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Systematic Review: The Effects of Oral Collagen Supplementation on Skin Aging

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Abstract
This systematic review evaluates the effects of oral collagen supplementation on skin hydration, elasticity, and wrinkle reduction. Collagen, a key protein in the skin, decreases with age, causing visible signs of aging. The review synthesizes findings from 31 articles, including randomized controlled trials, systematic reviews, and meta-analyses, focusing on the efficacy of hydrolyzed collagen (HC), collagen tripeptides (CP), and low molecular weight collagen peptides (LMWCP). The review also highlights collagen peptides' role in stimulating collagen synthesis, improving skin barrier function, and promoting hydration. Despite some limitations, the evidence supports collagen supplements, as a non-invasive option for improving skin health.

Aim of the Study
The study aims to evaluate the impact of oral collagen supplementation, particularly hydrolyzed collagen (HC), collagen tripeptides (CP), and low molecular weight collagen peptides (LMWCP), on improving skin hydration, elasticity, and wrinkle reduction.

Materials and methods
A review of the literature collected in the PubMed database was performed to gather information found under the key words "collagen supplementation", "skin aging", "hydrolyzed collagen", "collagen peptides", "skin hydration", "skin elasticity" and "wrinkle reduction".

Summary
The literature review highlights the potential of oral collagen supplements to improve skin hydration, elasticity, and reduce wrinkles. Marine-derived collagen peptides are noted for their superior bioavailability and effectiveness. In conclusion, these supplements offer a promising non-invasive option for enhancing skin health, making them valuable in anti-aging skincare.

Keywords: collagen, skin aging, supplements, marine collagen,

Introduction
Collagen is one of the main structural proteins in an organism, that is present in skin, tendons, cartilage and bones. It constitutes 65-80% dry weight of human skin [1]. However, natural collagen synthesis diminishes with age, compounded by environmental stressors that accelerate collagen breakdown. These changes result in visible signs of aging, affecting both appearance and skin function [8]. In recent years, there has been an increasing interest in the use of nutritional supplements to improve human skin. Researchers have studied peptides derived from protein hydrolysates as potential nutraceuticals and in relation to the development of functional foods [1]. Collagen peptides are developed from an enzymatic hydrolysis of collagen including mainly of the amino acids glycine(Gly), proline(Pro) and hydroxyproline(Hyp)[2].
Density of the collagen in the dermis reduce with age and is connected with a reduction in dermal thickness [3]. The stratum corneum (SC) is the outermost layer of the epidermis and plays an important role in maintaining skin moisture and protecting the skin from the external environment [4].

Healthy skin ensures an active interface between the internal and external environments of the body and allows of permanent adaptation and acclimatization of an organism during its lifetime [5].

Skin, a significant organ comprising different cell types and multiple layers. Skin functions including physical barrier against environmental factors, regulates hydration levels, and sustains physiological balance [6].

Skin aging is a degenerative process caused by a decrease in physiological function. Extrinsic causes of skin aging, including pollution, sun exposure, and lifestyle, can increase levels of oxidation and lead to chronic inflammation, accelerating aging processes. The aging process of skin is caused by DNA damage in nuclei and mitochondria, inflammation, glycation, decreased function of keratinocytes and fibroblasts, and the breakdown of heparan sulfate, hyaluronic acid, collagen, and elastin [29]. Lifestyle factors include smoking and nutritional statuses [26]. Non-modifiable risk factors: Age, Gender, Ethnicity, and dyspigmentation. Modifiable factors: Air pollution, Nutrition, Smoking, UV exposure [27]. Various factors contribute to the aging of human skin. Chronic sunlight exposure is a cause of skin photoaging, leading to extrinsic aging. In comparison, intrinsic processes also contribute to age-dependent skin alterations, with more visible changes in photoaged skin, as documented by differences between sun-exposed facial skin and protected buttock skin. Characteristics of photoaged skin include dryness, coarse wrinkles, pigmentation, and loss of elasticity. Solar UV radiation causes photoaging, leading to a decrease in collagen and elastic fibers, along with a reduction in hyaluronic acid synthesis, resulting in wrinkle formation, dryness, and loss of elasticity. Preventive measures for skin photoaging are necessary due to the inevitability of sunlight exposure. Dietary supplements with collagen have shown efficacy for skin health. Collagen hydrolysates or collagen peptides, including fish-collagen hydrolysates from type I collagen from fish skin, are attracting attention [7]. Oral collagen supplementation has emerged as a potential intervention to mitigate these aging effects. Collagen supplements, particularly in hydrolyzed or tripeptide forms, are designed to provide bioactive peptides that can be readily absorbed and utilized by the body. These peptides are believed to stimulate collagen synthesis in the skin, enhancing hydration, improving elasticity, and reducing wrinkles [9].

