REVIEW ARTICLE

CONTENTS

The role of collagen types I and II in the regeneration of temporomandibular joint and bone tissues - from molecular mechanisms to modern treatment protocols: Literature review

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ABSTRACT

Aim: The aim of this study is to analyze current data on the molecular and cellular mechanisms underlying the development of degenerative-dystrophic diseases of the temporomandibular joint (TMJ). The article explores the potential of collagen therapy as a pathogenetically substantiated approach to the comprehensive treatment of this disease.

Materials and Methods: A systematic review of the scientific literature over the past 20 years was conducted, indexed in PubMed/MEDLINE, Scopus, Web of Science, the Cochrane Library, RCSB Protein Data Bank until March 2026.

A comprehensive literature search identified 14,865 publications. Following a sequential analysis of titles, abstracts, and full texts based on predefined inclusion criteria (original experimental and clinical studies, systematic reviews and meta-analyses that revealed the molecular and cellular mechanisms of TMJ osteoarthritis, the therapeutic impact of types I and II collagen on joint and bone regeneration) and exclusion criteria (irrelevant papers, duplicates, TMJ rheumatoid arthritis, septic arthritis, systemic vasculitis). Ultimately, 37 primary sources were selected for the final review.

Conclusions: The authors summarized current data on the pathogenetic mechanisms of TMJ osteoarthritis, analyzed data on the use of collagen in the treatment of TMJ. The biological role of collagen types I and II as key structural components of fibrocartilage and subchondral bone is examined.

Special attention is given to the feasibility of using injectable tropocolagen to stimulate reparative processes in the TMJ.

KEYWORDS: temporomandibular joint, bone, osteoarthritis, treatment, cartilage regeneration, collagen type I, collagen type II, tropocollagen.

Wiad Lek. 2026;79(7):1654-1660. doi: 10.36740/WLek/225981 DOI

INTRODUCTION

The temporomandibular joint (TMJ) is a synovial joint that ensures jaw movement and function. Its complex anatomical structure and unique biomechanics, combined with the multifactorial nature of degenerative diseases, pose significant challenges for clinicians [1,2]. Osteoarthritis (OA) of the TMJ affects all joint structures, including articular cartilage, synovial membrane, subchondral bone, capsule, ligaments, periarticular muscles, sensory nerves, and innervating tissues [3,4].

OA develops primarily due to disruption of the metabolic homeostasis of cartilage and bone tissue. Deficient collagen and glycosaminoglycan synthesis leads to matrix dehydration, loss of cartilage elasticity, and the appearance of microcracks, erosions, and defibrosis [4,5].

Since collagen accounts for up to 70% of the dry mass of articular cartilage, it acts as a structural framework that provides three-dimensional strength and holds aggregates together. With age, collagen synthesis decreases, and the ratio of collagen types in tissues changes. When advanced glycation end products accumulate in the body, collagen fibers become rigid and lose their ability to stretch and cushion. This worsens the condition of the cartilage and subchondral bone. A decrease in the supply of nutrients and minerals to chondrocytes leads to their functional depletion and apoptosis, making the pathological process irreversible without external therapeutic support [6, 7]. It should be noted that, unlike the hyaline cartilage of large joints, the surfaces of the TMJ are covered with fibrous cartilage which contains both type I and type II collagen [8]. This underscores a critical demand not only for type II collagen but also for the structural reinforcement of the type I collagen scaffold.

AIM

The purpose of this study is to analyze current data on the molecular and cellular mechanisms underlying the

development of degenerative-dystrophic diseases of the TMJ. The article explores the potential of collagen therapy as a pathogenetically substantiated approach to the comprehensive treatment of this disease.

MATERIALS AND METHODS

A systematic review of the scientific literature over the past 20 years was conducted, indexed in PubMed/MEDLINE, Scopus, Web of Science, the Cochrane Library, and the RCSB Protein Data Bank until November 2025. Google Scholar and other sources were also used. The search utilized MeSH terms, keywords ("temporomandibular joint," "TMJ," "osteoarthritis," "treatment," "collagen type I," "collagen type II," "collagen supplement," "collagen therapy," "tropocollagen"), and the logical operators AND and OR.

