COLLAGEN 101

The Science of Collagen

Presented by: COLLAGEN STEWARDSHIP ALLIANCE

WHAT IS COLLAGEN?

A group of abundant, fibrous proteins found in vertebrates, and is the primary building block of skin, connective tissue, cartilage, tendons, and bones. Supplemental collagen, comes in a variety of forms and is found as an ingredient for both cosmetic and dietary applications.

Today we will cover:

- What collagen is and its role in the body.
- Why there are so many supplemental forms and what they are.
- How collagen works to improve skin, reduce inflammation, and ease joint pain.

WHAT IS COLLAGEN?

COLLAGEN STEWARDSHIP ALLIANCE

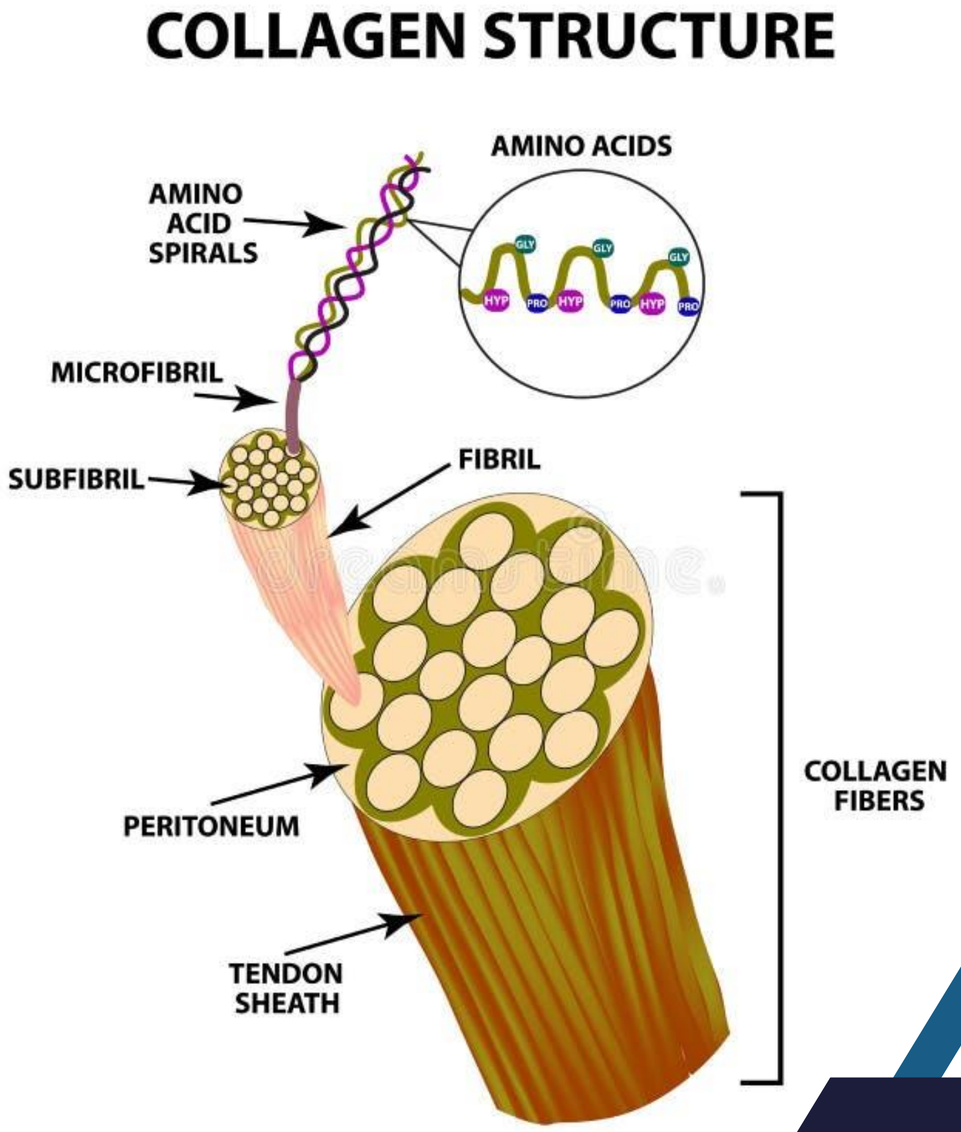
A group of fibrous proteins found in vertebrates.