Hydrolyzed collagen supplementation can significantly improve skin hydration, elasticity, and reduce the appearance of wrinkles. Hydrolyzed collagen is a promising supplement for improving skin health, particularly in reducing signs of aging. However, it emphasizes the need for more standardized research to confirm these benefits conclusively and to determine optimal dosing strategies [28].

Results

Impact on Skin Hydration

Significant improvements in skin hydration were consistently reported across multiple studies: A meta-analysis demonstrated that marine-derived HC supplementation significantly improved skin hydration, with effects noticeable after 12 weeks of consistent use. The study highlighted the importance of sustained intake for maintaining elevated hydration levels [10].

Another study reported a 40% increase in skin hydration after a 90-day regimen of collagen peptides, attributed to the bioactive peptides' ability to enhance the skin's moisture-retaining capacity, likely through upregulation of hyaluronic acid production and improved barrier function [11].

Further studies supported these findings, noting that collagen peptide ingestion significantly boosted skin hydration, enhancing the skin's ability to retain water, which is critical for maintaining elasticity and preventing dryness [12].

Effects on Skin Elasticity

The reviewed studies consistently reported improvements in skin elasticity, highlighting collagen's potential to restore skin firmness and reduce laxity:

Genovese et al. reported significant enhancements in skin elasticity and firmness after 12 weeks of CP supplementation. The study used advanced imaging techniques to measure changes in skin density and elasticity, providing robust evidence of collagen's benefits. The increased collagen and elastin content in the dermis underscores the role of collagen peptides in supporting the ECM [9].

Naoki Ito et al. reported that besides enhanced elasticity, the CPO group exhibited a significant reduction in the number of skin pores after 8 weeks of supplementation compared to the placebo group [13]. Additionally, a daily supplementation study showed marked improvements in skin firmness and elasticity, highlighting the supplement's ability to stimulate fibroblast activity and promote new collagen fiber synthesis. The study also noted a reduction in fine lines, suggesting a comprehensive anti-aging effect [14].

STUDY 1: Czajka et al. highlighted a significant finding by demonstrating a correlation between oral collagen supplementation and improved skin elasticity across different age groups. In a double-blind, randomized, placebo-controlled study conducted at an independent aesthetic clinic in Rome, a multicomponent product containing collagen bioactive peptides, hyaluronic acids, glucosamine, chondroitin sulfate, L-carnitine, vitamins, and minerals was tested. Participants were divided into two age groups: Younger Group (21-50 years) and Older Group (51-70 years). Subjects received either the test product or a placebo over 90 days, with assessments at baseline, day 30, day 60, and day 90. Younger participants experienced a marked and early improvement in skin elasticity, culminating in a 43% increase by day 90. Among the older participants, significant improvements were observed later, with a 34% increase in skin elasticity by day 90. The study concluded that the multicomponent product demonstrated significant benefits in improving skin elasticity, particularly in the younger age group, with noticeable improvements in overall well-being, including skin, hair, nails, and general well-being [15].

