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Supplementation of hydrolyzed collagen to the aging process of the skin: A review



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ABSTRACT

Background: The aging of the skin has emerged as a significant concern, not only among older individuals but also among the younger population, given the increasing trend of longevity. Consequently, there has been a notable rise in the utilization of dietary supplements in recent years. Furthermore, a substantial body of scientific research suggests that the inclusion of hydrolyzed collagen in supplementation can play a significant role in mitigating the visible signs of skin aging. The primary aim of this study is to compile and present a comprehensive summary of the existing evidence pertaining to the effects of hydrolyzed collagen supplementation on human skin.

Methods: This study conducted a narrative review to assess the efficacy of collagen administration in addressing skin aging. The literature search employed the keywords (collagen) AND (skin aging) to identify

relevant articles, and the search was conducted on the PubMed database. The included articles' findings were systematically reviewed and presented in a narrative format to provide an overview of the current understanding of collagen supplementation in relation to its impact on skin aging.

Results: We included fourteen articles in this review based on the eligibility criteria. Skin hydration was higher in most of the studies that favored collagen compared to placebo. Ten of 14 articles reported higher skin elasticity following collagen administration. There were six articles assessing skin roughness between both groups and all of them reported lesser skin roughness in the collagen group.

Conclusion: Hydrolyzed collagen can delay and improve the signs of skin aging by improving skin hydration and elasticity, and reducing skin roughness.

Keywords: aging, collagen, elasticity, hydration, roughness, skin.

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INTRODUCTION

Collagen constitutes a significant portion (25-30%) of the body's proteins, playing a crucial role in the structural integrity of connective tissues like skin, tendons, cartilage, and bones.¹ In the context of skin tissue, collagen plays a crucial role as a primary component of the extracellular matrix, constituting 75% of its overall weight. Its primary function involves providing mechanical support by creating a supportive network along with other fibers such as hyaluronic acid, reticulin, and elastin within the extracellular matrix. This intricate network offers support to diverse skin cells, encompassing fibroblasts, keratinocytes, melanocytes, and specialized immune cells.²

With aging, the dermal collagen fiber network undergoes fragmentation, exhibiting shorter and less organized fibers. This results in the accumulation of degraded collagen fragments.³ Furthermore, the aging process enhances the production of metalloproteinases, which are enzymes responsible for breaking down collagen fibers. As a result, there is a decrease in the production of new components within the extracellular matrix, including the specific type of collagen generated by skin fibroblasts.⁴ The intersection of intrinsic and extrinsic aging processes initiates structural and functional modifications in the dermis. These alterations involve a loss of volume, decreased elasticity, diminished epidermal thickness, and increased wrinkles. This

is linked to a reduced concentration of hyaluronic acid in the extracellular matrix. Hyaluronic acid is pivotal in preserving moisture within the skin structure, and its decline results in a compromised ability of the skin to retain moisture.^{3,5}

Beyond conventional systemic antioxidants, diverse nutritional supplements are employed to enhance skin health and attain a more youthful appearance. Examples include macromolecules derived from marine proteins.^{6,7} Nevertheless, hydrolyzed collagen (HC) has emerged as a recent and highly promising systemic anti-aging supplement, supported by various scientific studies demonstrating its functional and beneficial impact on the skin. It primarily focuses on enhancing

clinical symptoms associated with aging skin.^{2,8,9} Oral bioactive collagen peptides can prevent age-related decline in collagen synthesis.¹⁰ Derived through enzymatic hydrolysis of natural collagen, these peptides undergo metabolism in the gastrointestinal tract, transforming into dipeptides and tripeptides. Subsequently, these compounds are transported through the bloodstream and deposited in the skin, contributing to the formation of new collagen fibers.¹¹

Hydrolyzed collagen (HC) supplements are rich in amino acids, particularly hydroxyproline, proline, and glycine. Hydroxyproline is unique to collagen. Studies suggest that proline hydroxyproline (Pro-Hyp) and hydroxyproline glycine (Hyp-Gly) are absorbed in the form of dipeptides, rather than individual amino acids, upon ingestion. These dipeptides are then deposited in the upper layers of the skin.³ These dipeptides elevate the bioactivity of dermal fibroblasts, promoting collagen synthesis, ultimately enhancing skin hydration and elasticity while reducing the appearance of wrinkles.^{3,12}

With the rising number of scientific publications and global clinical trials assessing collagen supplementation, there is a growing necessity to gather and analyze this data for informed supplementation decisions. Consequently, the objective of this study is to consolidate and summarize the evidence regarding

the effects of hydrolyzed collagen (HC) supplementation on human skin.

