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Advantages of oral collagen supplementation. Review of the literature

Zuzanna Kotowicz
Voivodeship Clinical Hospital No.2 in Rzeszow
St. Lwowska 60, 35-301 Rzeszów, Poland
kotowiczzuzia@gmail.com
https://orcid.org/0009-0009-5711-3229
Aleksandra Pich-Czekierda
St Michael the Archangel Hospital - Medical Centre in Łańcut
St. Ignacego Paderewskiego 5, 37-100 Łańcut, Poland
aleksandrapich22@gmail.com
https://orcid.org/0009-0002-6774-3282
Patrycja Proszowska
University Clinical Hospital named after F. Chopin in Rzeszow
St. F. Chopin 2 35-055 Rzeszów, Poland
proszowska.patrycja@gmail.com
https://orcid.org/0009-0005-5421-4009
Adrianna Orzeł
University Clinical Hospital named after F. Chopin in Rzeszow
St. F. Chopin 2 35-055 Rzeszów, Poland
adaorzel98@gmail.com
https://orcid.org/0009-0003-3093-2482
Daria Sieniawska
University Clinical Hospital named after F. Chopin in Rzeszow
St. F. Chopin 2 35-055 Rzeszów, Poland
sieniawska.daria@gmail.com
https://orcid.org/0009-0004-1019-6227
Magda Madoń
City Hospital of John Paul II in Rzeszow
St. Rycerska 4, 35-241 Rzeszów, Poland
magmad2505@gmail.com
https://orcid.org/0009-0002-1711-6571

Julia Sieniawska
Rzeszów University
Al. Rejtana 16c 35-959 Rzeszów, Poland
julia.sieniawska01@gmail.com
https://orcid.org/0009-0002-3737-5079

ABSTRACT

Introduction

Collagen is a protein that has found widespread use both as an ingredient in cosmetics applied externally and as an oral supplement. This substance is obtained from a number of animal sources, including bovine tissues, as well as marine fish. The characteristic properties of collagen peptides, such as scientifically proven anti-inflammatory effects, activation of fibroblast skin cells, stimulation of synovial cells to produce hyaluronic acid, and much more make this type of supplement promising in improving the body's general condition and in alleviating the symptoms of many ailments. Numerous scientific studies have shown that supplementation with hydrolyzed collagen has a beneficial effect on both the overall condition of the skin by improving its elasticity, hydration level, and positive action on its protective barrier and on the musculoskeletal system, where, when combined with appropriately selected physical activity, it can help to reduce pain associated with conditions such as osteoarthritis and even increase the range of movement in the joints. Easy availability, user-friendly forms of administration, such as powders or ready-to-drink liquid formulations, and a low incidence of side effects make this supplementation highly beneficial for users.

Aim of the study

This study aims to discuss the known processes and review the evidence supporting the beneficial effects of hydrolyzed collagen supplementation on the human skin and musculoskeletal system.

Material and method

This article presents the current state of knowledge about the benefits of oral collagen peptide supplementation in various scientific articles. Publications describing the mechanisms of action and the effects of collagen supplementation on skin conditions and the musculoskeletal system, including recent reports in this field, were reviewed using the PubMed platform. The search included the keywords ‘collagen’, ‘collagen supplementation’, ‘nutritional supplement’, ‘recovery’.

Keywords: collagen, collagen supplementation, nutritional supplement, recovery

Introduction and Description of Collagen

Collagen, the primary structural protein in the skin comprises up to 30% of all proteins in the body and is the principal protein that creates structure in tissues including skin, cartilage,

tendons, bones and hair. Seventy-five percent of the extracellular matrix's weight is made up of collagen [1,2]. Collagen's unique triple-helix shape is made up of a high concentration of three amino acids: glycine, proline and hydroxyproline [3]. There are 28 different forms of collagen that have been found and described at the molecular level [4]. Each form differs in its own characteristics. They can be discovered in a variety of tissues throughout the human organism. More than 90 percent of collagen in the human body is composed of type I, II and III fibrillar collagens. Type I is the most prevalent in the skin, bones, teeth, and tendons, while type III accounts for about 15% of the collagen content in skin. Type II is responsible for the structure of cartilage and corresponds to 90% of the collagen content in these structures [5,6,7,8].