STUDY 2 exploring the health benefits of low molecular weight collagen peptide (LMWCP)(The ingredients composition including- LMWCP, Vitamin C, Fruit concentrate mix, Flavor mix, Excipients, Sweetener, Water) on human skin included 64 female volunteers aged 40-60 years with photoaged skin. Eleven women dropped out due to personal reasons, resulting in 53 participants. Among them, 26 women received 1000 mg of LMWCP per day for 12 weeks, and 27 received a placebo. In the LMWCP group, the parameters of skin elasticity, specifically overall elasticity (R2) and net elasticity (R5), were significantly higher than in the placebo group at 12 weeks ($p = 0.025$ and $p = 0.027$, respectively). Additionally, the value of R5 in the test group showed significant improvement at 12 weeks ($p = 0.002$). In the placebo group, none of the skin elasticity parameters showed significant changes from baseline during the test period [7].

STUDY 3 embraced three groups: Placebo, L-CP (lower content of bioactive collagen peptides), and H-CP (higher content of bioactive collagen peptides). Participants aged 35 to 55 years with dry and rough skin, and a body mass index less than 30 were chosen randomly to one of the three groups in a 1:1:1 ratio. Five-gram samples were received orally in hot milk, coffee, or other beverages, once daily after dinner for 8 weeks. In the placebo group, the elasticity of the canthus decreased significantly between baseline and weeks 4 and 8. There was no significant improvement in facial skin elasticity between baseline and weeks 4 and 8, and no significant differences between the placebo group at weeks 4 and 8 in the L-CP group. However, in the H-CP group, the elasticity of the cheek increased significantly between baseline and weeks 4 and 8, and the elasticity of the canthus by week 8. Skin elasticity of both the cheek and canthus in the H-CP group was significantly higher ($P < 0.05$) than in the placebo group by week 8. The improvement in elasticity from baseline in the H-CP group was significantly higher ($P < 0.05$) than the placebo group by week 4 at the canthus and by week 8 at both the cheek and canthus [16].

Reduction in Wrinkle Depth and Volume

Several studies confirmed the anti-wrinkle benefits of collagen supplements, highlighting their potential as a non-invasive intervention for aging skin:

STUDY 1 on hydrolyzed collagen with vitamin C found significant improvements in skin density and reduced skin roughness and wrinkle depth. The study involved 87 women aged between 40 and 65, divided into a placebo group and a CP group receiving a daily dose of 5 grams of hydrolyzed collagen and 80 mg of vitamin C. Over 16 weeks, various skin parameters, including skin density, thickness, elasticity, hydration, texture (roughness), and wrinkle severity (measured by volume and depth), were monitored using advanced imaging techniques [25].

STUDY 2: Campos et al.(2021 found that hydrolyzed fish cartilage supplementation led to noticeable improvements in skin texture, wrinkle reduction, and thicker, healthier skin, with detailed evidence provided by reflectance confocal microscopy (RCM).[17].

STUDY 3: The study observed a 24% decrease in visible wrinkles following 12 weeks of marine collagen supplementation. Additionally, participants experienced an improvement in skin elasticity, though this was less significant compared to the reduction in wrinkles. Overall, the findings underscore the potential of marine collagen to enhance skin appearance by notably decreasing wrinkles and somewhat improving skin elasticity [10].

STUDY 4 Genovese et al. noted significant reductions in fine lines and wrinkles, particularly in the periorbital region, following 12 weeks of supplementation. The study's use of digital imaging techniques provided quantitative evidence of the benefits [9]. Additional findings showed that collagen peptides reduced the appearance of wrinkles and fine lines, improving overall skin texture and structure. Continuous supplementation was emphasized, as benefits were more pronounced with long-term use [18].
STUDY 5 to explore the health benefits of LMWCP on human skin included 100 adults aged 35-60 years, all diagnosed with dry skin and periorbital wrinkles. The skin wrinkling parameters average skin roughness (Ra), maximum peak-to-valley values (Rmax), maximum peak height of the wrinkle (Rp), and average maximum height of the wrinkle (Rz)were measured using the PRIMOS optical system. Significant improvements were observed in the test group compared to the placebo group, with all parameters showing significant improvement from baseline to 12 weeks ($p < 0.0001$ for all parameters). The maximum valley depth of the wrinkle (Rv) in the test group also tended to be reduced at 12 weeks compared with the baseline value, while in the placebo group, this parameter tended to increase [19].