Primary building block of:

- Skin
- Connective tissue
- Cartilage
- Tendons
- Bones

Importance: Provides strength, elasticity, and structural support.

Supplements: Available in various forms for cosmetic and dietary use.



COLLAGEN SOURCES:

Bovine Collagen

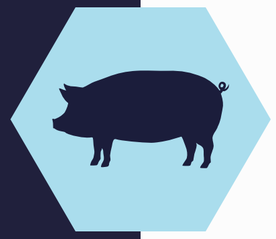
Source: Extracted from the hides, bones, and cartilage of cows [1]

Features:

- Composed of type I and type III collagen, known for supporting skin, bone, and joint health.
- Widely used in dietary supplements, cosmetics, and medical products.

Applications:

- Promotes skin elasticity and hydration.
- Supports joint health and cartilage integrity.
- Often used in protein supplements for muscle repair and recovery.



Porcine Collagen

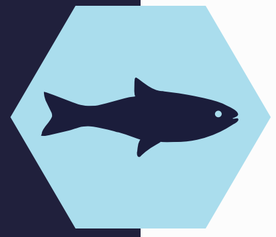
Source: Extracted primarily from pig skin [1]

Features:

- Rich in type I and type III collagen, with similar structural and functional properties to bovine collagen.

Applications:

- Enhances skin health and hydration.
- Supports joint health and cartilage integrity.



Marine Collagen

Source: Extracted from fish skin and scales [1, 2]

Features:

- Known for its high bioavailability due to smaller peptide sizes.
- Primarily composed of type I collagen, beneficial for skin, hair, and nails.
- Thought of as a more sustainable and environmentally friendly option.

Applications:

- Formulations for skincare.
- Nutritional supplements designed to support healthy skin and hair.

COLLAGEN SOURCES: (CONTINUED)

Chicken Collagen

Source: Extracted from chicken cartilage [1, 3]

Features:
- Rich in type II collagen, which specifically supports joint and cartilage health.
- Often included in supplements targeting arthritis and joint pain relief.

Applications:
- Joint support and cartilage repair.
- Used to alleviate symptoms of osteoarthritis.

Eggshell Membrane Collagen

Source: From the thin membrane lining eggshells [4]

Features:
- Contains a mix of collagen types along with other beneficial compounds like glycosaminoglycans.
- Recognized for its ability to support both skin and joint health.

Applications:
- Improves joint flexibility and reduces pain.
- Promotes smoother, healthier skin.
- Possible concern due to egg allergy.

Emerging Collagen Sources [2]

While less common, research is exploring other collagen sources:
- Jellyfish, starfish and Marine Sponges: Valued for their bioactive potential and eco-friendly harvesting.

VEGAN COLLAGEN CONUNDRUM

We support the position as expressed by New Hope Informa:

We have set a precedent with companies making collagen, whey, or other animal-identical molecules, that does not allow the use of a vegan claim in reference to those products. We do this to protect the integrity of the term for vegans who avoid animal products in the interest of their health. While it may be fair to call products vegan in terms of the processing, it is misleading to call it vegan in terms of the actual physical properties of the product itself because, by definition, collagen is an animal protein. Such products should be revised to “animal-free collagen”.

TYPES & FORMS OF COLLAGEN

The human body naturally produces various types of collagen, each with distinct roles in different tissues. Type I collagen is predominantly found in skin and bones, providing structural support. Type II collagen is a key component of cartilage in joints. Type III collagen is naturally present in blood vessels and plays a role in the body's healing processes. These different collagen types work together to maintain the integrity and function of various bodily structures.

Available forms on the market include collagen peptides, hydrolyzed collagen, gelatin, and undenatured collagen, each offering distinct applications for health and wellness.

TYPES OF COLLAGEN:

TYPE I COLLAGEN:

Type I collagen is a fibrillar type collagen, is the most abundant collagen and is expressed in almost all connective tissues and is the predominant component of the interstitial membrane.

It forms large, eosinophilic fibers known as collagen fibers. It is present in scar tissue, the end product when tissue heals by repair, as well as tendons, ligaments, the endomysium of myofibrils, the organic part of bone, the dermis, the dentin, and organ capsules. Often paired with Type III.

