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The Role of Collagen Supplementation in Improving Skin Quality and Joint Function: Mechanisms of Action, Effectiveness, and Future Research Directions

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ABSTRACT

Introduction

Collagen is one of the most abundant proteins in the human body and the most prevalent component of the extracellular matrix. It provides mechanical support and guides tissue development. It is fundamental in maintaining elasticity, hydration, and overall structural integrity of the skin. Collagen is also essential for joint health, contributing to cartilage resilience and mobility. However, natural collagen synthesis declines with age, exacerbated by environmental factors such as UV radiation, environmental factors, lifestyle, and oxidative stress, leading to visible skin ageing and joint degeneration.

Methods and Materials

This study utilises data from databases such as PubMed, Frontiers, and Google Scholar to analyse the effectiveness of collagen supplementation in improving skin and joint health. A systematic review of clinical trials and *in vitro* studies was conducted to explore mechanisms of action, bioavailability, and outcomes associated with various forms of collagen supplementation.

Conclusions

Evidence indicates that hydrolysed collagen improves skin elasticity, hydration, and wrinkle reduction by stimulating fibroblast activity. Additionally, it supports joint health by promoting cartilage regeneration and reducing inflammation, particularly in conditions like osteoarthritis. The evidence for the positive impact of supplementing good quality collagen on the condition of the skin and musculoskeletal system is increasing. Further research into long-term effects and personalised supplementation strategies is necessary to optimise clinical outcomes.

Keywords: collagen supplementation, skin health, joint health, hydrolysed collagen, ageing, cartilage regeneration, antiaging

INTRODUCTION

Collagen is one of the basic structural proteins in the human body, accounting for about 30% of the total body protein mass. Collagen structure is based on a triple helix composed of three polypeptide chains (consisting of mainly glycine, proline, and hydroxyproline), which gives it exceptional mechanical strength and resistance to stretching. There are 40 collagen genes in vertebrates which code for 28 types of collagen, the most common ones being types I, II and III [7,8]. Collagen is constantly replaced, albeit at different rates, depending on the type of tissue or organ. For example, collagen replacement in the bones is a yearly (the longest) process, while in the liver it occurs every month.

Collagen fibers are located mainly in the skin, cartilage and soft tissues [2]. The dominant types of collagen found in the skin are type I (85–90%) and type III (up to 15%). Collagen performs many important functions in the body: ensuring the mechanical strength of tissues, participating in regenerative processes, and maintaining the integrity of the extracellular matrix (ECM). The exact structure of collagen depends on its role in a given tissue. In the skin, collagen is responsible for its firmness, flexibility, and ability to retain water.

Collagen's regenerative properties are particularly important in wound healing and reconstruction of damaged tissues [9,10].

The problem of collagen degradation is becoming increasingly important in the context of an ageing population. After 25 years of age, the natural synthesis of collagen slows down, its fibers thinen, and solubility decreases. After the age of 40, collagen production drops by an average of 1% each year. After the age of 80, collagen synthesis is reduced by about 75% [13,14]. At the same time, degradation processes intensify under the influence of UV radiation, oxidative stress and environmental factors. This results in visible signs of ageing, such as the appearance of wrinkles. In joints, a decrease in collagen levels leads to the weakening of cartilage and the development of degenerative diseases, mainly degenerative arthritis [4,12]. The degradation of collagen fibers leads to the formation of wrinkles, loss of elasticity and the appearance of sagging skin [11]. Collagen is used as a biomaterial in pharmacy, cosmetology, and many areas of medicine such as orthopedics, dermatology or aesthetic medicine. As a result, collagen is an important part of prevention and numerous therapies [1]. This work aims to analyze the mode of action of collagen, its applications in various fields of medicine, and the potential benefits resulting from supplementation based on clinical studies.

THE IMPORTANCE OF COLLAGEN - STRUCTURE AND CLASSIFICATION

28 different types of collagen are distinguished based its structure. Collagen is classified into fibrillar and nonfibrillar types. Fibrillar collagens are collagen types I, II, III, V, XI, XXIV, and XXVII. Nonfibrillar collagens include collagen types IV, VI, VII, VIII, IX, X, XII, XIII, XIV, XV, XVI, XVII, XVIII, XIX, XX, XXI, XXII, XXIII, XXV, XXVI, XXVIII, and XXIX. Depending on their structure, the different collagen types are present in various tissues or organs (Table 1).