Initially, 14,865 publications were identified. The inclusion criteria were original experimental and clinical studies, systematic reviews and meta-analyses that revealed the molecular and cellular mechanisms of TMJ osteoarthritis, as well as the effect of collagen types I and II on joint regeneration. Studies with poor methodology, irrelevant studies (rheumatoid arthritis, septic arthritis, systemic vasculitis), and unreviewed publications were excluded.

The papers were excluded by sequential analysis of titles, abstracts, and then full texts based on established selection criteria. After full text analysis, 37 primary sources that fully met the inclusion criteria were included in the final analysis.

The authors summarized current data on the pathogenetic mechanisms of TMJ OA and the potential therapeutic effects of collagen therapy. The results of in vitro and clinical trials of collagen preparations of various origins: bovine, porcine, marine and recombinant were studied. Particular attention was given to studies that shed light on the pathogenesis of inflammatory and degenerative diseases of the TMJ and the characteristics of its fibrocartilage.

ETHICS

All sources used in this literature review are publicly available.

AI STATEMENT

The following artificial intelligence tools were used in this work: [Gemini 3 Flash]. They were used for [linguistic editing, translation refinement, reference editing]. All sections using artificial intelligence were reviewed and edited personally by the author(s). The scientific statements, conclusions, and results are the author(s)'s own intellectual contribution.

REVIEW AND DISCUSSION

COLLAGEN TYPE I

More than 90% of collagen in the human body is type I collagen due to its widespread distribution in almost all connective tissues. The molecular formula of type I collagen is $[\alpha 1(I)]_2\alpha 2(I)$ ($\alpha 1$, $\alpha 2$ are proteins encoded by the COL1A1 and COL1A2 genes (Fig.1).

Type I collagen is the main component of calcified tissue in teeth and bones; it is present in skin, tendons, blood vessels, lungs, and the heart. Type I collagen plays a critical role in maintaining the integrity of subchondral bone, as it constitutes approximately 90% of its organic matrix and forms a highly ordered fibrillar network, which provides bone with the ability to withstand tensile loads and serves as the basis for hydroxyapatite mineralization. Impaired type I collagen synthesis leads to a decrease in the mechanical stability of the condylar process of the mandible, which accelerates the destruction of the cartilage above it. Modern protocols consider the use of bioactive collagen peptides type I as a means of stimulating osteoblasts and restoring subchondral bone density, which can slow the progression of osteoarthritis [6].

OA develops as an acute inflammatory process with a tendency to chronic development: chondrocytes enter the joint cavity, the osmotic pressure in the articular cartilage changes, and proteoglycans progressively migrate into the joint space, interfering with the natural stages of healing. Proinflammatory factors (synoviocyte tumor necrosis factor (TNF-β), interleukins: IL-6, IL-1α and IL-1β) are released, stimulating enzymes that degrade cartilage: disintegrin and metalloproteinase with thrombospondin motifs (ADAMTS) and matrix metalloproteinases (MMP) [9]. These enzymes cause degradation of the extracellular matrix (ECM), including collagen. For this reason, exogenous collagen administration has been investigated as a possible symptomatic adjuvant or independent method of treating osteoarthritis [10].

COLLAGEN TYPE II

Collagen type II is a common matrix molecule of cartilage, with the molecular formula $[\alpha 1(II)]3$ (Fig.2).

Collagen type II is associated with many diseases, such as skeletal dysplasia, rheumatoid arthritis, osteoarthritis, and OA. The degradation of type II collagen (COL2A1) induces chondrocyte hypertrophy via the bone morphogenetic protein (BMP) signaling pathway,