Collagen is now widely used as an ingredient in cosmetics and nutrisupplements. It is used both externally, on the skin formulated as creams or serums, for example, which aim to improve skin elasticity, increase the level of hydration, enhance its appearance and reduce wrinkles, and is also used in the form of pharmaceuticals or oral supplementation, usually as a powder to be mixed with water or a ready-to-drink liquid [9,10].

Oral ingestion of hydrolyzed collagen results in considerably better postprandial absorption compared to non-hydrolyzed collagen, indicating that supplements containing the hydrolysed form are associated with better absorption and bioavailability [11]. Collagen hydrolysates are products that have a low molecular weight - usually around 3-6 kDa. Enzymatic hydrolysis involves breaking down its peptide chains into smaller, low-mass molecules [8]. Hydrolysis usually occurs through the action of acidic or alkaline substances followed by high temperatures, usually above 40°C [8].

Nowadays, thanks to modern production and extraction methods, it is possible to extract collagen from a variety of animal tissues, including connective tissue, tendons, bones, as well as skin and scales in the case of marine collagen [3].

Collagen made from fish has become a popular alternative in recent times. Because collagen peptides derived from marine fish have a low molecular weight, they are better absorbed by the gastrointestinal tract and show greater bioavailability than collagens derived from other animal sources e.g. bovine [12]. Also, they have a structure that closely resembles those of humans when passing through the gastrointestinal barrier, which may make them more effective [13]. A further advantage of dietary supplements containing collagen, especially those that include hydrolyzed collagen peptides, is that they are both safe and economical when compared with different collagen-based tactics [3].

Metabolism of collagen in the human body

Collagen, as a protein, is digested in the gastrointestinal tract by enzymes, such as pancreatic protease in the small intestine. The first step in this process is the breakdown of the collagen molecule into smaller dipeptides, tripeptides or individual amino acids, which will then be absorbed into the blood [7]. The peak level of peptides derived from collagen in the blood occurs 2 hours after oral consumption, followed by a decline in serum levels thereafter [14]. Then, they are transported with the blood to the tissues, e.g. skin, where they participate in the formation of new collagen fibers [15].

A specific characteristic of collagen is its ability to resist proteolytic enzymes, which limits the hydrolysis and degradation of its molecules. The presence of the amino acids proline (Pro) and hydroxyproline (Hyp) is most probably responsible for this phenomenon [7].

The presence of bioactive peptides, e.g., Pro-Hyp dipeptide, in the blood plasma of people after oral ingestion of hydrolyzed collagen has been verified in human-based clinical studies [8,14]. It has also been shown that the aforementioned peptides, collagen derivatives, were excreted in the urine after oral ingestion. This allows us to conclude that after oral consumption of collagen in hydrolyzed form, its metabolites are absorbed in the blood and then, in a stable form, excreted into the urine and removed from the body [8,16].

Effects of collagen supplementation on the skin

As the biggest organ exposed to the outside environment, the skin experiences aging due to both internal and external causes [10]. As the standards of beauty continue to rise, there has been a significant increase in the amount of attention paid to the process of skin aging. The growing demand for effective treatments to alleviate the psychological effects of skin aging is due to the increasing number of aging populations in many countries. In recent years, dietary supplements and nutricosmetics such as collagen have gained considerable popularity [10,17].

Reduced collagen production and decreased skin blood circulation are two factors that contribute to the deterioration of skin quality with aging, which results in dehydration, reduction in epidermal thickness, less elasticity of the skin and the development of wrinkles [1,18].

One of the many functions characterising collagen is to provide mechanical support to keratinocytes, fibroblasts, melanocytes and other cells that represent the building elements of

the skin. This action is made possible by the interaction of collagen with other skin components, including elastin, hyaluronic acid and reticulin [1,19].