TYPE IV COLLAGEN:

Found in the basal lamina, the layer of extracellular matrix supporting the epithelium.

TYPE II COLLAGEN:

As a protein, fibrillar collagen is composed of three identical polypeptide chains that represent the main components of the cartilage and other types of connective tissues in animals and humans, usually provided from chicken, sometimes bovine sources. As an oral ingredient, it appears as native type II collagen.

TYPE V COLLAGEN:

Found within the dermal/epidermal junction as well as in most interstitial (the space between structures) and in placental tissues. Frequently found in association with Type-I collagen.

TYPE III COLLAGEN:

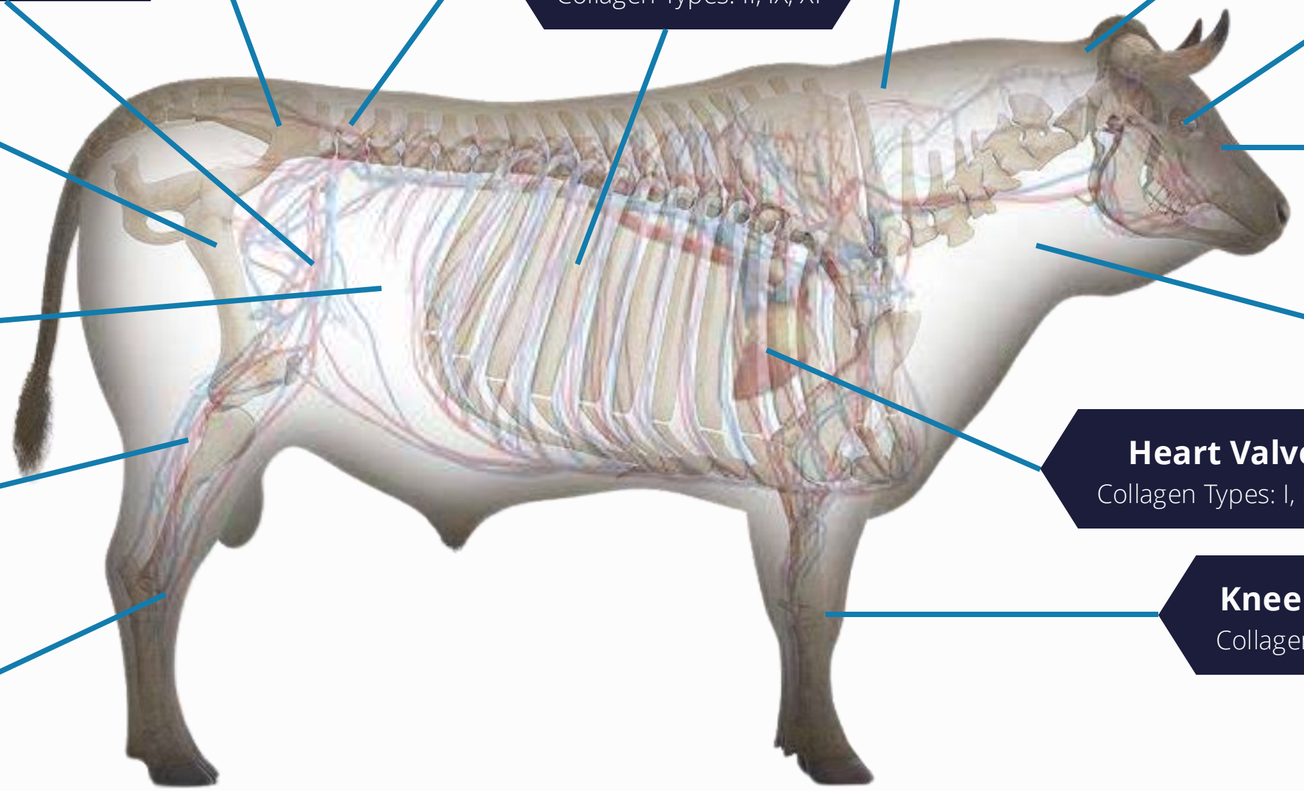
Type III collagen, one of the major fibrillar collagens, is found as a major structural component in hollow organs such as large blood vessels, uterus and bowel.