METHODS

This was a narrative literature review study. We created a PICO framework to determine the eligibility criteria for this review. In this review, the population of interest was all people; the interest was the administration of hydrolyzed collagen; the comparator was placebo administration; and the outcome of interest was signs of skin aging. Based on the PICO framework, we can determine the keywords to obtain eligible literature in the online database. The keywords were (collagen) AND (skin aging) which we used to find eligible literature in the PubMed database. Articles that have been written in English that describe the effect of collagen on sign of skin aging were included in this review. We restrict the year of publication to the past 10 years. The included studies were reviewed further and narratively elaborated. In this literature review, we included fourteen articles that describe the effect of collagen on signs of skin aging.

RESULTS

We included fourteen articles in this review based on the eligibility criteria. The characteristics of the included studies can be seen in **Table 1**. The total samples that were given collagen was 456 samples and the placebo was 420 samples. All studies

included female samples except the study by Genovese *et al.* which included 111 females and 9 males. The age of the samples was ranging from 21-70 years old. The duration of intervention ranged from 4 weeks to 12 weeks where the most common duration was 12 weeks and less common was 4 weeks. The dose of collagen was ranging from 0.6 gram to 10 gram which composed of hydrolyzed collagen and collagen peptides.

As can be seen in **Table 2**, this article review the effect of collagen administration to skin hydration, skin elasticity, and skin roughness. There were nine articles assessing skin hydration following collagen and placebo administration. The value of skin hydration was higher in most of the studies which favor collagen compared to placebo. There were 14 articles comparing skin elasticity between collagen and placebo administration. Ten of them reported higher skin elasticity following collagen administration. There were six articles assessing skin roughness between both groups. All of the six articles reported lesser skin roughness in the collagen group.

DISCUSSION

Although there are differences between studies using different collagen peptide concentrations, formulations, sources, and oral supplement forms (liquid vs solid), most studies report improved skin hydration and elasticity, as well as

Table 1. Characteristic of included studies

Author (Year)	Samples	Gender	Age (years)	Duration	Intervention
Proksch <i>et al.</i> ⁸ (2014)	I = 30; C = 30	F = 60; M = 0	35 – 55	8 weeks	2.5 grams HC
Koizumi <i>et al.</i> ¹² (2017)	I = 37; C = 34	F = 71; M = 0	30 – 60	12 weeks	3 grams CP
Bolke <i>et al.</i> ¹³ (2019)	I = 36; C = 36	F = 72; M = 0	> 35	12 weeks	2.5 grams CP
Sugihara <i>et al.</i> ¹⁴ (2015)	I = 27; C = 26	F = 53; M = 0	35 – 55	8 weeks	2.5 grams HC
Inoue <i>et al.</i> ¹⁵ (2016)	I = 54; C = 26	-	35 – 55	8 weeks	2.5 grams CP
Nomoto and Iizaka ¹⁶ (2020)	I = 20; C = 19	-	> 65	8 weeks	12 grams CP
Choi <i>et al.</i> ¹⁷ (2014)	I = 8; C = 8	F = 16; M = 0	-	5 weeks	CP
Genovese <i>et al.</i> ¹⁸ (2017)	I = 60; C = 60	F = 111; M = 9	40 – 60	12 weeks	5 grams HC
Zmitek <i>et al.</i> ¹⁹ (2020)	I = 16; C = 15	F = 31; M = 0	40 – 65	12 weeks	4 grams HC
Yoon <i>et al.</i> ²⁰ (2014)	I = 22; C = 22	F = 44; M = 0	> 44	12 weeks	3 grams HC
Schwartz <i>et al.</i> ²¹ (2019)	I = 58; C = 55	F = 113; M = 0	36 – 59	12 weeks	0.6 gram HC
Czajka <i>et al.</i> ²² (2018)	I = 61; C = 59	-	21 – 70	12 weeks	4 grams HC
Ito <i>et al.</i> ²³ (2018)	I = 10; C = 11	-	30 – 50	8 weeks	10 gram fish CP
Sangsuwan and Asawanonda ²⁴ (2020)	I = 17; C = 19	F = 36; M = 0	50 – 60	4 weeks	5 grams HC