As we age, the structure of collagen fibers in the skin becomes fragmented, leading to shorter molecules that form a less organized structure. In addition, there is an increased synthesis of enzymes with age, whose action is based on the degradation of collagen fibers – they are known as metalloproteinases. These enzymes also have an inhibitory effect on fibroblasts, causing these cells to produce less ammount of new collagen fibers [1].

It has been proven that after oral ingestion of collagen in hydrolysed form, high concentrations of small-molecule collagen peptides are recorded in the blood [20,21,22,23]. Research has demonstrated that prolylhydroxyproline (Pro-Hyp) is absorbed as dipeptide after consumption and then it is accumulated in the layers of skin [1].

The biologically active form of the Pro-Hyp dipeptide initiates fibroblast migration and the growth of these cells in the skin. This action has a positive effect on the skin's structure, as the fibroblasts stimulate the synthesis of collagen and elastic fibers, resulting in a reduction in the signs of skin aging and an increase in skin elasticity [22,23]. Pro-Hyp dipeptide in the skin has also been shown to promote hyaluronic acid (HA) production. Hyaluronic acid is known for its ability to bind water in skin cells, which translates into an increase in skin hydration [24,25].

In addition, evidence has demonstrated that consuming collagen peptides boosts the synthesis of filaggrin, an essential component in repairing the skin's protective barrier. This substance enhances the amounts of amino acids, which are crucial elements of the skin's natural moisturizing factor (NMF) in the stratum corneum, resulting in enhancing skin hydration [21,26]. Collagen use also contributes to increased synthesis of ceramides, important components of the skin's lipid profile, by upregulating the expression of ceramide synthases. This action also improves skin barrier condition, its hydration and reduces transepidermal water loss [26].

The oral use of collagen peptides in various formulations helps to increase skin hydration, improve elasticity, reduce wrinkles, and increase epidermal density and thickness. These supplementation effects were already visible after 2 or 3 months of regular consumption [1].

The effectiveness of collagen as a dietary supplement and its effect on skin condition is supported by a number of scientific studies.

Kim et al. [22] investigated how oral collagen supplementation affects human skin. 64 healthy women aged 40-60 years who had dermatologists-diagnosed wrinkles participated in this

study. Every day each woman consumed 1 bottle, containing 1000 mg of low-molecular-weight collagen peptide, derived from the sutchi catfish's skin for a period of 12 weeks. It was then examined how supplementation affected hydration, wrinkle advancement and skin elasticity. After 12 weeks, a significant improvement in skin hydration was shown in the group of patients taking oral collagen supplementation, compared to women in the placebo group. In the study group, the structure of wrinkles visually on the skin improved significantly, according to the placebo group. At 12 weeks, the skin-elasticity measurements were notably enhanced in the test group compared to the placebo group. All of the participants in the study did not exhibit any adverse effects while the research was being conducted [22].

In a similar study by Evans et al. [13] a group of women with visible signs of skin aging consumed 10g of hydrolysed collagen, which was derived from freshwater fish. The participants took it every morning, on an empty stomach, dissolving a dose of collagen in 100ml of water. The effects of supplementation in women were measured using advanced systems analyzing the level of skin wrinkle advancement and the skin's elasticity. The study group that ingested collagen experienced significant enhancements in firmness, hydration, elasticity, and reduction of the depth and advance of skin wrinkles. This indicates that hydrolyzed collagen supplementation positively impacted self-perceived skin appearance. During the course of the study, oral supplementation of hydrolysed collagen was shown to be well tolerated and safe. The occurrence of adverse effects was reported with equal frequency in the placebo group and the study group, none of which were directly related to supplementation [13].

Choi et al. [27] studied the effects of collagen peptide supplementation on skin elasticity, hydration and the presence of erythema and pigmentation on the skin. They also aimed to test whether adding vitamin C to the supplement taken by the study participants would enhance the effect of collagen. In the study, they obtained results that suggested that the use of collagen peptides enhanced skin elasticity and hydration levels. In contrast, this supplementation did not significantly affect the severity of pigmentation changes and erythema in the study subjects. Also, the addition of vitamin C to the supplement taken was not shown to enhance the benefits in skin hydration and elasticity derived from its use [27].