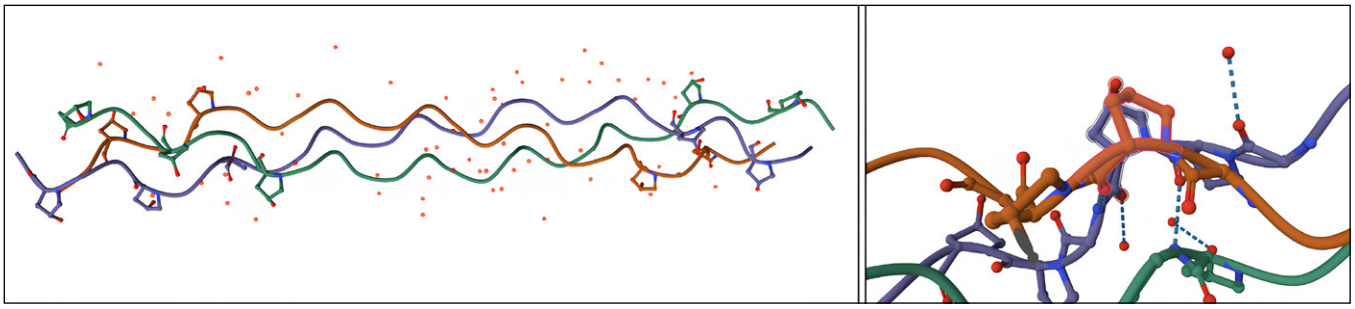

Fig. 1. Structure of the triple helical region of human collagen type I by Trautec from RCSB protein data bank
Source: compiled by the authors based on [https://www.rcsb.org/structure/8K4W]

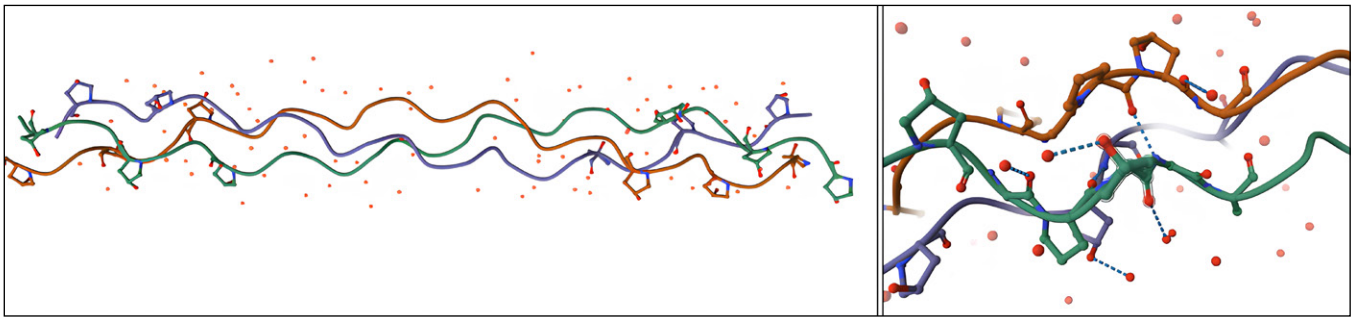

Fig. 2. Structure of the triple helical region of human collagen type II by Trautec from the RCSB protein data bank
Source: compiled by the authors based on [https://www.rcsb.org/structure/9J23]

consequently accelerating the progression of TMJ OA [11]. A significant number of preclinical, experimental, and clinical studies over the past 20 years have demonstrated the effectiveness of type II collagen preparations (including its native form UC-II®) in the treatment of joint inflammation [12,13].

UCII® is a triple helix with bioactive regions called epitopes. These promote binding of undenatured type II collagen to Peer's plaques in the small intestine, which underlies its unique mechanism of action inducing oral tolerance. After binding, a Peer's plaque dendritic cell determines that this antigen is harmless to the body and initiates the activation of immune cells, specifically regulatory T-lymphocytes. The importance of regulatory T-cells stems from their ability to reach sites of inflammation and cartilage destruction and secrete anti-inflammatory cytokines such as IL10 and transforming growth factor β (TGF-β). IL10 inhibits the synthesis of IL1, IL6, and TNFα, preventing the latter from stimulating chondrocytes to release aggressive enzymes and nitric oxide. TGF-β stimulates the synthesis of cartilage matrix components by chondrocytes: collagen, chondroitin sulfate, and hyaluronic acid (HA). Therefore, the use of UC-II® helps reduce inflammation, renew cartilage, and improve joint movement [13].

SOURCES OF COLLAGEN

Nowadays, collagen is obtained using a variety of methods, including natural sources and specially developed recombinant systems based on bacteria, yeast, insects, or mammalian cells [14]. Chemical or enzymatic hydrolysis is typically used to process raw materials, resulting in hydrolyzed collagen. This group of peptides dissolves better than their original (native) form. Extraction is easy, so peptides are actively used in production [15].

