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## The Role of Hydrolyzed Collagen in Combating Skin Aging: A Literature Review

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## **Abstract**

### **Introduction**

Skin aging has become an increasingly common issue. As time passes, the skin undergoes degenerative changes, including the loss of elasticity and reduction in collagen content. In this context, the use of nutricosmetics as supplements has increased in recent years. Numerous scientific studies have shown the benefits of hydrolyzed collagen supplementation in improving the signs of skin aging. In this article, we summarize some of the most promising studies available in the literature and evaluate the effectiveness of oral collagen supplementation in the context of skin health.

**Purpose of the work:** This study aims to review and characterize the effectiveness of hydrolyzed collagen in the skin anti-aging process.

**Materials and Methods:** A comprehensive analysis of research papers available on PubMed, Google Scholar and Embase was conducted using search terms including the following keywords: hydrolyzed collagen, supplementation, skin aging, anti-aging.

**Results:** Hydrolyzed collagen supplementation has been shown to improve skin elasticity, hydration, and reduce wrinkles. Although generally safe and well-tolerated, minor side effects have been reported in some cases. An individualized approach to supplementation, along with ongoing research to optimize dosages and formulations, is essential. Future studies should focus on understanding the long-term effects of collagen supplementation, exploring its impact on different demographic groups, and comparing the efficacy of various collagen sources, such as marine and bovine collagen.

**Keywords:** hydrolyzed collagen, skin aging, wrinkle reduction, anti-aging supplementation

### **Introduction**

The problem of skin aging is currently very relevant, mainly due to the increased average life expectancy of people [1]. Skin aging is a degenerative process that involves a decrease in epidermal thickness, degeneration of elastic fibers, and a reduction in collagen content – the main protein that determines the physiology of the skin, maintaining its structure and enabling its numerous functions [2].

Skin aging is influenced by both genetic factors and external factors such as environmental pollution, sun exposure, and lifestyle (smoking, consumption of an unbalanced diet, and micronutrient deficiencies related to stress), which increase oxidation levels, contribute to chronic inflammation, and lower collagen content. Clinically, this manifests as skin laxity and the formation of wrinkles [3].

In recent years, oral collagen supplements have become a popular and trendy solution in the field of skin health. They are widely advertised to consumers as a way to reduce wrinkles, rejuvenate the skin, reverse signs of aging, and increase its volume [3]. The effects of oral collagen supplementation have been controversial due to the inefficient absorption of native collagen in the gastrointestinal tract. However, numerous pieces of evidence point to the beneficial role of small peptides derived from collagen, which have high absorbability compared to native collagen, for various tissues, including bones, joints, and skin in humans [4]. This paper presents findings on the effects of hydrolyzed collagen supplementation on human skin through a systematic literature review of available studies on PubMed and Google Scholar, using terms such as: collagen, supplementation, and anti-aging. Its effectiveness has been confirmed, and benefits such as skin anti-aging protection have been described.

### **Structure and Function of Collagen in the Human Body**

Collagen is a strong structural protein of the extracellular matrix (ECM) found in various connective tissues such as skin, tendons, cartilage, and bone. It makes up a significant portion of the body's total protein content, approximately 25 % [5]. Collagen is characterized by a triple helix structure formed by the repetition of glycine every third residue, and particularly by proline and hydroxyproline in the other residues. The triple helix is a rigid, rope-like protein conformation that, depending on the type of collagen, can be interspersed with small, flexible, non-helical regions or larger, globular non-collagenous regions [6, 7].

There are approximately 29 types of collagen [5]. Their distribution varies by tissue, and their specific characteristics arise from differences in post-translational modifications. The primary types of collagen found in the dermis include:

- Type I collagen - is the primary type of collagen in adult human skin, making up about 80% of the dermis. It is also found in all connective tissues, including skin, bones, teeth, tendons, ligaments, and vascular structures.
- Type II collagen - classified as fibrillar collagen, constitutes approximately 15% of the dermis. It works in synergy with type I collagen in the skin, ligaments, tendons, periodontal ligaments, vascular walls, and synovial membranes [8,9].

Collagen plays several essential roles in the human body, including:

- acting as a building material to connect cells,
- protecting tissues from mechanical damage, including skin and other organs, due to its very high tensile strength and resistance to breaking,
- mediating the transmission of cell signals,
- regulating cell proliferation and migration within tissues,
- playing a crucial role in wound healing, tissue growth, regeneration, and also participating in the processes of cell adhesion, growth, and differentiation [10].