C: Control; CP: Collagen peptide; F: Female; HC: Hydrolyzed collagen; I: Intervention; M: Male

Table 2. Description of skin hydration, elasticity, and roughness between intervention and control among included studies

Author (Year)	Hydration	Elasticity	Roughness
Proksch <i>et al.</i> ⁸ (2014)	-	I = 4.32; C = 0.938	-
Koizumi <i>et al.</i> ¹² (2017)	I = 10.9; C = 4.01	I = 0.938; C = 4.32	I = -0.45; C = 11.274
Bolke <i>et al.</i> ¹³ (2019)	I = 44.5; C = 36.6	I = 0.81; C = 0.75	I = 118; 161.7
Sugihara <i>et al.</i> ¹⁴ (2015)	I = 73.98; C = 70.85	I = 0.758; C = 0.697	I = 22.15; C = 23.42
Inoue <i>et al.</i> ¹⁵ (2016)	I = 31.08; C = 25.42	I = 0.758; C = 0.738	I = 22.32; C = 23.42
Nomoto and Iizaka ¹⁶ (2020)	I = 51.7; C = 41.4	I = 0.74; C = 0.66	-
Choi <i>et al.</i> ¹⁷ (2014)	I = 71.09; C = 61.3	I = 0.786; C = 0.718	-
Genovese <i>et al.</i> ¹⁸ (2017)	-	I = 8.07; C = 7.52	-
Zmitek <i>et al.</i> ¹⁹ (2020)	I = 200; C = 194.1	I = 1.38; C = 1.59	-
Yoon <i>et al.</i> ²⁰ (2014)	-	I = 0.6097; C = 0.6446	-
Schwartz <i>et al.</i> ²¹ (2019)	I = 61.31; C = 62.08	I = 5.29; C = 5.32	I = 4.19; C = 4.36
Czajka <i>et al.</i> ²² (2018)	-	I = 9.8; C = 7	-
Ito <i>et al.</i> ²³ (2018)	I = 60.3; C = 60.9	I = 0.784; C = 0.779	I = 1,610; C = 1,755
Sangsuwan and Asawanonda ²⁴ (2020)	-	I = 0.56; C = 0.48	-

C: Control; I: Intervention

increased skin elasticity, strength, density and reduces mimic wrinkles. Positive effects became noticeable within 60 to 90 days of commencing supplementation and continued for 30 days after the intervention concluded. Hence, the advantages of this supplement for skin health appear to be linked to its maintenance cycle. Multiple clinical studies have investigated the effects of oral hydrolyzed collagen (HC), revealing enhancements in skin collagen synthesis, increased fibroblast collagen synthesis, improved skin hydration and elasticity, as well as a reduction in wrinkles.^{4,7,8}

In a study conducted by Bolke *et al.*, women over 35 years of age exhibited heightened hydration levels, improved skin elasticity, increased dermis density, and a reduction in wrinkle area following supplementation with 2.5 grams of collagen peptides per day for a period of 90 days.¹³ The validity of these outcomes was affirmed through both objective and subjective evaluation methods, including surveys. Furthermore, the sustained results were noticeable even 30 days after the intervention concluded. Supporting these findings, a clinical trial involving 5 grams of collagen peptide yielded similar positive results, suggesting that supplementing with 2.5 grams of collagen peptide for 90 days was adequate for beneficial effects. It's noteworthy that Proksa *et al.* did not observe improvements

in skin hydration with 2.5 or 5 grams of hydrolyzed collagen, and this discrepancy may be attributed to differences in the measurement site, specifically the inner arm.⁸ The selection of the measurement site is pivotal, considering that areas protected from solar radiation generally experience slower aging compared to exposed skin. Therefore, assessing regions more prone to external factors such as radiation and pollution enables a more precise observation of positive effects.