Traditionally, the most common sources of animal collagen remain the tissues of cattle, pigs, poultry, and marine organisms [16]. Such products may carry a risk of transmitting spongiform encephalopathy. Clinical observations of patients receiving bovine collagen implants indicate that immune reactions are almost nonexistent and subside when the material is completely absorbed [14]. Furthermore, this collagen is well suited as a precursor to peptides that reduce the activity of angiotensin-converting enzyme, helping to correct blood pressure [17,18].

In parallel, porcine collagen is widely used in medical practice; due to its high similarity to human protein, it causes virtually no allergic reactions. Its peptides demonstrate significant potential in the prevention and treatment of osteoporosis [19], and collagen membranes based on porcine tissue have confirmed their biocompatibility in bone regeneration processes [20]. Chicken feet and sheep and goat tendons are rich in beneficial nutrients and have therefore proven themselves to be alternative collagen sources. Collagen obtained from goat tendons has been shown to be similar in its physical and chemical properties to calf collagen and has demonstrated better cytocompatibility [21].

At the same time, religious restrictions on the consumption of pork or veal products, as well as epidemiological threats, are stimulating the development of the marine collagen segment [14]. Collagen from fish or marine invertebrates yields a high yield and does not transmit zoonotic diseases. Although marine collagen has somewhat lower thermal stability and mechanical strength due to its lower amino acid content, the use of cross-linking methods allows its successful use as a biomaterial in tissue engineering [22]. Over the past twenty years, marine organisms and their derivatives have increasingly been used in the development of new drugs [23,24].

TMJ AND COLLAGEN

Modern collagen preparations, given their wide range of sources and high biocompatibility, open up new perspectives in the treatment of degenerative-dystrophic joint diseases. This issue is particularly relevant in the treatment of TMJ, as the structural integrity of its cartilage and subchondral bone directly depends on collagen metabolism.

Unlike the large joints of the limbs, the TMJ has a unique histological structure. Its articular surfaces are covered not by hyaline cartilage, but by fibrous cartilage—a dense fibrous connective tissue where type I collagen predominates [25]. This influences the choice of treatment, since in TMJ OA, the collagen framework is destroyed due to progressive degradation of the collagen matrix. Consequently, the joint space narrows, crunching occurs, and jaw mobility is limited [5].

The use of collagen hydrolysates in the complex therapy of degenerative-dystrophic diseases of the TMJ not only inhibits the activity of proinflammatory cytokines but also stimulates chondrocytes and fibroblasts to restore damaged structures. Furthermore, given the complex etiology of degenerative-dystrophic processes in the TMJ, modern protocols include a combination of collagen peptides with B vitamins and other cofactors. This helps build new modified, mechanically stable collagen fibers [26].

Collagen can help with osteoarthritis of the TMJ not only by replenishing protein deficiency. Its effects are complex, influencing molecules and cells. A key aspect in the pathogenesis of this disease is changes in metabolism in fibrocartilage. The matrix then degrades faster than it can be restored, as metalloproteinases begin to break it down more rapidly. Therefore, oral administration of hydrolyzed collagen initiates anabolic processes in the joint due to the accumulation of specific peptides, namely proline-hydroxyproline, in the synovial fluid. These bioactive molecules act as ligands for receptors on the surface of chondrocytes and fibroblasts of the TMJ, stimulating them to increase the expression of genes responsible for the synthesis of endogenous collagen types I and II, as well as aggrecan [5,25].

Of particular importance for the TMJ is the ability of collagen peptides to influence the local immune response through the mechanism of oral tolerance. The interaction of native collagen molecules with intestinal lymphoid tissue promotes the differentiation of specific T-regulatory cells, which migrate to the site of inflammation in the TMJ area and secrete anti-inflammatory cytokines [26]. This helps stop secondary synovitis and slow the destruction of the collagen framework of the articular disc. At the same time, restoration of the structural integrity of the subchondral bone of the condylar process of the mandible with the participation of type I collagen provides the necessary biomechanical support to the articular surfaces, preventing further deformation of bone structures. Optimization of the rheological properties of synovial fluid by stimulating the synthesis of its own HA complements this complex multicomponent mechanism, providing the necessary lubrication and reducing mechanical friction during articulation [27].