### **The process of collagen degradation**

The natural aging process involves changes in the composition, as well as the structural and mechanical integrity of connective tissue, and a decline in cellular function due to the accumulation of damaged cellular components. Fibroblasts—the connective tissue cells responsible for maintaining the homeostasis of collagen, elastin, and related glycosaminoglycans (GAGs)—become less active starting in early adulthood, with collagen production declining by approximately 1.0%–1.5% per year. This decline can be further exacerbated by smoking and external factors such as sun exposure. Prolonged sunlight exposure and a reduced efficiency in eliminating free radicals contribute to additional damage. Furthermore, post-translational modifications of collagen and an increased accumulation of oxidized proteins occur during aging due to impaired degradation mechanisms [11,12,14].

Type I collagen, the primary protein of the extracellular matrix (ECM), provides tissue stiffness and elasticity through the spatial organization of collagen fibers. Disruptions in the organization of collagen macromolecules caused by aging or pathological processes can impair their reorganization and mechanical properties [13].

Aging-related changes in the ECM are attributed to reduced collagen synthesis and uncontrolled degradation by matrix metalloproteinases (MMPs), which are essential for tissue remodeling. During aging, collagens undergo modifications such as mineralization, glycation (leading to the formation of advanced glycation end products, or AGEs), and the loss of GAGs. These changes compromise fiber stability and affect their susceptibility to degradation by MMPs. Tissue mineralization and AGE accumulation hinder collagen degradation by cathepsin K (CatK), a cysteine protease critical for ECM remodeling. These processes can lead to extracellular matrix destruction and increased tissue stiffness [11,13]. Consequently, the dermis and subcutaneous layers of the skin are altered, resulting in decreased elasticity and increased stiffness of the skin [12].

### **Collagen Supplementation**

Over the past several years, there has been a growing body of scientific research aimed at developing various anti-aging therapies, including the use of oral supplements. Scientific evidence indicates that bioactive peptides, such as collagen hydrolysate—categorized as nutraceuticals—have chemotactic properties for skin fibroblasts, aiding in the skin regeneration process [15,16].

Nutraceuticals ("foods" + "pharmaceuticals") are substances of natural origin with specific physiological effects, but without side effects, used to improve health. Hydrolyzed collagen has been recognized as safe [17]. Lopez-Morales et al. conducted a detailed experimental study to characterize HC through various in vitro techniques using CaCo-2 and HepG2 cell lines. They concluded that HC was safe and non-toxic in the cell lines evaluated [17,18].

Several studies have shown that blood levels of collagen-derived peptides increase significantly after the oral ingestion of HC, suggesting that collagen molecules are absorbed into human plasma [15]. In a rat study by Yamamoto and colleagues, the absorption of HC tripeptides (Gly-Pro-Hyp) or dipeptides (Pro-Hyp) into the bloodstream was documented as early as 10 minutes after oral administration [17,19].

Studies on products containing collagen-derived peptides have shown an increase in skin elasticity after 90 days of use. Bioactive peptides in the dermis help form collagen fibers and bind to receptors on the membrane of fibroblasts, stimulating their proliferation and, thus, the production of hyaluronic acid, collagen, and elastin [15].

Collagen is widely available, as it can be obtained from many animal sources. Hydrolyzed collagen is most commonly derived from bovine, fish, porcine, or poultry proteins. Plant collagen is not as widely used as animal collagen because it is difficult to obtain and exhibits inferior properties compared to animal collagen [15]. Marine fish collagen has been found to have homology with human collagen, so it is widely used. It has an excellent safety profile, high bioavailability across the human gastrointestinal barrier, and high bioactivity [20].

## Clinical Study Review

We conducted a literature search in the Google Scholar and PubMed databases using the following terms: collagen or hydrolyzed collagen, supplementation, and skin anti-aging. The identified studies were published in articles prior to 2020. The studies included in the analysis met the following criteria: (1) use of a randomized controlled trial (RCT) design; (2) inclusion of healthy adults (aged  $\geq 18$  years); (3) inclusion of patients receiving hydrolyzed collagen (HC); (4) full-text articles written in English. Studies were excluded if they: (1) assessed the combined effect of a collagen supplement with another supplement or (2) were RCTs not written in English.

### STUDY 1

In one of the 6-week studies on collagen supplementation, the tested product was COLLIstant® LMW - an oral dietary supplement based on bioactive hydrolyzed bovine collagen peptides. Each sachet contained 2.5 g of the product. This study was a prospective, randomized, placebo-controlled, double-blind, monocentric trial conducted at GALA Laboratories in Don Benito–Villanueva.