Other functions of type III collagen include interaction with platelets in the blood clotting cascade and it is also an important signaling molecule in wound healing. It constitutes between 5-20% of the entire collagen content of the human body. Often paired with Type I. [9]

TYPE X COLLAGEN:

Rare type of collagen that is involved in the growth, mineralization and remodeling of articular cartilage.

TYPES OF COLLAGEN:[10]



Interverbal Disc
Collagen Types: I, II, III

Fecet Joint Cartilage
Collagen Types: II, IX, XI

Skeletal Muscle
Collagen Types: I, III, VI

Articular Cartilage
Collagen Types: I, II, III

Blood Vessels
Collagen Types: I, III, IV

Costal Cartilage
Collagen Types: II, IX, XI

Cornea
Collagen Types: I, V, VI

Bone
Collagen Types: I, III, V

TMJ Disc
Collagen Types: I, III, V

Adipose Tissue
Collagen Types: I, V, VI

Skin
Collagen Types: I, III, VI

Tendons & Ligaments
Collagen Types: I, III, V

Heart Valve
Collagen Types: I, III, V

Knee Meniscus
Collagen Types: I, II, III

Articular Cartilage
Collagen Types: II, IX, XI

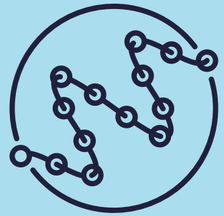
COLLAGEN FORMS:

Gelatin	Produced by controlled thermal hydrolysis of animal bones, cartilage, and skin in water. Usually sourced from cows or pigs. High protein ingredient that can enhance the flavor, texture, and nutritional value of certain foods, such as mousses, stews, and gelled desserts. [11]	Typical dosage range: No current consensus on dosage [12]
Hydrolyzed Collagen/ Collagen Peptides	Hydrolyzed collagen (HC) is a group of collagen peptides with low molecular weight (0.3 and 8 kDa) and average molecular weight of 2-3kDa, that can be obtained by enzymatic action in acid or alkaline media at a specific incubation temperature. HC can be extracted from different sources such as bovine or porcine. Intake of collagen hydrolysates has been reported to exert various beneficial effects, mainly at skin and joint levels. [13, 14]	Typical dosage range: 2.5 - 15 g/day [12]
Undenatured/Native Type II Collagen	Not broken down or hydrolyzed (into peptides), undenatured in its original form, with a triple helix structure.	Typical dosage range: 2-40 mg per day [12, 15]

COLLAGEN FORMS: (CONTINUED)

Collagen Matrix	Commonly associated to scaffolds, dressings and grafts, the extracellular matrix represents a complex alloy of variable members of diverse protein families defining structural integrity and various physiological functions. The most abundant family is the collagens with more than 20 different collagen types identified so far.[16]	Typical dosage range: • Chondroitan sulfate - 800-1200 mg/day[17] • Hyaluronic acid - 100-200 mg/day[18]
Collagen Boosters	Collagen boosters are often vegan products, that contain a number of amino acids derived from other sources, as well as vitamins and other nutrients intended to support or boost the body's ability to make (and retain) collagen. Common ingredients used in this way include hyaluronic acid, vitamin C and various antioxidants.	Typical Glycine dosage range - 10 g/day[19] Typical vitamin C dosage range:[20] • 15–75 mg for children • 75 mg for adult women • 90 mg for adult men • 85–120 mg for pregnant or breastfeeding women

HOW DOES COLLAGEN WORK?



Stimulates Collagen Synthesis

Supplementation of collagen products may increase the internal production of collagen. [5]

Supports Essential Amino Acids Status

While collagen is not a complete source of protein, supplementing collagen offers high levels of the non-essential amino acids, glycine and proline. [6]