Previous studies have shown that the dipeptides Pro-Hyp and Hyp-Gly have an improved effect on dermal fibroblasts, stimulating their metabolism, migration, and proliferation, producing collagen fibers in the dermis.³ In a clinical study conducted by Koizumi *et al.*, a 90-day intervention incorporating the consumption of 3 grams of tilapia-scale collagen peptide, notable for its high content of Hyp, Gly, and Pro, resulted in significant reductions in eye wrinkles. Additionally, improvements in skin moisture (hydration) and elasticity were observed among the participating women.¹² Moreover, a study by Sugihara, Inoue, and Wang revealed that the consumption of 2.5 grams of hydrolyzed collagen (HC) peptides, derived from fish scales and containing bioactive dipeptides Pro-Hyp and Hyp-Gly, led to improvements in hydration, elasticity, and the smoothing of facial wrinkles within a four-week period.¹⁴ In a study conducted

by Inoue, Sugihara, and Wang, the impact of concentrations of Pro-Hyp and Hyp-Gly was investigated, demonstrating efficacy in both groups. Notably, the group with higher dipeptide concentrations exhibited faster changes in parameters, aligning with clinical improvement. This observation supports the hypothesis that the composition directly influences the results.¹⁵

Collagen peptides effectively improve the condition of the skin, regardless of the source (fish, pig, cow, or chicken), depending on the composition and concentration of the peptides. Some studies in which type II HC was administered mentioned the effectiveness of improving the collagen structure of the dermis, reducing wrinkles and elasticity, and obtained positive results in subjective questionnaires. This suggests that supplementation of both type I and type II HC may contribute to beneficial effects on the skin. However, due to the limited number of studies that performed biopsy analysis of skin samples, the evaluated studies were unable to demonstrate structural modifications of dermal collagen. In the reported cases, the intervention was shorter, and the reduction in wrinkles and increased elasticity may be due to increased skin hydration rather than changes in collagen structure alone.

In a study conducted by Nomoto and Iizaka, which involved hospitalized older

adults and non-healthy individuals, the results demonstrated that hydrolyzed collagen (HC) peptide supplementation was effective in reducing surgically induced skin lesions in bedridden elderly patients.¹⁶ The study conducted by Choi et al. assessed the impact of hydrolyzed collagen (HC) supplementation on skin regeneration following laser therapy. The primary outcome revealed an enhancement in the recovery process among patients who utilized dietary supplements.¹⁷⁻²¹

The majority of the selected studies employed commercial hydrolyzed collagen (HC) supplements in ready-to-use forms as interventions.²²⁻²⁴ These commercially available brands exhibited variations in ingredient percentages, incorporating not only collagen peptides but also vitamins, minerals, antioxidants, coenzyme Q10, hyaluronic acid, and chondroitin sulfate. Importantly, in these studies, the positive effects attributed to these additives were exclusively linked to collagen, with no comparative evaluation of the formulation carrier's effects. Consequently, the observed beneficial effects may arise from the synergistic impact of these substances with collagen.²⁰⁻²⁶ For instance, coenzyme Q10, functioning as a significant antioxidant, neutralizes free radical damage during skin aging, thereby improving signs of aging. Additionally, vitamins like vitamin C and hyaluronic acid actively contribute to and stimulate collagen biosynthesis. Nevertheless, it is crucial to acknowledge that studies employing isolated forms of collagen have also demonstrated effectiveness.