The study included 80 healthy women aged 30–65 years with Fitzpatrick skin phototypes I–IV, who were mentally and physically healthy, had a body mass index (BMI) of 20.0–29.9 kg/m<sup>2</sup>, and showed visible signs of natural and photoaging on the face (crow's feet), classified as moderate to severe. All participants (test group and placebo group) were instructed to consume the contents of one sachet daily in the morning on an empty stomach for 6 weeks. The product had to be dissolved in at least 100 mL of liquid. Participants agreed to refrain during the study from prolonged exposure to ultraviolet (UV) radiation, taking similar dietary supplements, and undergoing skincare treatments such as facial masks/creams, wraps, or massages.

Skin assessment was performed based on wrinkle analysis using the Visioface 1000D device, cutometry (examining elasticity and fatigue), and corneometry (evaluating skin hydration) at the start of the study and after 6 weeks. After 6 weeks, participants who received collagen demonstrated significant improvements in biometric skin wrinkle parameters compared to baseline: a 46% reduction in wrinkle volume, a 44% reduction in wrinkle area, and a 9% reduction in wrinkle depth, as well as a greater increase in skin hydration (34%) compared to the placebo group ( $p < 0.001$ ).

The tested product was well tolerated. The observed effects aligned with the subjective assessments reported by the study participants. The study provides confirmed evidence of the effectiveness of low-molecular-weight collagen peptides in restoring altered skin biometric parameters, as objectively assessed. Thus, regular supplementation with this nutraceutical may contribute to achieving smoother and more radiant skin [21].

### STUDY 2

In another study, the product CollaSel Pro® – a hydrolyzed bovine collagen peptide without additives – was tested. Each sachet contained 10 g of the product. The placebo group received maltodextrin, and each product was administered once daily for eight weeks. The study involved 112 women aged 35 to 60 years, who had normal physical examination results, did not take any medications or supplements, and had not used moisturizers or undergone skincare treatments (e.g., laser or peeling) within three months prior to the study. Measurements of skin elasticity, hydration, and roughness were taken five times (at baseline and weeks 1, 4, 8, and 12) using the

Callegari Soft-Plus device, which is designed to assess skin condition. Facial scanning in seated and supine positions was also performed using the Artec EVA 3D Light Scanner to evaluate morphological changes in facial soft tissues caused by gravity due to changes in head position.

The following results were obtained:

- Skin elasticity: in the test product group, skin elasticity significantly improved at week 8 and week 12 compared to baseline and week 1 values. Week 8 values were also significantly higher than those at week 4. No significant changes in skin elasticity were observed in the placebo group during the study period.
- Skin hydration: significantly improved as early as week 1 of supplementation, with values continuing to increase and reaching their highest levels at weeks 8 and 12. In the placebo group, no significant changes in skin hydration were observed during the eight-week treatment period.
- Skin roughness: was reduced in the test group starting from week 1, with further significant improvements in subsequent weeks. In the placebo group, skin roughness also increased; however, it was not as significant compared to the test group.

Three-dimensional surface analysis was available for 28 women in the test product group and 25 in the placebo group. A significant decrease in RMS values—indicating a reduction in sagging of facial soft tissues caused by gravity—was observed at week 8 compared to baseline in the test product group. Improvements from baseline were also noted at week 12. No significant changes in RMS values were observed in the placebo group during the study period.

In total, 43 adverse events were reported (most commonly nausea [20.9%] and constipation [9.3%]) among 19 patients. A probable link to the test product was reported for 32 (74.4%) of the 43 adverse events, 95.3% of which were mild, and no serious adverse events (SAEs) were reported.

The study confirmed the efficacy and good tolerability of the hydrolyzed collagen peptide CollaSel Pro®. Beneficial effects of the product were observed as early as one week of use for skin hydration and roughness, and after at least eight weeks of use for skin elasticity and facial configuration [22].

### STUDY 3

Another study, this time with the product Collagen-Tripep20™/Tripep20, containing liquid fish collagen, was conducted to assess the enhancement of skin health and quality after daily consumption of 1000 mg of the product in a 50 ml bottle for 12 weeks. The study involved 85 healthy women aged 35–60 with diagnosed photoaging of the skin (including crow's feet graded from 2 to 6 according to dermatologists' assessment using the Global Photodamage Scoring system), who were randomly assigned to receive either Tripep20 or a placebo.