Extra Cellular Matrix (ETC) Support

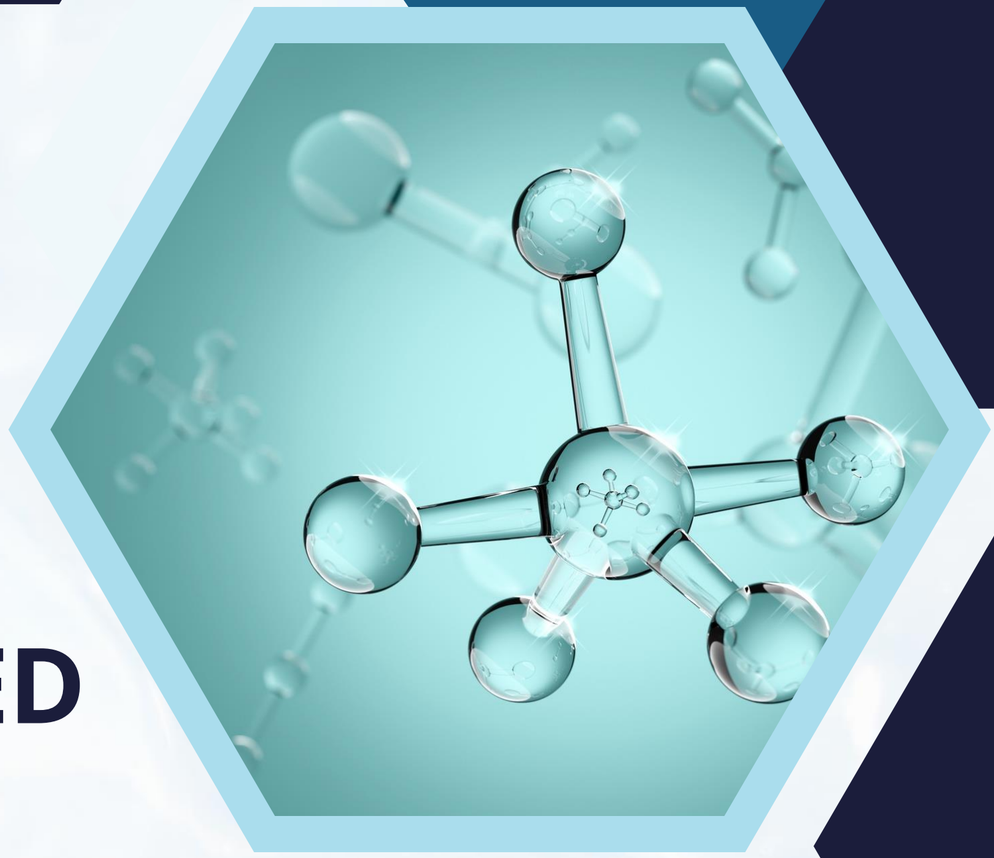
Collagen plays a role in maintaining ETC remodeling, which is critical for elasticity in muscles and connective tissue. [6,7]

Oral Tolerance Mechanism

Native (undenatured) collagen, particularly type II may exhibit more immune-related effects, influencing inflammation in conditions such as such as autoimmune rheumatoid arthritis and osteoarthritis. [8]

NATIVE/UNDENATURED VERSUS HYDROLYZED/DENATURED

The two primary forms available on the market are native/undenatured and hydrolyzed/denatured collagen. These differ significantly in structure, production processes, mechanisms of action, as well as clinical applications.



STRUCTURE AND PRODUCTION

Native/Undenatured Collagen:
Native collagen retains the original triple-helix structure and large molecular size, which is approximately 300 kDa. This form utilizes low temperatures and without denaturation agents to maintain its natural configuration. [21]

The Two Types of Native Collagen:

1. **Soluble Native Collagen:** Maintains the triple helix but has fewer crosslinks, which increases solubility. This is done by destabilizing the covalent bonds contained within its structure. [8]
2. **Insoluble Undenatured Collagen:** Retains its triple helix and natural crosslinks, making it water-insoluble. [8]

Hydrolyzed/Denatured Collagen:
Hydrolyzed collagen is produced by enzymatically or chemically breaking down native collagen. This process reduces molecular size to 2–9 kDa by breaking the original triple-helix structure, allowing for enhanced bioavailability. [21, 22]

MECHANISMS OF ACTION

Native/Undenatured Collagen

Native collagen, particularly undenatured type II collagen, is thought to work through oral tolerance, an immune-mediated process involving gut-associated lymphoid tissues. Preserved antigenic epitopes within the triple-helix structure may help modulate the immune response, potentially reducing inflammation in conditions like osteoarthritis. [8, 21]

Hydrolyzed/Denatured Collagen

Hydrolyzed collagen, due to its smaller peptide size, has different mechanisms:

1. **Enhanced Absorption:** These smaller peptides are absorbed in the small intestine, increasing bioavailability.
2. **Cartilage Support:** After absorption, collagen peptides may stimulate chondrocytes to synthesize cartilage components, as well as modulate osteoblast and osteoclast activity [8, 22]

HOW COLLAGEN IMPROVES SKIN

Hydrolyzed collagen:

- Absorbed as peptides in the small intestine.
- Stimulates fibroblasts to produce dermal collagen.