Therefore, both type I and type II collagen help ensure pathogenetically based restoration of all parts of the temporomandibular joint as a unified system. This allows for a synergistic effect, as the combination of different collagen types allows for the joint to be treated as a holistic biomechanical structure.

When planning the treatment of TMJ osteoarthritis, the clinical picture, the degree of joint destruction, and the intensity of the pain syndrome are primarily taken into account. Although many different methods exist for achieving stable treatment, individualized and comprehensive treatment is essential. Timely and comprehensive treatment is essential for slowing the pathological process [4, 28]. Early diagnosis and treatment strategies for osteoarthritis can improve outcomes and reduce disability and social burden associated with this disease [29].

COLLAGEN AND BONE METABOLISM

In vitro studies of collagen preparations with varying degrees of hydrolysis or polymerization have demonstrated their positive effects on synovial and cartilage cells in animals and humans. Collagen stimulated increased chondrocyte proliferation and the synthesis of cartilage extracellular matrix proteins, increased HA synthesis, and reduced the release of inflammatory mediators [30]. Purified atelocollagen of porcine ori-

gin is a soluble form of type I collagen. This collagen is readily absorbed by the body and has little immune response. Purified atelocollagen has a long half-life and is resistant to enzymatic degradation. This collagen has demonstrated the ability to directly reduce the inflammatory response and promote tissue repair, serving as a scaffold matrix for regenerative processes in the area of injury [31].

Recent meta-analyses show that collagen supplementation helps alleviate the symptoms of osteoarthritis. They found an overall significant improvement in knee joint mobility and pain reduction [32]. Following oral administration of collagen, an improvement in bone mineral density was observed in individuals with early bone loss, particularly in postmenopausal women with osteopenia [33].

Massicotte F. et al. (2002) investigated intra-articular injection of type I collagen as a possible symptomatic adjuvant or standalone treatment for OA. The results showed that collagen injection stimulates chondrocytes to produce hyaline cartilage and inhibits the normal inflammatory response, leading to the formation of fibrous tissue, reducing symptoms, and improving functionality [34].

In studies by Tsai K.S. et al. (2010) of different types of biomaterial coatings, collagen type I has proven to be the best extracellular matrix protein for enhancing osteogenesis, as it promotes the proliferation and osteogenesis of human mesenchymal stem cells (hMSC) by activating the extracellular signal-regulated kinase (ERK), protein kinase B (Akt) pathways [35].

In vivo studies by Tarantino D. et al. (2023) of intra-articular administration of collagen type II solution demonstrated therapeutic efficacy and cartilage regeneration efficiency similar to that of HA in rats with osteoarthritis induced by meniscectomy of the knee (MNX). In this study, treatment of articular cartilage with collagen type II solution attenuated the loss of collagen type II expression, thereby maintaining chondrocyte and cartilage density, similar to HA. Treatment with a solution of collagen II and HA increased aggrecan, which acted as a protective mechanism in osteoarthritis, and expression of SRY-box transcription factor 9 (SOX-9) reduced cartilage damage, thereby preventing significant destruction of chondrocyte collagen in the articular cartilage of rats with MNX-induced OA, similar to that of HA [30].

Porcine collagen, obtained by tangential filtration and sterilization with controlled molecular weight, is contained in an injectable preparation of tropocollagen type I with a molecular weight of 300 kDa (MD-Collagen (GUNA SpA, Milan, Italy)). The obtained injectable tropocollagen type I is a pure product that has standardized physicochemical characteristics with high clinical safety. In addition to biochemical and phylogenetic similarity with collagen of human tissues, it contains high concentrations of the main collagen-forming amino acids: glycine (22.8%), proline (13.8%), hydroxyproline (13%). The average content of other amino acids is only 3% (maximum glutamic acid 9.5%, minimum tyrosine 0.4%). The MD-Collagen line of products includes MD-TISSUE, which, in addition to tropocollagen type I, contains other biologically active substances in its formula, namely a complex of vitamins C, B1, B2, B6, and Mg gluconate, essential for collagen synthesis [31]. This tropocollagen normalizes metabolic processes in the joint at the cellular level, stimulates biorevitalization and protects against the effects of free radicals, promoting tissue regeneration in the event of damage. It has proven itself in orthopedics and traumatology for the treatment of degenerative-dystrophic joint diseases, lumbago, osteoporosis, and rheumatoid arthritis. In dentistry, it is used to improve tissue regeneration in the alveolar bone of the jaws and the oral mucosa, particularly during oral surgery on both soft and hard tissues.

