REVIEW

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Collagen Supplementation

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ABSTRACT

The use of nutritional supplements for antiaging purposes has been rising in the past decade. Collagen is one of the most prevalent proteins in the human body. Aging is a multifactorial process; and the thinning and sagging of the skin is due to the loss of collagen and elastin fibers. Oral collagen supplementation, via collagen dipeptides and tripeptides triggers neocollagenesis. Therefore there is a rise in the market of collagen supllementation recently. This review article dwells on the biochemistry and sources of collagen as well as the recent studies about collagen supplementation.

Keywords: Anti-aging, Collagen, Supplementation

Introduction

Skin homeostasis is affected by nutrition. The use of nutritional supplements for antiaging purposes has been rising in the past decade and the estimated market value for nutritional supplementation in 2025 is 60 billion Turkish liras. Although the demand has been rising, enough evidence for the use of oral collagen supplementation in anti-aging is still lacking [1].

Biochemistry of Collagen

Collagen is one of the most prevalent proteins in the human body. It compromises one third of the human protein component, three quarters of the dry weight of human skin; and it is the most abundant component of the extracellular matrix. Collagen is a protein that is unique for its sturcture: Three polipeptide strands forming a helix [2]. Gelatin is a product that is produced when collagen is denatured by heat. Gelatin is used as a part of traditional medicine in Europe and China. Collagen hydrosylates, peptides of varying lengths, are produced by the further hydrolisis of gelatin. Collagen hydrosylates can be easily formulated into liquid drinks and jelly sticks due to its lower molecular weight and higher water solubility. In the human body, the collagen hydrosilates are further divided into dipeptides and tripeptides, which are resistant to degradation and are bioactive. The dipeptide and tripeptide degradation products of collagen are found in the human blood stream after oral collagen hydrosilate intake. Previously, animal studies have shown that these dipeptides are incorporated to the skin for two weeks. Furthermore, *in vitro* studies have demostrated that the ingestion of collagen hydrosilates induces mRNA transciption and translation of the protein and thus the collagen synthesis. Besides, it promotes anti-oxidative activity within the cells. Dipeptides induce chemotaxis, cell proliferation and the production of hyaluronic acid by fibroblasts. Thus, oral collagen supplementation has a potential therapeutic value for aging since it helps to produce stronger collagen fibers [1].

Aging

Aging is a multifactorial process. The reduction and repositioning of adipose tissue, bone remodelling and decreased production of collagen contribute to aging [3]. Histologically, aged skin shows abnormally deposited amorphous elastin fragments and fragmented collagen. The aged skin is lax, rough, shallow and has decreased elasticity [4]. First signs of dermal aging are shown in the human

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body around 30 years of age. Fine wrinkles ocur around the eyes and the mouth. The thinning and sagging of the skin is due to the loss of collagen and elastin fibers [5]. Oral collagen supplementation, via collagen dipeptides and tripeptides triggers neocollagenesis [1].

Sources of Collagen

The most commonly used source of collagen are the bovine and porcine sources. The age of the animal effectes the solubility of collagen obtained. Collagen of older animals are less soluble than that of the younger animals. The technology for acquiring collagen has been advancing as well. Bovine collagen, extracted as gelatin from the bovine bone, was used in the treatment of osteoarthitis previously. However, due to the increasing risk of bovine encephalopathy the use of this source has diminished. As a result the search for other sources of collagen began, which include vegetable source, algea and marine organisim including the fish [6].

The use of marine organisms is preferred in the cosmetic industry as a source of collagen. The marine organisms from which collagen can be extracted are jellyfish, sponges, seaurchin, octopus, cod, salmon and marine mammals. The biocompatibility and amino acid content of marine collagen is similar to that of bovine collagen. Yet, it has a lower molecular weight, is more soluble and has a lower potential for contamination or inflammatory reactions. In addition to these, type 1 collagen is more abundant in marine sources. The previous uses of marine collagen in the cosmetic industry were would healing, antimicrobial protection, prevention of loss of heat and humidity from the injured tissues [7,8]. The only limitation of the use of marine collagen is its possible contamination with heavy metals [9].