Class	Type	Distribution
Fibril-forming (Fibrillar)	I	Bone, skin, tendon, ligaments, cornea
	II	Cartilage, vitreous humor in the eyes
	III	Skin, blood vessels
	V	Bone, dermis, co-distribution with type I
	XI	Cartilage, inverterbral discs, co-distribution with type II
	XXIV	Bone, cornea
	XXVII	Cartilage
Fibril-associated collagens with interrupted triple helices (FACIT)	VII	Bladder, dermis
	IX	Cartilage, cornea
	XII	Tendon, dermis
	XIV	Bone, dermis, cartilage
	XVI	Kidney, dermis
	XIX	Basement membrane
	XX	Cornea of chick
	XXI	Kidney, stomach
	XXII	Tissue junctions
	XXVI	Ovary, testis
Network-forming	IV	Basement membrane
	VI	Muscle, dermis, cornea, cartilage
	VIII	Brain, skin, kidney, heart
	X	Cartilage
	XXVIII	Dermis, sciatic nerve
Membrane-associated collagens with interrupted triple helices (MACIT)	XIII	Dermis, eyes, endothelial cells
	XVII	Hemi desmosomes in epithelia
	XXIII	Heart, retina
	XXV	Heart, testis, brain
Multiple triple-helix domains and interruptions (MULTIPLEXINs)	XV	Capillaries, testis, kidney, heart
	XVIII	Liver, basement membrane

Table 1. Types of collagen and their distribution in tissues and organs [reprint from 7].

Fibrillar collagens maintain the structural integrity of tissues and organs by providing mechanical strength and interacting with cellular receptors and other components of the extracellular matrix [20]. Collagen types I, II, and III are the most common collagens in the body. In the bones, collagen types I, V, XXIV, and XIV can be found. In articular cartilage, primarily collagen type II is found but also the types IX, X, XII, XII, and XIV. The collagen types forming the fibers of the extracellular skin matrix are mainly types I and III, but it has been proven that other types are present in human skin, such as types V, VI, VII, VIII, XII, XII, XIII, XIV, and XVI. Type III collagen is often co-present with type I, and is also present in the composition of reticular fibers [2,5,6,16]. Collagen is produced by specialized cells called fibroblasts. The synthesis of collagen in the body is a multi-step process involving the production of procollagen, which after hydroxylation and glycosylation is secreted via exocytosis outside the fibroblasts, where it undergoes numerous modifications and is transformed into mature collagen fibers [23]. Physiologically, collagen synthesis depends on genetic conditions, hormonal regulation (mainly cortisol and sex hormones), as well as environmental factors such as diet and physical activity. Vitamin C, which is a strong antioxidant that protects against UV rays, also has a stimulating effect on the formation of collagen.. Additionally, the type of physical activity affects collagen synthesis, due to the involvement of different units of the musculoskeletal system during different types of exercise [2].

SKIN AGEING

Skin ageing is an inevitable process characterized by loss of elasticity, reduction in epidermal thickness and level of hydration, and the appearance of wrinkles. This is due to reduced collagen synthesis in the body. Due to an ageing population, there is an increasing need for anti-ageing interventions in many countries [25]. Therefore, the use of nutraceuticals as dietary supplements has increased in recent years. As a result of skin ageing, a decrease in enzymes involved in the post-translational processing of collagen can be observed. This is due to a reduced number of fibroblasts [19]. There is a decrease in epidermis and dermis thickness as fibroblasts synthesize fewer new extracellular matrix components, and collagen degradation is accelerated through the action of the matrix metalloproteinase. The network made up of collagen fibers is fragmented and as a result, the skin becomes more wrinkled and flaky. In the elderly, the skin is more prone to dryness due to a decrease in the amount of hyaluronic acid and the skin's ability to retain moisture [15]. Two types of ageing can be distinguished: internal ageing and ageing related to environmental factors, such as air pollution, smoking, poor nutrition, and ultraviolet (UV) light. The main factors affecting the acceleration of ageing processes are oxidative stress, UV radiation, and the effects of an unhealthy lifestyle. Oxidative stress contributes to skin ageing by increasing the production of reactive oxygen forms and reducing cellular repair capacity.

Photoaging is a process of skin degeneration caused by excessive exposure to UV radiation, which is responsible for most damage and skin ageing. UV radiation can be divided into UVA, UVB, and UVC rays. It is estimated that about 80% of visible signs of skin ageing are the result of radiation. UVA and UVB rays penetrate through the layers of the skin (epidermis, dermis), while UVC rays are mostly absorbed by the ozone layer.

UVB radiation can cause mutations and initiate skin carcinogenesis by inducing photoproducts. UVA affects DNA damage indirectly by raising the level of free radicals, thus leading to oxidative damage. About 50% of UVA radiation reaches the dermis.