Given the pronounced regenerative therapeutic effect of tropocolagen type I, its use is advisable for the treatment of inflammatory, degenerative-dystrophic processes in the TMJ, osteoporosis, and degenerative-dystrophic changes in bone structure.

The effectiveness of collagen therapy for the treatment of degenerative-dystrophic diseases of the TMJ is determined by the presence of specific cofactors. Vitamin C helps hydroxylate proline and lysine residues. This maintains the stability of the collagen triple helix. B vitamins reduce neurogenic pain, which often occurs during the treatment of TMJ diseases, and improve bone structure by promoting the metabolic processes necessary for collagen formation and metabolic regulation [37].

CONCLUSIONS

The conducted systematic review showed that, taking into account the above-mentioned anti-inflammatory effect of collagen, slowing down the destruction of the collagen skeleton of the articular disc, restoring the structural integrity of the subchondral bone, the bone of the mandible head, ensuring biomechanical support of the articular surfaces, improving the rheological properties of the synovial fluid, etc. in the tissues of the joint, it is advisable to use collagen preparations of types I and II for the treatment of degenerative-dystrophic diseases of the TMJ, osteoporosis, and degenerative changes in the bone structure.

REFERENCES

1. Kostiuk TM. Kompleksna diahnostyka, klinika, ortopedychne likuvannia ta profilaktyka miazovo-suhlobovoi dysfunktsii skronevo-nyzhnoshchelepnoho suhloba [Comprehensive diagnostics, clinical features, orthopedic treatment, and prevention of temporomandibular joint myofascial dysfunction]. [author's abstract]. Kyiv: Bogomolets National Medical University; 2021. https://surl.li/jkfctw [Accessed 17 April 2026] (Ukrainian)
2. Kostiuk TM, Shynchukovskyi IA. Alhorytmy likuvannya ta diahnostyky m'yazovo-suhlobovoyi dysfunktsiyi skronevo-nyzhn'oshchelepnykh suhlobiv: metodychni rekomendatsiyi dlya studentiv, kursantiv tsykliv spetsializatsiyi ta praktychnykh likariv [Algorithms for treatment and diagnostics of muscular-articular dysfunction of temporomandibular joints: guidelines for students, residents of specialization cycles and practitioners.] Kyiv: Bogomolets National Medical University. 2021, p.51. (Ukrainian)
3. Xu J, Ren H, Zhao S et al. Comparative effectiveness of hyaluronic acid, platelet-rich plasma, and platelet-rich fibrin in treating temporomandibular disorders: a systematic review and network meta-analysis. Head Face Med. 2023;19(1):1-39. doi: 10.1186/s13005-023-00369-y. DOI
4. Li B, Guan G, Mei L et al. Pathological mechanism of chondrocytes and the surrounding environment during osteoarthritis of temporomandibular joint. J Cell Mol Med. 2021;25(11):4902-4911. doi:10.1111/jcmm.16514. DOI
5. Cardoneanu A, Macovei LA, Burlui AM et al. Temporomandibular Joint Osteoarthritis: Pathogenic Mechanisms Involving the Cartilage and Subchondral Bone, and Potential Therapeutic Strategies for Joint Regeneration. Int J Mol Sci. 2022;24(1):171. doi:10.3390/ijms24010171. DOI
6. Wang H, Yuan T, Wang Y et al. Osteoclasts and osteoarthritis: Novel intervention targets and therapeutic potentials during aging. Aging Cell. 2024;23(4):e14092. doi:10.1111/acel.14092. DOI
7. Hu Y, Chen X, Wang S et al. Subchondral bone microenvironment in osteoarthritis and pain. Bone Res. 2021;9(20). doi: 10.1038/s41413-021-00147-z. DOI