Another study by Pyun et al. [28] was conducted in which participants were hairless mice that were exposed to UVB radiation, resulting in degradation of collagen and elastic fibers in their skin. After oral administration of a low-molecular-weight collagen peptide, extracted from

fish, the regeneration of collagen and elastic fibers in the skin of these animals was observed [28].

Impact on joint function and injury recovery

An interest is growing in therapeutic approaches to enhance joint health due to the rising occurrence of long-term joint and bone injuries resulting from sports activity [29]. Studies have shown that collagen peptides can serve as a safe and beneficial supplement to alleviate symptoms associated with orthopaedic conditions such as osteoarthritis (OA) and osteoporosis [30].

Given the lack of therapeutic choices and absence of authorized disease-modifying medications, it is important to explore the possible impact of dietary components and supplements in treating osteoarthritis. Early management is crucial for patients with initial phase or symptomatic osteoarthritis to slow down its development and avoid surgical procedures [8].

Articular cartilage is formed by the combination of an extracellular matrix and chondrocytes, which are cartilage-producing cells. The extracellular matrix consists mostly of water and proteins like collagen and proteoglycans [8]. Type I collagen is the predominant element of the extracellular matrix (ECM) and serves as a supporting component, facilitating cell migration, wound repair, and tissue regrowth. The bone extracellular matrix is highly abundant in type I collagen, making it valuable for use in bone tissue development and treatment [31].

Hydrolyzed collagen nutritional supplementation, when combined with physical activity, has the potential to be effective for alleviating the symptoms of degenerative bone and joint conditions. This is probably a result of the invigorating impact of collagen supplementation and physical activity on the extracellular matrix of connective tissues resulting in a enhancing its architecture [29]. Additionally, there is significant proof that collagen supplementation prevents bone collagen degradation and relieves painful signs related to degenerative joint diseases [32].

In individuals using oral collagen supplementation, there is a high concentration of Pro-Hyp dipeptides in the blood [14], which stimulate hyaluronic acid synthesis by synovial cells [33], and this action is particularly beneficial for the condition and structure of ligaments and tendons.

Furthermore, collagen peptides have the potential to exhibit anti-inflammatory characteristics. It has been shown that the glycine contained in them has the ability to reduce the production of cytokines that promote inflammation such as interleukin-6 [34].

Consumption of products containing collagen peptides has been shown to significantly increase the synthesis of type I, II and IV collagen molecules in cartilage located on articular surfaces. The effect of this supplementation also promotes the synthesis of proteoglycan and elastin in articular cartilage. The result of these actions is an improvement in tissue condition [35].

Studies were conducted, which demonstrated that oral supplementation with specific collagen peptidescan additionally promote the synthesis of extracellular matrix (ECM) compounds, resulting in improved connective tissue density and structure. The mentioned supplementation has also the potential to inhibit the activity of specific enzymes, called matrix metalloproteinases, which destroy the collagen molecules in the ECM [29].

Scientific experiments revealed that people who consumed collagen supplements showed a decrease in the concentration of the plasma marker cross-linked C-telopeptide of type II collagen, the concentration of which corresponds to the cartilage degradation process. These findings suggest that collagen supplementation may contribute to a decrease in structural joint damage [32,36].

It is concluded that further studies in humans are needed to better comprehend and describe the mechanisms underlying the action of collagen peptides.

Numerous scientific studies undertaken to date have demonstrated the favourable effects of collagen supplementation on the state and function of the musculoskeletal system.

A study by Dressler et al. [37] was conducted with 50 athletic participants. Each took 5g of collagen peptides daily, while performing a series of exercises at home three times a week, for a period of six months. In the group including those taking the collagen peptide-based supplement, the vast majority of study participants showed improvements in perceived ankle function, compared to the group taking placebo. Also, at the three-month monitoring, ankle sprains were considerably decreased in participants who consumed the particular collagen peptides compared to the control group. The study demonstrated that a daily 5 g intake of certain collagen peptides had a significant impact on ankle stability in individuals with persistent instability in the ankle over a 6-month period [37].