Benefits:

- Increased hydration and elasticity.
- Reduced wrinkles and smoother texture.
- Enhanced collagen density in skin.

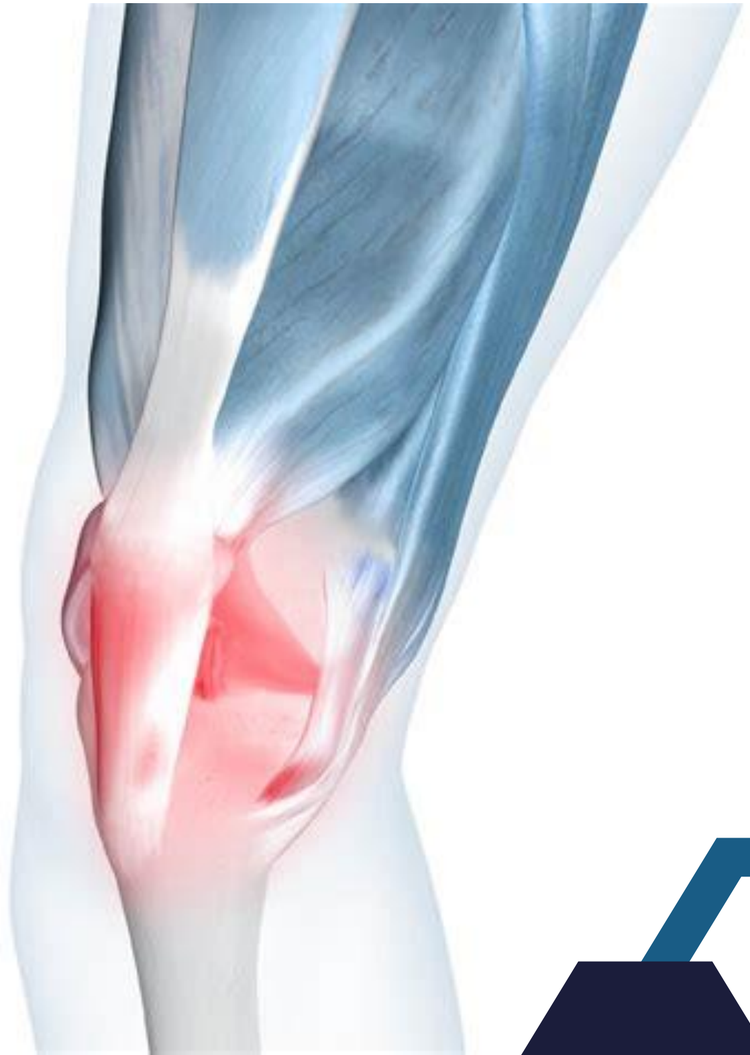
HOW COLLAGEN REDUCES INFLAMMATION & PAIN

Native Collagen (Type II):

Mechanism: Oral tolerance in gut that modulates immune response.
Effect: Reduces inflammation in joints (e.g., osteoarthritis).

Hydrolyzed Collagen:

Mechanism: Stimulates chondrocytes for cartilage repair.
Effect: Supports joint recovery, reduces pain.



ADDITIONAL BENEFITS

Muscle Recovery:

- Faster recovery post-exercise.

Bone Health:

- Increases bone mineral density.
- Enhances calcium absorption.

Versatility:

- Benefits tied to form and type used.

Randomized Controlled Trial > Nutr J. 2023 Mar 15;22(1):17.
doi: 10.1186/s12937-023-00837-w.

Randomized, double-blind, four-arm pilot study on the effects of chicken essence and type II collagen hydrolysate on joint, bone, and muscle functions

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Affiliations + expand

PMID: 36918892 PMCID: PMC10015953 DOI: 10.1186/s12937-023-00837-w

Abstract

Background: Knee osteoarthritis (OA) is a leading cause of disability among older adults. Medical and surgical treatments are costly and associated with side effects. A natural nutraceutical, collagen hydrolysate, has received considerable attention due to its relieving effects on OA-associated symptoms. This study investigated the effects of hydrolyzed collagen type II (HC-II) and essence of chicken (BRAND'S Essence of Chicken) with added HC-II (EC-HC-II) on joint, muscle, and bone functions among older adults with OA.