8. Lu K, Ma F, Yi D et al. Molecular signaling in temporomandibular joint osteoarthritis. Journal of Orthopaedic Translation. 2021;32:21–27. doi: 10.1016/j.jot.2021.07.001. DOI
9. Siddiq MAB, Oo WM, Hunter DJ. New therapeutic strategies in osteoarthritis. Joint Bone Spine. 2024;91(6):105739. doi: 10.1016/j.jbspin.2024.105739. DOI
10. Liu S, Deng Z, Chen K et al. Cartilage tissue engineering: From proinflammatory and anti-inflammatory cytokines to osteoarthritis treatments (Review). Mol Med Rep. 2022;25(3):99. doi:10.3892/mmr.2022.12615. DOI
11. Li B, Guan G, Mei L et al. Pathological mechanism of chondrocytes and the surrounding environment during osteoarthritis of temporomandibular joint. Journal of Cellular and Molecular Medicine. 2021;25(11):4902–4911. doi: 10.1111/jcmm.16514. DOI
12. Di Cesare Mannelli L, Micheli L, Zanardelli M, Ghelardini C. Low dose native type II collagen prevents pain in a rat osteoarthritis model. BMC Musculoskelet Disord. 2013;14:228. doi:10.1186/1471-2474-14-228. DOI
13. Sahin E, Orhan C, Erten F et al. The effect of oral administration of undenatured type II collagen on monosodium iodoacetate-induced osteoarthritis in young and old rats. Sci Rep. 2023;13(1):6499. doi:10.1038/s41598-023-33763-2. DOI
14. Wang H. A Review of the Effects of Collagen Treatment in Clinical Studies. Polymers. 2021;13(22):3868. doi:10.3390/polym13223868. DOI
15. Amirrah IN, Lokanathan Y, Zulkiflee I et al. A Comprehensive Review on Collagen Type I Development of Biomaterials for Tissue Engineering: From Biosynthesis to Bioscaffold. Biomedicines. 2022;10(9):2307. doi:10.3390/biomedicines10092307. DOI
16. Naomi R, Ridzuan PM, Bahari H. Current Insights into Collagen Type I. Polymers. 2021;13(16):2642. doi:10.3390/polym13162642. DOI
17. Yan Z, Gui Y, Liu C et al. Gastrointestinal digestion of food proteins: Anticancer, antihypertensive, anti-obesity, and immunomodulatory mechanisms of the derived peptides. Food Res Int. 2024;189:114573. doi:10.1016/j.foodres.2024.114573. DOI
18. Adebayo SD, Poddar S, Yu J. Antihypertensive Peptides and Hydrolysates Derived from Plant Proteins and Their Bioavailability. Foods. 2026;15(5):900. doi:10.3390/foods15050900. DOI
19. Zhu L, Xie Y, Wen B et al. Porcine bone collagen peptides promote osteoblast proliferation and differentiation by activating the PI3K/Akt signaling pathway. J Funct Foods. 2020;64:103697. doi:10.1016/j.jff.2019.103697. DOI
20. Tai A, Landao-Bassonga E, Chen Z et al. Systematic evaluation of three porcine-derived collagen membranes for guided bone regeneration. Biomater Transl. 2023;4(1):41-50. doi:10.12336/biomatertransl.2023.01.006. DOI
21. Sallent I, Leon Lopez A, Aguirre-Álvarez G, Zeugolis DI. Assessing the Potential of Caprine Collagen Type I in the Development of Medical Devices. Biomacromolecules. 2025;26(10):6418-6429. doi:10.1021/acs.biomac.5c00309. DOI
22. Pozzolini M, Tassara E, Dodero A et al. Potential Biomedical Applications of Collagen Filaments derived from the Marine Demosponges Ircinia oros (Schmidt, 1864) and Sarcotragus foetidus (Schmidt, 1862). Mar Drugs. 2021;19(10):563. doi:10.3390/md19100563. DOI
23. Coppola D, Oliviero M, Vitale GA et al. Marine Collagen from Alternative and Sustainable Sources: Extraction, Processing and Applications. Mar Drugs. 2020;18(4):214. doi:10.3390/md18040214K. DOI
24. Carvalho DN, Gonçalves C, Sousa RO et al. Extraction and Purification of Biopolymers from Marine Origin Sources Envisaging Their Use for Biotechnological Applications. Mar Biotechnol (NY). 2024;26(6):1079-1119. doi:10.1007/s10126-024-10361-5. DOI