None of the studies reported any adverse side effects associated with the supplements. The assessed studies indicated that the utilization of both liquid and solid forms of hydrolyzed collagen (HC), including dissolvable capsules and powder supplements, was well-received by patients. This positive reception was attributed to the ease of swallowing and the perceived safety of administration.

CONCLUSION

According to the findings of this study, hydrolyzed collagen (HC) supplements, or collagen peptides, exhibit the potential to delay and improve the manifestations

of skin aging. This is evidenced by a reduction in facial wrinkles and enhancements in skin hydration and elasticity, with sustained effects observed post-supplementation. Most studies indicate that a 90-day intervention period is necessary to slow down skin aging, and the positive results persist for up to four weeks after the supplementation concludes. Studies involving supplements with higher concentrations of Pro-Hyp and Hyp-Gly dipeptides demonstrated notable improvements within four weeks. The use of HC supplements appears to be both effective and safe, as no reported side effects were noted in the analytical studies. However, further research is warranted to assess the long-term effects of HC peptides, considering that the longest intervention study lasted for 90 days and an additional 120 days were required to evaluate the effects. Additionally, there is a need for further investigations into the impact of carriers and other substances combined with collagen, particularly vitamins and coenzyme Q10. These substances may act either collaboratively or synergistically with collagen, potentially enhancing the measured effects.

CONFLICT OF INTEREST

The authors declared the absence of a conflict of interest regarding the preparation of this manuscript.

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AUTHOR CONTRIBUTION

The author made equal contributions during the preparation of this manuscript and agrees to accept equal responsibility regarding the content of the article.

REFERENCES:

1. Squire JM, Parry DAD. Fibrous protein structures: Hierarchy, history and heroes. In *Subcellular Biochemistry*. 2017;1-33
2. Dini I, Laneri S. Nutricosmetics: a brief overview. *Phyther Res*. 2019;33:3054-3063.
3. De Miranda RB, Weimer P, Rossi RC. Effects of hydrolyzed collagen supplementation on skin aging: A systematic review and meta-analysis. *Int J Dermatol*. 2021;60(12):1449-1461.

4. Quan T, Little E, Quan H, Qin Z, Voorhees JJ, Fisher GJ. Elevated matrix metalloproteinases and collagen fragmentation in photodamaged human skin: Impact of altered extracellular matrix microenvironment on dermal fibroblast function. *J Invest Dermatol*. 2013;133:1362-366.
5. Calleja-Agius J, Brincat M, Borg M. Skin connective tissue and ageing. *Best Pract Res Clin Obstet Gynaecol*. 2013;27:727-740.
6. Suleria HAR, Osborne S, Masci P, Gobe G. Marine-based nutraceuticals: an innovative trend in the food and supplement industries. *Mar Drugs*. 2015;13:6336-6351.
7. De Luca C, Mikhal'chik EV, Suprun MV, Papacharalambous M, Truhanov AI, Korkina LG. Skin anti ageing and systemic redox effects of supplementation with marine collagen peptides and plant-derived antioxidants: a single-blind case-control clinical study. *Oxid Med Cell Longev*. 2016;2016:1-14.
8. Proksch E, Segger D, Degwert J, Schunck M, Zague V, Oesser S. Oral supplementation of specific collagen peptides has beneficial effects on human skin physiology: a double-blind, placebo-controlled study. *Skin Pharmacol Physiol*. 2014;27:47-55.
9. Proksch E, Schunck M, Zague V, Segger D, Degwert J, Oesser S. Oral intake of specific bioactive collagen peptides reduces skin wrinkles and increases dermal matrix synthesis. *Skin Pharmacol Physiol*. 2014;27:113-119.
10. Sato K. The presence of food-derived collagen peptides in human body-structure and biological activity. *Food Funct*. 2017;8:4325-4330.
11. Choi FD, Sung CT, Juhasz MLW, Mesinkovsk NA. Oral collagen supplementation: a systematic review of dermatological applications. *J Drugs Dermatol*. 2019;18:9-16.
12. Koizumi S, Inoue N, Shimizu M, Kwon C, Kim HY, Park KS. Effects of dietary supplementation with fish scales-derived collagen peptides on skin parameters and condition: a randomized, placebo-controlled, double-blind study. *Int J Pept Res Ther*. 2017;24:397-402.
13. Bolke L, Schlippe G, Gerß J, Voss W. A collagen supplement improves skin hydration, elasticity, roughness, and density: results of a randomized, placebo-controlled, blind study. *Nutrients*. 2019;11:7-11.
14. Sugihara F, Inoue N, Wang X. Clinical effects of ingesting collagen hydrolysate on facial skin properties: A randomized, placebo-controlled, double-blind trial. *Jpn Pharmacol Ther*. 2015;43:67-70.
15. Inoue N, Sugihara F, Wang X. Ingestion of bioactive collagen hydrolysates enhance facial skin moisture and elasticity and reduce facial ageing signs in a randomised double-blind placebo-controlled clinical study. *J Sci Food Agric*. 2016;96:4077-4081.
16. Nomoto T, Iizaka S. Effect of an oral nutrition supplement containing collagen peptides on stratum corneum hydration and skin elasticity in hospitalized older adults: a multicenter open-label randomized controlled study. *Adv Ski Wound Care*. 2020;33:186-191.
17. Choi SY, Ko EJ, Lee YH, Kim BG, Shin HJ, Seo DB, et al. Effects of collagen tripeptide