Methods: Patients (n = 160) with grade 1-3 knee OA according to the Kellgren-Lawrence classification system, joint pain for ≥ 3 months, and a Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score of > 6 were randomly assigned with equal probability to consume EC-HC-II, HC-II, glucosamine HCl, or a placebo for 24 weeks in combination with resistance training. Outcome measurements were WOMAC score, visual analogue scale (VAS) pain score, grip strength, fat-free mass (FFM), and bone mass.

Results: All groups exhibited similar levels of improvement in WOMAC index scores after 24 weeks. HC-II significantly reduced VAS pain score by 0.9 ± 1.89 (p = 0.034) after 14 days. A repeated-measures analysis of variance showed that HC-II reduced pain levels more than the placebo did (mean ± standard error: - 1.3 ± 0.45, p = 0.021) after 14 days; the EC-HC-II group also had significantly higher FFM than the glucosamine HCl (p = 0.02) and placebo (p = 0.017) groups and significantly higher grip strength than the glucosamine HCl group (p = 0.002) at 24 weeks.

Conclusion: HC-II reduces pain, and EC-HC-II may improve FFM and muscle strength. This suggests that EC-HC-II may be a novel holistic solution for mobility by improving joint, muscle, and bone health among older adults. Large-scale studies should be conducted to validate these findings.

Randomized Controlled Trial > BMC Musculoskelet Disord. 2025 Jan 4;26(1):17.
doi: 10.1186/s12891-024-08244-w.

The effect of supplementation with type I and type III collagen peptide and type II hydrolyzed collagen on pain, quality of life and physical function in patients with meniscopathy: a randomized, double-blind, placebo-controlled study

Ahmet Serhat Genç [1], Ali Kerim Yılmaz [2], Berna Anıl [3], Esra Korkmaz Salkılıç [3], Enes Akdemir [3], Berna Güzel [4], Ahmet Mor [5], Hacı Ahmet Yarar [6], Nizamettin Güzel [7], Lokman Kehribar [7]

Affiliations + expand

PMID: 39755603 PMCID: PMC11699701 DOI: 10.1186/s12891-024-08244-w

Abstract

Background: Menisci, one of the most important anatomical structures of the knee joint, plays a role in load transfer, stability, shock absorption, prevention of articular cartilage degeneration, and proprioception. Type I collagen, the main component of the meniscus, and type II collagen fibers play an important role in the stability of the knee joint. This study aimed to evaluate the effects of Naturagen® 4 Joint product containing type I, II, and III collagen on pain, quality of life, and physical functions in patients with meniscopathy.

Methods: This randomized, double-blind, placebo-controlled clinical study included 32 patients (collagen = 17 and placebo = 15) with meniscopathy. Patients completed the Visual Analog Scale (VAS), Western Ontario and McMaster Universities Osteoarthrtis Index (WOMAC), Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS), Oxford Knee Score (OKS), Tampa Scale for Kinesiophobia (TSK), Short Form Health Survey (SF-12), Lower Extremity Functional Scale (LEFS), Foot Function Index (FFI), proprioceptive sensation, Timed Up and Go (TUG), 6-Minute Walking Test (6MWT), The Five Repetition Sit to Stand Test (5STS), Stair Climbing Test (SCT), Berg Balance Scale (BBS) and back and leg strength tests and scales were applied. All tests were repeated before and after eight weeks of collagen supplementation.

Results: The study showed that eight weeks of supplementation with various collagen types had statistically significant effects on pain, quality of life, kinesiophobia, and foot function scale scores in patients with meniscopathy ($p < 0.05$). Similarly, eight weeks of supplementation showed a statistically significant difference in leg strength ($p = 0.057$), but no significant difference was found in back strength, proprioception, balance, and various functional test results ($p > 0.05$).

Conclusions: The results of the study showed that the eight-week collagen-based supplement had a positive effect on pain and quality of life levels and some functional test results in patients with meniscopathy. Longer-term studies and diversification of subject groups will help to understand better the effects of the product on meniscal tears and symptoms.