Another study by Lugo et al. [38] involves 55 participants who experienced discomfort in their knee joints after exercising with a step machine. Participants were given a supplement,

UC-II which contains a patented form of undenatured type II collagen derived from chicken or a placebo for 120 days. There was an increase in mean knee extension in the UC-II subgroup after 120 days of supplementary intake in comparison to the control group. The placebo group did not show any notable change in knee extension throughout the study. After 120 days, the group who took the supplement were able to exercise for a longer period of time before noticing joint pain. There were no notable alterations observed in the placebo group. In this way, it was shown that collagen peptide supplementation in the study group improved mobility in the knee joint and prolonged the time participants could indulge in physical exercise without experiencing pain. The study suggests that the positive outcomes of collagen peptide supplementation could be attributed to the stimulation of regulatory T cells that specifically target UC-II. Type II collagen molecules have the capacity to develop anti-inflammatory cytokines (like transforming growth factor-β and interleukin-10), which are possible able to prevent the pro-inflammatory pathway that is linked to intense physical activity. No negative side effects connected to the collagen supplement were noted during the research [38].

Studies have demonstrated that supplementation of collagen peptides may have positive impacts on pain associated with joint function. This supplementation also contributes to an increase in the duration of intense physical activity without feeling pain and it can help to decrease the need for other therapies. These benefits are particularly evident when collagen supplements are used in conjunction with physical activities and a rehabilitation plan. [37,38,39].

The therapeutic potential of collagen peptides in the management of joint disorders continues to receive attention in scientific circles. One of the topics examined is the suggested dose of the supplement. In the majority of research studies conducted on individuals with osteoarthritis, the administration of an everyday dose of 10 g of collagen peptides over a period of 3 months has shown efficacy in considerably enhancing mobility and alleviating joint pain when compared to placebo groups [40]. In contrast, another study, which highlighted the amount of collagen-containing supplement used, found that supplementation with 5g of collagen peptides per day improved ankle joint function throughout everyday and sports activities compared to the placebo group [37].

Conclussion

It is now widely recognised that collagen, which is one of the main components of tissue, is considered as safe to use. It also benefits from its easy availability, simplicity of dosage and various forms of administration. There have been no reports of significant adverse effects associated with the use of hydrolyzed collagen peptides as an oral supplement up until this point, coming to the conclusion that it is a safe substance. According to the findings of a notable amount of scientific research, the utilisation of this dietary supplement has the potential to greatly enhance the condition of the skin. Collagen has been shown to have a beneficial impact on the components of the skin barrier, as well as an improvement in the hydration of the skin, a reduction in the advancement of signs of ageing, and an enchancement in the overall appearance of the skin. In addition to the favourable impacts that collagen peptide supplementation has on the skin, there are other positive elements that arise from using this substance. Studies included in this review show that collagen can improve joint function and reduce discomfort, especially when supplementation is accompanied by physical activity. Thus, its administration may be beneficial for people with osteoarthritis or during rehabilitation after musculoskeletal injuries. More randomised controlled studies on a wide scale are required in order to conduct a comprehensive investigation into the potential advantages of oral collagen supplements and the relationship between those benefits and the doses that are administered.

Author's contribution

Conceptualization, Zuzanna Kotowicz; methodology, Zuzanna Kotowicz, Aleksandra Pich-Czekierda; software, Patrycja Proszowska; check, Zuzanna Kotowicz, Daria Sieniawska and Julia Sieniawska; formal analysis, Adrianna Orzeł, Aleksandra Pich-Czekierda; investigation, Zuzanna Kotowicz; resources, Magda Madoń; data curation, Adrianna Orzeł; writing - rough preparation, Zuzanna Kotowicz; writing - review and editing, Zuzanna Kotowicz; visualization, Aleksandra Pich-Czekierda; supervision, Patrycja Proszowska; project administration, Zuzanna Kotowicz, Magda Madoń and Daria Sieniawska; receiving funding, Zuzanna Kotowicz, Julia Sieniawska;

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