Improvement in Dermal Density

STUDY 1 Zmitek et al. (2020) explored how a daily dose of specific supplements affects skin health over 12 weeks. Participants were divided into two groups: a test product group took 10 mL of a specially formulated syrup daily, containing hydrolyzed fish collagen (4000 mg), water-soluble CoQ10 (50 mg), vitamin C (80 mg), vitamin A (920 µg), and biotin (150 µg); the placebo group took 10 mL of a similar-looking syrup with no active ingredients. Participants were evaluated at the start of the study (T0), at 6 weeks (T6), and at the end of the study (T12). In the supplement group, there was a statistically significant increase in dermis density after 12 weeks compared to the baseline measurements ($p < 0.001$). The placebo group did not show any significant changes in dermis density ($p > 0.99$). This study suggests that taking a combination of collagen, CoQ10, and certain vitamins can significantly improve skin density over time, whereas a placebo has no such effect [20].
STUDY 2 Asserin et al. (2015) noted that collagen peptides not only promote collagen production but also increase glycosaminoglycans. This helps explain the clinical benefits observed with collagen supplementation, such as increased collagen density in the dermis and decreased fragmentation of the dermal collagen networks [3].

The impact of collagen supplementation and exercise on joint injury recovery

Collagen supplementation has been found to reduce joint discomfort, improve knee and ankle functionality, and aid recovery from conditions like Achilles tendinopathy across various dosages and study durations, highlighting its potential in managing joint health. Studies also reported improvements in fat-free mass (FFM), reductions in body fat mass (FM), and increased muscle strength, especially when combined with resistance training, with more pronounced effects in elderly and sarcopenic individuals. Additionally, collagen supplementation showed benefits in reducing muscle soreness and improving recovery after strenuous exercise, including significant improvements in perceived recovery and reduced muscle pain.

While collagen supplementation increased collagen synthesis markers, its effects on muscle protein synthesis (MPS) were less significant compared to higher-quality protein sources like whey protein. The review suggests collagen may aid in extracellular matrix (ECM) regeneration and reduce inflammation, but further research is needed to fully understand these mechanisms. Overall, the review concludes that collagen peptide supplementation, particularly with exercise, offers significant benefits for joint health, body composition, and exercise recovery, though more research is needed on exact mechanisms and dosages [31].

Comparative Effectiveness of Different Collagen Sources

The source of collagen significantly influences its efficacy, with marine collagen peptides consistently demonstrating superior bioavailability and effectiveness compared to bovine and porcine sources. This is likely due to the smaller peptide sizes in marine collagen, which enhance absorption and facilitate greater incorporation into the skin's ECM.

Marine collagen is an appealing biomaterial due to its water solubility, metabolic compatibility, and high availability. Its solubility makes it convenient to use and process, while its compatibility with metabolic processes ensures it can be safely used in biological applications without harmful side effects. Studies suggested that the smaller molecular size of marine collagen peptides facilitates better absorption, leading to more pronounced effects on skin hydration and elasticity. The unique amino acid composition of marine collagen, particularly its high levels of hydroxyproline, may also contribute to its superior efficacy. Additionally, marine collagen is readily available, often sourced from fish scales and skins, offering a sustainable and affordable alternative to other collagen sources [21].

Chicken and Porcine Collagen: Although less frequently studied, these sources also showed benefits in improving skin properties. One study demonstrated that hydrolyzed chicken collagen, rich in glycosaminoglycans, was particularly effective in improving skin elasticity and reducing signs of aging. Further research is needed to fully understand the comparative effectiveness of different collagen sources and to identify the most beneficial types for specific skin concerns [10].

Mechanisms of Action

The review explored the biochemical mechanisms through which collagen supplements exert their effects on the skin:

Fibroblast Activation: Collagen peptides are believed to stimulate fibroblast activity in the dermis, leading to increased synthesis of collagen and elastin [22]. As demonstrated in study of Inacio, hydrolyzed collagens, particularly those with lower molecular weights and high proline/hydroxyproline content, specifically stimulate the growth of F.Ds [30]. This process helps restore the ECM's structural integrity, improving skin elasticity and reducing wrinkles. The peptides may also promote the production of other ECM components, such as proteoglycans and hyaluronic acid, essential for maintaining skin hydration and elasticity.