Previous Studies Regarding the Use of Oral Collagen Supplementation in Human Subjects

Collagen Hydrosilates

In 2006, Lee et al. [10] investigated the use of collagen hydrosilate in pressure ulcers with 89 patients. Each patient either received 15 g oral collagen three times daily or placebo. The investigators concluded that collagen hydrosilates were effective in the treatment of pressure ulsers compared to placebo [10].

Proksch et al. [11] investigated the use of 2.5 g oral bioactive collagen product use daily for the treatment of eye wrinkles in 116 healthy females. As a result of daily collagen use, procollagen type 1 and elastin has increased within the skin. There was a significant reduction in the periorbital wrinkles after the daily use of collagen hydrosilate. A year after, Proksch et al. [12] investigated the use of porcine collagen for impro ving skin elasticity. Sixty-nine females with dry forearm skin were divided into three groups of equal participants. The first group recevied 2.5 g oral daily porcine collagen hydrosilate, the second group received 5 g oral porcine collagen hydrosilate and the third group was the placebo group. The authors concluded that daily use of porcine collagen hydrosilates (2.5 g or 5 g) were effective in improving the skin quality and elasticity [11,12].

In 2014, Yoon et al. [13] compared the use of oral 2 mg astaxhantin and 3 g fish collagen hydrosilate to placeboin 44 women with wrinkles. Skin elasticy and transepidermal water loss improved significantly with the use of collagen hydrosilates. The expression of procollagen type 1 mRNA increased and the expression of the matrix metalloproteinases decrased as a result of collagen ingestion [13].

Asserin et al. [14] compared the use of porcine collagen to that of fish collagen in 33 women with dry skin. Ten grams of fish colllagen peptide, used daily was compared to 10 g porcine peptide used daily and the investigators report that fish collagen hydrosilate increased the skin moisture by 12 percent, whereas pig collagen hydrosilate increased the skin moisture by 28 percent. Asserin et al. [14] also compared the effect of fish collagen hydrosilates to placebo. They reported that the collagen density increased significantly and collagen fragmentation decreased significantly with the use of 10 g fish collagen hydrosilate daily compared to placebo [14].

Schunck et al. [15] gave 2.5 g porcine bioactive collagen peptide daily to 105 female patients with moderate cellulite. They reported a significant decrease in cellulite, reduced skin waviness and significantly improved dermal collagen density in women with normal weight. The effects were less pronounced in overwieght patients [15].

Genovese et al. [16] investigated the use of oral 50 mL blend of 5 g fish collagen bioactive peptides, hyaluronic acid, borage oil, N-acetylglucose amine and antioxidants on 120 healthy volunteers. They reported that skin elasticity improved significantly with the use of collagen [16].

Collagen Tripeptides

Choi et al. [17] investigated the use of oral 3%, 15 g collagen tripeptide for the treatment of post-laser erythema and skin elasticity in 8 females that have recieved laser therapy. The authors reported that the collegen supplementation led to faster recovery of post-laser erythema and skin hydration starting at the third day of treatment; and increased skin elasticity by the 14th day of treatment [17]. In another study, Choi et al. [17] compared the use of oral 3%, 15 g collagen alone or along with vitamin C supplementation 500 mg dailiy in 24 female and 8 male patients with wrinkles. They concluded that daily collagen peptide supplementation improves skin elasticty and hydration; however, the synchronous intake of vitamin C supplementation does not enhance this effect [18].

Collagen Dipeptides

Inoue et al. [19] investigated the use of oral fish collagen in 85 female patients for the improvement of facial skin moisture, elasticity,

wrinkles and roughness. They compared the use of collagen hydrosilates with low (0.5 mg) and high (10 mg) dipeptide content. The authors concluded that oral collagen hyrdosilate solutions with higher dipeptide content were superior to those with lower dipeptide content in the treatment of decreased skin moisture and elasticity, wrinkles and roughness due to aging [19].

Hexsel et al. [20] researched the efficacy of oral collagen supplementation in improving nail brittleness. Twenty-five patients with brittle nail syndrome received 2.5 g oral daily collagen supplementation for 24 weeks. Bioactive collagen peptides decreased the nail break rate by 42% and increased the nail growth rate by 12%. Eighty percent of the patients were satisfied with the results. Thus, oral collagen supplementation is effective in treating brittle nails [20].