During photoaging, collagen degradation, production of reactive oxygen forms, and matrix metalloproteinase activity are increased. There is also increased fragmentation and degradation of skin collagen, resulting in an imbalance in the extracellular matrix and a decrease in the amount of collagen [9,31,34]. Bioactive peptides derived from collagen supplementation can reach the skin and thus effectively counteract the skin damage caused by photoaging. Structurally, the skin in which photoaging occurs appears to be thicker, there are deep wrinkles, as well as abnormal pigmentation spots [32]. As a result of careless exposure to the sun in one day, a person can lose up to 20% of collagen.

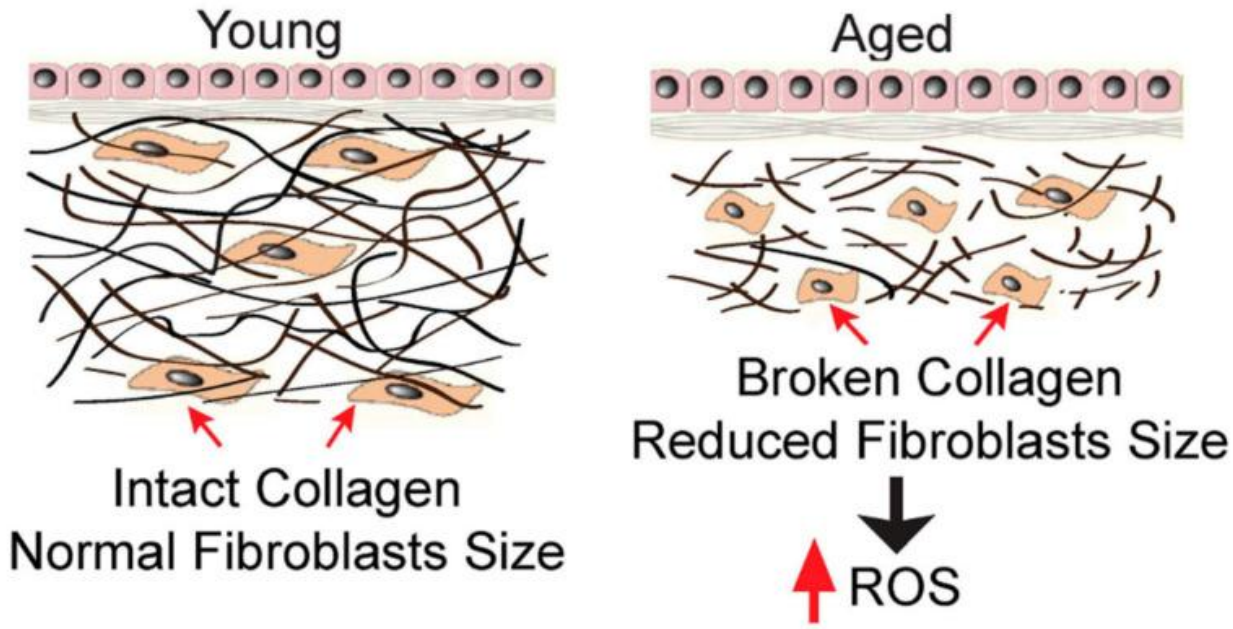

Figure 1. Comparison of the skin structure of a young (left) and old (right) individual. [reprint from 33]

SOURCES OF COLLAGEN AND FORMS OF ITS ADMINISTRATION

The topic of using collagen in prophylaxis is becoming more and more popular, which is why many products with collagen in their composition can be found on the market. Collagen can be obtained from fish scales, bones, and skins, as well as from beef skin, pork skin, calfskin, and beef tendons. The most commonly used source of collagen is beef, especially from the bones and skin of cows, but due to the danger associated with the transmission of diseases dangerous to humans (BSE, TSE, FMD, mad cow disease) and the possible risk of allergic reactions (about 3% of the total population is allergic), safer sources of collagen are being sought.

In medicine, collagen-containing medicinal preparations are administered orally, transcutaneously, and by injection. Injections of collagen preparations can be performed subcutaneously, intradermally, intramuscularly, intra-articularly, and peripherally.

The advantage of injectable products is that they can fill irregular spaces of various types of cavities. Collagen is also used in joint tissue engineering in the form of sponges, films, membranes or scaffolds. A scaffold is designed to create a special support structure for bone regeneration.