25. Lu K, Ma F, Yi D et al. Molecular signaling in temporomandibular joint osteoarthritis. J Orthop Translat. 2021;32:21-27. doi:10.1016/j.jot.2021.07.001. DOI
26. Olson GB, Savage S, Olson J. The effects of collagen hydrolysat on symptoms of chronic fibromyalgia and temporomandibular joint pain. Cranio. 2000;18(2):135-141. doi:10.1080/08869634.2000.11746125. DOI
27. Sohn HS, Choi JW, Jhun J et al. Tolerogenic nanoparticles induce type II collagen-specific regulatory T cells and ameliorate osteoarthritis. Sci Adv. 2022;8(47):eabo5284. doi:10.1126/sciadv.abo5284. DOI
28. Spadon-Brito LG, Souza CSP, Mélo AM et al. Effectiveness of treatments for temporomandibular joint osteoarthritis: a systematic review and meta-analysis. Clin Oral Investig. 2025;29:513. doi:10.1007/s00784-025-06581-1. DOI
29. Im GI. The Concept of Early Osteoarthritis and Its Significance in Regenerative Medicine. Tissue Eng Regen Med. 2022;19(3):431-436. doi:10.1007/s13770-022-00436-6. DOI
30. Tarantino D, Mottola R, Palermi S et al. Intra-Articular Collagen Injections for Osteoarthritis: A Narrative Review. Int J Environ Res Public Health. 2023;20(5):4390. doi:10.3390/ijerph20054390. DOI
31. Lee HS, Oh KJ, Moon YW et al. Intra-articular Injection of Type I Atelocollagen to Alleviate Knee Pain: A Double-Blind, Randomized Controlled Trial. Cartilage. 2021;13(1):342S-350S. doi:10.1177/1947603519865304. DOI
32. Simental-Mendía M, Ortega-Mata D, Acosta-Olivo CA et al. Effect of collagen supplementation on knee osteoarthritis: an updated systematic review and meta-analysis of randomised controlled trials. Clin Exp Rheumatol. 2025;43(1):126-134. doi:10.55563/clinexprheumatol/kflfr5. DOI
33. Zulfiqar Z, Kot J, Lee K et al. Collagen Supplementation and Bone Health: A Narrative Review. Wiadomości Lekarskie. 2026;(3):548–52. doi:10.36740/WLek/218222. DOI
34. Massicotte F, Lajeunesse D, Benderdour M et al. Can altered production of interleukin-1beta, interleukin-6, transforming growth factor-beta and prostaglandin E(2) by isolated human subchondral osteoblasts identify two subgroups of osteoarthritic patients. Osteoarthritis Cartilage. 2002;10(6):491-500. doi:10.1053/joca.2002.0528. DOI
35. Tsai KS, Kao SY, Wang CY et al. Type I collagen promotes proliferation and osteogenesis of human mesenchymal stem cells via activation of ERK and Akt pathways. J Biomed Mater Res A. 2010;94(3):673-682. doi:10.1002/jbm.a.32693. DOI
36. Martin Martin LS, Massafra U, Bizzi E et al. A double blind randomized active-controlled clinical trial on the intra-articular use of Md-Knee versus sodium hyaluronate in patients with knee osteoarthritis ("Joint"). BMC Musculoskelet Disord. 2016;17:94. doi:10.1186/s12891-016-0948-4. DOI
37. Boyera N, Galey I, Bernard BA. Effect of vitamin C and its derivatives on collagen synthesis and cross-linking by normal human fibroblasts. Int J Cosmet Sci. 1998;20(3):151-158. doi:10.1046/j.1467-2494.1998.171747.x. DOI

CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 10.03.2026
ACCEPTED: 30.06.2026