Crow's feet wrinkles around the eyes were measured using an optical in vivo 3D skin measurement device, PRIMOS, which after 12 weeks showed a significant improvement in the appearance of crow's feet and skin roughness compared to the placebo group. Skin hydration in the test group was significantly higher from week 6 compared to baseline, when compared to the placebo group. Consuming the liquid collagen Tripep20 also significantly improved skin elasticity within 6 weeks compared to the placebo group. No adverse symptoms or events occurred during the study period in participants taking either Tripep20 or the placebo [23].

### ANOTHER STUDIES

Apart from studies conducted on humans, animals have also been examined to assess the impact of collagen. In one study, mice were fed a diet containing collagen hydrolysate for about 3 months. The study revealed an improvement in the water content of their skin and an increase in elasticity, compared to the mice in the control group, who did not experience such benefits. In another study, mice were observed on a diet rich in prolylhydroxyproline and hydroxypropylglycine for around 5 weeks. Mice that received collagen hydrolysates showed increased skin hydration [20].

### Conclusions from the above studies

Studies on collagen supplementation show a positive impact on skin elasticity, hydration, and wrinkle reduction, both in human trials and animal models. Collagen supplementation, especially in the form of hydrolyzed

peptides, shows benefits after just a few weeks of use. However, most studies are limited to short-term periods, making it difficult to assess long-term effects. Additionally, there is a lack of data on optimal dosages and the impact of collagen on different skin types.

## **Discussion**

The conducted studies on collagen supplementation show a consistent trend indicating its effectiveness in improving skin parameters such as elasticity, moisture retention, and wrinkle reduction. Hydrolyzed collagen peptides are effectively absorbed and function as bioactive compounds that stimulate the activity of dermal fibroblasts and support the synthesis of the extracellular matrix, including collagen, elastin, and hyaluronic acid.

While reviewing the available literature, we did not find studies that directly compared the effects of marine collagen and bovine collagen on skin aging. Some sources support marine collagen, which is metabolically compatible and offers advantages over animal-derived collagens such as bovine or porcine collagen. One of its main benefits is the availability of the raw material, as marine collagen is obtained from large amounts of fishing industry waste, such as fish skin (with a high content of Type I collagen), which helps reduce environmental pollution and ensures high yields at lower costs. Additionally, marine collagen has higher biocompatibility and lacks the risk of transmitting animal diseases such as bovine spongiform encephalopathy (BSE), making it a safer alternative [24]. Another source notes that despite concerns related to mad cow disease in Europe and the United States, bovine bones still remain one of the most abundant sources of gelatin, accounting for 23.1% of gelatin production. Bovine collagen, in addition to its anti-aging effects on the skin, has a beneficial impact on bone metabolism, including inhibiting bone mass loss and improving osteoarthritis [25]. In conclusion, both types of collagen show anti-aging effects on the skin. This lack of direct comparison may suggest a direction for future scientific research in this area, such as analyzing the bioavailability and effectiveness of both types in individuals with varying health needs.

The safety profile of collagen supplements, according to the studies presented, is generally favorable, although minor side effects (e.g., gastrointestinal discomfort) have been reported. It has also been shown that collagen supplements do not significantly interact with other dietary components, supporting their classification as safe nutraceuticals.

Despite the positive results, there are some limitations that need to be discussed. First, many studies on collagen supplementation are short-term, typically lasting from 6 to 12 weeks, limiting the ability to assess long-term effects and cumulative benefits. Second, differences in study designs, such as collagen doses, formulation types, or participant characteristics, make comparing and generalizing the results challenging. Additionally, most studies focus on middle-aged women, and data on other demographic groups, such as men, people from various age groups, or individuals with different skin types, are limited.

Further research involving standardized protocols, diverse population groups, and long-term observations is essential to strengthen the evidence base and determine optimal dosages and formulations of collagen supplements.

## **Conclusions**

Research indicates that supplementation with hydrolyzed collagen improves skin elasticity, hydration, and reduces wrinkles. Collagen stimulates skin fibroblasts and supports the production of collagen, elastin, and hyaluronic acid. Supplements are safe, and side effects are rare and usually mild. Both marine and bovine collagen show similar anti-aging benefits, although marine collagen has better bioavailability. However, there are no direct comparisons between the two types. Most studies are short-term (6-12 weeks) and focus primarily on middle-aged women, which limits the generalizability of the results. Further research, particularly long-term studies involving diverse demographic groups, is needed to determine the optimal doses and forms of supplementation.

## **Disclosures**

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