The types of collagen most commonly used in biomedical engineering are type I and type III. In aesthetic medicine, the preparations used are in the form of creams, gels, nutraceuticals containing collagen or collagen hydrolysates, and injectable products. Nutraceuticals have usually been used for the prevention of diseases related to connective tissue. With the desire to delay the ageing process, products that have a positive effect on the condition of skin, hair, and nails are becoming more and more common. Collagen can be administered in various forms: powders, tablets, capsules, beverages or gels. Due to its proven efficacy and high absorption, the most commonly used form of collagen is low molecular weight collagen peptides, which are rich in the amino acids hydroxyproline, glycine, and proline [2].

USE OF COLLAGEN IN ORTHOPAEDICS AND SPORTS MEDICINE

Collagen is increasingly used in the prevention and treatment of injuries. Being the main component of joint cartilage, ligaments and tendons, it plays a key role in cushioning, reducing friction during movement, and also participates in regeneration. By improving flexibility and endurance, it can reduce the risk of injury. Type II collagen fibers dominate in articular cartilage, which is why they are most often used in cartilage therapy. Type II collagen forms a scaffold and allows the retention of proteoglycans and water, which gives tit unique elastic properties. It can also be used to treat bone tissue, even though type I collagen dominates in bones. It is used mainly because of its greater flexibility. In medicine, the type of collagen is usually selected based on the type of tissue being repaired and matched to the type of natural collagen found in that tissue. The structure of collagen, in particular the triple helix, contributes to considerable mechanical stability, as well as strength and thermal stability [5,21,22]. Joint health is a key element in maintaining mobility and quality of life, especially in the face of ageing or intense physical activity. Collagen supplementation, especially hydrolyzed collagen, is gaining increasing recognition as a potential support for joint cartilage regeneration, improving joint mobility, and reducing pain. The results of scientific studies confirming its effectiveness and the possibility of using supplementation in the prevention and treatment of joint diseases will be discussed in the following part. A 2024 meta-analysis of collagen supplementation in people with osteoarthritis included information from 870 participants of 11 different randomized controlled clinical trials. Randomized clinical trials have shown that supplementation with a hydrolyzed form of collagen results in a significant improvement in mobility and a reduction in pain severity in people with osteoarthritis [18].

THE USE OF COLLAGEN IN DERMATOLOGY AND AESTHETIC MEDICINE

Collagen and its peptides, which are collagen derivatives, are now increasingly used in dermatology and aesthetic medicine. To improve skin health and prevent ageing, various nutrients and dietary supplements are used. In dermatology and aesthetic medicine, there is a large selection of products, mainly topical creams, fillers administered in the form of injections or products used orally, so-called nutraceuticals, which are intended to stimulate the skin to produce collagen. Creams in which composition collagen can be found are designed to improve the hydration and firmness of the skin. However, the effectiveness of products administered orally may be severely limited due to their limited ability to penetrate deeper layers of the skin [26,27]. Collagen in the form of injections belongs to the group of oldest tissue fillers. The disadvantage of these treatments is their high price and the possibility of side effects such as infection, swelling, discoloration, itching, and bruising.

Collagen supplements, especially those containing hydrolysates, have become the subject of research due to their potential to improve skin integrity and counteract skin ageing. Studies prove that they are safe and cost-effective compared to other collagen-based strategies. The advantage of collagen supplements is that oral intake can contribute to regularity in supplementation and thus improve their effectiveness. In the context of natural ageing processes, collagen peptides show promising properties that can increase skin hydration as well as improve its elasticity and density without causing significant side effects. To obtain collagen hydrolysates, which are peptides of different lengths, collagen must be subjected to enzymatic modulation. In subsequent stages, peptides can be broken down into peptidase-resistant small dipeptides and tripeptides. It has been shown that they can be found as early as 1–2 hours after oral intake [29, 30]. Another study showed that tripeptides: Ala-Hyp-Gly and Ser-Hyp-Gly can also be detected in the blood 1 hour after taking oral hydrolyzed collagen [19].

Several *in vivo* studies have revealed the underlying mechanisms of oral collagen supplementation, in particular decreased expression and activation of metalloproteinase after exposure to UVB radiation. As a result, greater synthesis of collagen and elastic fibers will be obtained and collagen fragmentation will be reduced. In addition, reduced expression of matrix metalloproteinase and higher levels of tissue inhibitor MMP-1 are thought to be involved in the anti-ageing effects of collagen peptides. Also, bioactive collagen peptides, consisting mainly of hydroxyproline, stimulate chemotaxis and proliferation of skin fibroblasts, thus enabling the production of skin components: hyaluronic acids, elastin fibers, and collagen [15]. In this work, selected scientific studies on the effectiveness of collagen supplementation will be analyzed. Their goal is to assess the impact of this protein on improving skin quality. Randomized trials will allow for a deeper understanding of the mechanisms of action of collagen, confirming its benefits.