Randomized Controlled Trial > J Cosmet Dermatol. 2024 Feb;23(2):554-562.
doi: 10.1111/jocd.16026. Epub 2023 Oct 11.

Low-molecular-weight collagen peptides supplement promotes a healthy skin: A randomized, double-blinded, placebo-controlled study

Seol Hwa Seong [1 2], Young In Lee [1 2], Joohee Lee [1], Sooyeon Choi [1], In Ah Kim [3], Jangmi Suk [3], Inhee Jung [3], Chaemin Baeg [3], Jinhak Kim [4], Dongchan Oh [4], Ju Hee Lee [1 2]

Affiliations + expand

PMID: 37822045 DOI: 10.1111/jocd.16026

Abstract

Background: Oral collagen peptides supplementation was reported to improve skin integrity and counteract skin aging.

Aims: A randomized, double-blinded, placebo-controlled study was conducted to clinically evaluate the impact of low-molecular-weight collagen peptides on the human skin.

Patients/methods: Healthy adult participants (n = 100) were randomly assigned to receive a test product containing low-molecular-weight collagen peptides or a placebo. Parameters of skin wrinkles, elasticity, hydration, and whitening (melanin and erythema indexes) were measured at baseline and after 4, 8, and 12 weeks.

Results: Compared with the placebo group, the average skin roughness, maximum of all peak-to-valley values, maximum peak height of the wrinkle, and average maximum height of the wrinkle were significantly improved in the test group. Parameters of skin elasticity, including overall elasticity, net elasticity, and biological elasticity, were also significantly improved in the test group at Week 12 as compared with the placebo group. Moreover, skin hydration and whitening parameters changed more significantly in the test group than in the placebo group. None of the participants experienced adverse events related to the test product.

Conclusions: Taken together, these findings suggest that low-molecular-weight collagen peptides supplementation can safely ehance human skin wrinkling, hydration, elasticity, and whitening properties.

Keywords: clinical study; collagen peptide; photoaging; wrinkles.

MISPERCEPTIONS/MISUNDERSTANDINGS:

“All collagen supplements are the same.”	This is a prevalent misconception. In reality, collagen supplements differ significantly in several ways: type (e.g., Type I, II, III), source, form (powder, capsule, liquid), processing methods, and molecular weight (hydrolyzed vs. native). These differences can significantly impact the effectiveness. [5, 23]
“Collagen source doesn’t matter.”	While more research is necessary, evidence indicates that different types and sources of collagen may be more, or less effective for specific health concerns, such as skin health, or osteoarthritis pain. Furthermore, factors such as stability, bioavailability, and individual dietary restrictions, whether due to allergies or religious beliefs, can influence the choice of collagen source. [23, 26]
“Since our bodies make collagen, supplementation is not necessary.”	Although our bodies do produce collagen, this process tends to decline with age, starting in the late 20s to early 30s. Collagen supplementation can be beneficial in this context, helping support skin elasticity, hydration, and wrinkle reduction while also promoting joint health and function. [23, 27]
“Dietary protein vs. collagen supplements: Do we need supplementation in the context of sufficient protein.”	It’s true that our diet provides amino acids—such as glycine, proline, and hydroxyproline—that are essential for collagen production. However, when collagen is consumed as a supplement, it delivers unique bioactive peptide sequences that offer benefits not found in single amino acids or through simply increasing overall protein intake. [5]

WHO SHOULD TAKE COLLAGEN?

Everyone may benefit from collagen supplementation. Many individuals do so to make up for lower intake of collagen through dietary sources. Others may want to increase their collagen intake through supplementation to support an area of concern. Collagen supplementation has been shown to be beneficial for:

Skin Health:

Significant benefits for skin health:

- Improved skin hydration and elasticity
- Reduced wrinkles and improved skin texture
- Enhanced dermal collagen density [5]

Joint Health:

Potential benefits for joint health:

- Improved recovery from exercise-induced joint stress [7]
- Potential reduction in osteoarthritis symptoms
- Supports joint comfort and mobility [8]

Muscle Recovery and Performance:

Supplementation may support:

- Faster recovery
- Improved markers of muscular recovery [5]

Bone Health:

Research suggests:

- Increased bone mineral density
- Enhanced calcium absorption
- Potential support for osteoporosis [25]

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