A Shift in Perspective: Marine Collagen Sources

Due the possible adverse effects faced with the use of bovine collagen sources, the resaerchers have shifted to a newer perspective and started investigating the marine sources [6]. Marine collagen peptides have high homology to human collagen, they are safe, stable, highly biocompatable and have high bioavalibilty through the gastrointestinal tract. However, due to the increased hydroxyproline levels in collagen, marine sources have the potential of causing higher oxidative stress. Besides, they can activate innate immune response through the activation of neutrophils and macrophages via the toll-like receptors which leads to NADPH activation and the production of reactive oxygen species [21].

De Luca et al. [21] investigated the use of marine collagen peptides acquired from the fish skin on the skin quality in 41 healthy volunteers. Each participant received marine collagen peptides combined with coenzyme Q, grape skin extract, seleinum and luteolin. Skin properties such as the moisture, elasticity, sebum production, and biological age were assed subjectively; and the ultrasonic markers such as the epidermal/dermal thickness and acoustic density were assesed objectively. The authors concluded that marine collagen peptides improved the skin properties measured by both objective and subjective parameters. Furthermore, the addition of plant derived antioxidants (coenzyme Q, grape skin extract, selenium and luteolin) were beneficial in reducing the oxidative stress. Thus, the combination of marine collagen peptides with the skin targeting anti-oxidants is effective and safe for improving skin properties [21].

Costa et al. [22] investigated the use of marine collagen for improving skin wrinkles in male patients. Forthy-seven male pateints received two tablets of the following content: marine protein (105 mg), vitamin C (27 mg), grape seed extract (13.75 mg), zinc (2 mg), and tomato extract (14.38 mg) every day for 180 consecutive days. As a result of the treatment, the facial erythema and pH decreased significantly, skin hydration increased significantly and the dermal density measured by ultrasound increased significantly. Thus, marine collagen supplement containing biomarine complex, vitamin C, grape seed extract, zinc, and tomato extract was effective in improving skin quality in men [22].

An animal study on hairless mice has previously shown that collagen hydrosilates derived from the type 1 collagen in the fish skin, promoted the recovery of collagen fibers from degraded collagen and enhanced the formation of normal elastic fibers rather than the abnormal elastic fibers which were due to the solar elastosis due the ultraviolet B damage. This effect was caused by the reduction of matrix metalloproteinases which degrade collagen and gelatins. This reduces skin wrinkling and transepidermal water loss; and increases skin elasticty and hydration. Kim et al. [23] investigated the use of collagen hydrosilates derived from the sutchi catfish's skin (Pangasius hypophthalmus), with >15% tripeptide content in the treatment of photoaged skin. Sixty-four female volunteers, ages ranging from 40 to 60 years received 1g low molecular weight collagen hydrosilate daily for 12 weeks. The authors concluded that the skin hydration and elasticity were significantly higher and wrinkling was less pronounced in the treatment group than in the placebo group. Thus, the low molecular weigh collagen peptides obrtained from sutchi catfish can be used as a supplement for improving skin hydration, elasticity and wrinkling [23].

Sangsuwan and Asawanonda [24] conducted a study about the use of oral collagen supplement obtained from the fish scale and skin. Thirty-six post menopausal female patients were randomized into two groups, the first group received 5 g oral collagen hydrosilate derived from fish skin and scale; the second group received placebo. Authors reported that the skin elasticty of the cheeks (representing the sun exposed areas) imporved significantly after using the collagen supplementation for 4 weeks. Furthermore, the effects continued 4 weeks after the supplementation was discontinued [24].

Some other studies regarding the use of marine derived collagen were performed using enzymatic hydrolysis as well. It was shown that commercially available fish type I collagen hydrolysate from amino collagen (Meiji Seika, Tokyo, Japan) improved skin hydration in 25 female Japanese patients after using for 6 weeks. Collagen peptides stabilized orthosilicic acids rejuvenised the skin and caused no side effects, hypersensitiy or systemic symptoms. Marine sponge collagen also rejuvenised the skin via increasing cell proliferation and photoprotection [25]. Other uses of marine organism include the uses in skin regenerative medicine such as wound healing, prevention of biofilm formation and bacterial contamination [26].

Ethics

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: D.Ö., Ö.A., Concept: D.Ö., Ö.A., Data Collection or Processing: D.Ö., Ö.A., Analysis or Interpretation: D.Ö., Ö.A., Literature Search: D.Ö., Ö.A., Writing: D.Ö., Ö.A.

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