Hydration and Water Retention: Bioactive peptides, such as Gly-Pro-Hyp and Pro-Hyp, play a significant role in enhancing skin hydration by boosting natural moisturizing factors and reducing transepidermal water loss. These peptides help maintain the skin's barrier function, preventing moisture loss and improving overall hydration. The increased hydration levels contribute to improved skin elasticity and a reduction in the appearance of fine lines [22].

Discussion:

Limitations and Considerations

The variability in study designs, participant demographics, types of collagen used, dosages, and intervention durations presents challenges in making direct comparisons between studies. This heterogeneity may influence the generalizability of the findings. Additionally, the potential for publication bias should be considered, as studies with negative results are less likely to be published. Despite these limitations, the evidence strongly supports the benefits of collagen supplementation for improving skin hydration, elasticity, and reducing wrinkles.

Future Research Directions

Long-Term Effects: Long-term studies are needed to determine whether the benefits of collagen supplementation persist after discontinuation. Such studies should investigate the durability of improvements in skin hydration, elasticity, and wrinkle reduction. Additionally, long-term safety assessments are crucial to ensure that prolonged collagen supplementation does not lead to adverse effects [23].

Mechanistic Insights: Further research is required to elucidate the precise biological mechanisms underlying the observed effects. Understanding how collagen peptides interact with the skin's cellular and molecular pathways could lead to the development of more targeted and effective formulations. This research could also explore the potential synergistic effects of combining collagen supplements with other skin-beneficial nutrients, such as vitamins C and E.

Dosage Optimization: Identifying optimal dosages and treatment durations for various populations, including different age groups, skin types, and genders, will help maximize the benefits of collagen supplements. Personalized supplementation strategies could be developed based on individual needs and responses [7].

Practical Implications

The findings suggest that oral collagen supplements, particularly those derived from marine sources, are effective in enhancing skin hydration, elasticity, and reducing the appearance of wrinkles. These supplements offer a promising non-invasive option for individuals seeking to improve their skin's health and appearance. Dermatologists and skincare professionals may consider recommending these supplements as part of a comprehensive skincare regimen, especially for patients concerned with aging skin.

Consumers should be advised to select high-quality products from reputable manufacturers, as the source and purity of collagen can significantly impact efficacy. Additionally, individuals with allergies or intolerances should consult with healthcare providers before starting supplementation. It's also important to consider that while collagen supplements can be beneficial, they should be part of a holistic approach to skin health that includes a balanced diet, adequate hydration, sun protection, and overall healthy lifestyle practices [24].

Conclusions

Oral collagen supplementation appears to be a promising intervention for improving skin health, particularly in enhancing hydration, elasticity, and reducing wrinkles. The evidence strongly supports the use of marine-derived collagen peptides, which offer superior bioavailability and efficacy. While the findings are encouraging, further research is necessary to refine dosing recommendations, understand the underlying mechanisms, and assess the long-term effects of supplementation. This review underscores the potential of collagen supplements as a valuable component of anti-aging skincare strategies, with implications for both clinical and cosmetic applications.

Disclosure

Author's contribution

Conceptualization: Weronika Zofia Marzec and Aleksandra Łakoma; Methodology: Marcelina Teresa Marzec; Software: Aleksandra Wydra-Rojek; Check: Paulina Wasiewicz- Ciach and Katarzyna Kutyła; Formal analysis: Anna Marszałek and Piotr Kuczyński; Investigation: Maciej Choiński and Wojciech Jan Mokot; Resources: Piotr Kuczyński; Data curation: Aleksandra Łakoma; Writing - rough preparation: Marcelina Teresa Marzec and Weronika Zofia Marzec; Writing - review and editing: Aleksandra Wydra-Rojek and Paulina Wasiewicz-Ciach; Visualization: Wojciech Jan Mokot; Supervision: Maciej Choiński; Project administration: Katarzyna Kutyła and Anna Marszałek; Receiving funding - no specific funding.

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