In 2021, the latest publications were reviewed and analyzed. Only randomized, double-blind, controlled studies that evaluated the efficacy of hydrolyzed collagen supplementation were eligible for the analysis. The studies involved people who reported at least one of the problems such as skin wrinkles, lack of hydration, loss of elasticity and firmness. 19 studies with a total of 1,125 people aged 20 to 70 years (95% women) were selected. A group analysis of studies showed favorable results of hydrolyzed collagen supplementation compared to placebo in terms of skin hydration, elasticity, and wrinkles.

Based on these results, it was found that taking hydrolyzed collagen for 90 days is effective in reducing skin ageing as it reduces wrinkles and improves skin elasticity and hydration [28]. To understand the multi-faceted role of collagen supplementation in improving skin quality, it is necessary to analyze the results of the latest scientific studies. These studies provide valuable information about the mechanisms of action, potential benefits, and limitations of collagen supplementation. Analysis of data from various research papers allows for conclusions to be drawn and areas requiring further research to be identified.

A 2023 study showed that oral supplementation with low-molecular collagen peptides improves skin integrity and counteracts ageing. The study participants were healthy adults with dry skin and wrinkles around the eyes who were randomly assigned to a test or control group using a placebo to assess the effect of collagen on the skin. During the study, selected parameters such as skin wrinkles, elasticity, hydration level, and bleaching effect were analyzed, measured at the start and after 4, 8 and 12 weeks. Compared to the placebo group, levels of all aspects of the study were significantly improved in the test group [15]. A 2014 double-blind and placebo-controlled study evaluated the formation of wrinkles around the eyes and the efficacy of procollagen I, a specific bioactive collagen peptide. This study enrolled 114 women aged 45–65 years and measured skin wrinkles in all subjects before the start of treatment, after 4 and 8 weeks, as well as 4 weeks after the last treatment (4-week regression phase). The analysis showed that oral intake of bioactive collagen peptides reduced skin wrinkles and had a positive effect on skin matrix synthesis [17].

In another 2023 study, a 16-week, randomized, controlled clinical trial was conducted in which 87 people (women aged 40–65 years) participated. Participants received liquid dietary supplements containing a daily dose of 5 g of collagen with 80 mg of vitamin C or a combination of them with 30 mg of hyaluronic acid. Supplementation of both products resulted in improved skin density, reduced skin roughness and reduced severity of wrinkles. However, no noticeable effects on skin elasticity or hydration were observed after supplementation with any of the tested products [3]. However, not all collagen sources have the same effectiveness. Even at the same dose and time of administration, some specific collagen sources are more effective than others. In conclusion, long-term use of collagen has more beneficial effects on skin hydration and elasticity than short-term use [19]. To investigate the clinical benefits of oral collagen supplements, it is necessary to organize a randomized control trial with a large group of participants to determine the most beneficial duration and the safest and most absorbable source of collagen for long-term benefits.

CONCLUSIONS

Collagen plays a key role in maintaining the health of the skin and joints, and its supplementation can significantly support the body's regenerative processes. The results of previous studies confirm the effectiveness of hydrolyzed collagen in improving skin elasticity and reducing joint pain. Collagen is responsible for the stability, elasticity and regeneration of many tissues, such as skin, cartilage, ligaments and tendons. In recent years, there has been a dynamic increase in the number of studies on collagen supplementation, which indicates growing interest in its applications in medicine and cosmetology. Collagen's mechanisms of action include inhibiting the activity of enzymes such as metalloproteinases responsible for the degradation of collagen fibers.

As a result, collagen supplementation can not only support the skin's natural repair processes but also delay the ageing process by protecting the extracellular matrix from degeneration. The recent dynamic development of scientific research on the effectiveness of collagen supplementation has provided promising evidence for its potential to improve quality of life. A growing body of evidence indicates that regular use of collagen not only supports skin health but can also contribute to the regeneration of joint cartilage after injury and reduce pain symptoms, especially in people suffering from degenerative diseases. Further research is necessary to understand the full potential of this protein in aesthetic, sports, and orthopedic medicine. The benefits of collagen supplementation and other substances that have the potential to more efficiently absorb collagen in the body are being investigated. Of the currently used supplement forms of collagen, hydrolyzed collagen is the most popular and most promising anti-ageing nutraceutical for the skin. As observations and more scientific studies continue, we will learn more about the long-term effects of collagen supplementation. Therefore, the development of the technology and further research into the mechanisms of action of collagen offer hope to further understand its potential and discover further benefits.

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