- supplement on skin properties: a prospective, randomized, controlled study. *J Cosmet Laser Ther.* 2014;16(3):132-137.
18. Genovese L, Corbo A, Sibilla S. An insight into the changes in skin texture and properties following dietary intervention with a nutraceutical containing a blend of collagen bioactive peptides and antioxidants. *Skin Pharmacol Physiol.* 2017;30:146-158.
 19. Zmitek K, Zmitek J, Butina MR, Pogacnik T. Effects of a combination of water-soluble coenzyme Q10 and collagen on skin parameters and condition: results of a randomised, placebo-controlled, double-blind study. *Nutrients.* 2020;12:1-13.
 20. Yoon HS, Cho HH, Cho S, Lee SR, Shin MH, Chung JH. Supplementating with dietary astaxanthin combined with collagen hydrolysate improves facial elasticity and decreases matrix metalloproteinase-1 and -12 expression: a comparative study with placebo. *J Med Food.* 2014;17:810-816.
 21. Schwartz SR, Hammon KA, Gafner A, et al. Novel hydrolyzed chicken sternal cartilage extract improves facial epidermis and connective tissue in healthy adult females: a randomized, double-blind, placebo-controlled trial. *Altern Ther Health Med.* 2019;25:12-29.
 22. Czajka A, Kania EM, Genovese L, Corbo A, Merone G, Luci C, Sibilla S. Daily oral supplementation with collagen peptides combined with vitamins and other bioactive compounds improves skin elasticity and has a beneficial effect on joint and general wellbeing. *Nutr Res.* 2018;57:97-108.
 23. Ito N, Seki S, Ueda F. Effects of composite supplement containing collagen peptide and ornithine on skin conditions and plasma IGF-1 levels: a randomized, double-blind, placebo-controlled trial. *Mar Drugs.* 2018;16:1-12.
 24. Sangsuwan W, Asawanonda P. Four-weeks daily intake of oral collagen hydrolysate results in improved skin elasticity, especially in sun-exposed areas: a randomized, double-blind, placebo-controlled trial. *J Dermatolog Treat.* 2020;9:1-6.
 25. Pratama GM, Hartawan IG, Indriani IG, Yusrika MU, Suryantari SA, Sudarsa PS. Potency of Spirulina platensis extract as sunscreen on Ultraviolet B exposure. *Journal of Medicine and Health.* 2020;2(6):205-17.
 26. Gill TJ, Ratnayanti IG, Arijana IG. The effect of purple mangosteen (*Garcinia mangostana*) peel extract on collagen fiber in male Wistar rats after Ultraviolet-B (UV-B) exposure. *Intisari Sains Medis.* 2018;9(3):131-4.



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