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THE ROLE OF COLLAGEN SUPPLEMENTATION IN KNEE JOINT DISORDERS: A SYSTEMATIC REVIEW OF CLINICAL STUDIES

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ABSTRACT

Introduction and Purpose: Collagen is essential for maintaining the structure and function of the knee joint, making it a promising option for managing joint-related conditions. This review explores current clinical research on the impact of collagen supplements on knee pain, mobility, and overall joint health in individuals with osteoarthritis, early arthritis, meniscal injuries, and functional joint discomfort.
Materials and Methods: A literature search was conducted using PubMed and Google Scholar, focusing on studies from 2016 onward. Keywords included "collagen," "knee joint," "supplementation," and "osteoarthritis" to identify relevant clinical trials and studies.
Main Findings: The review indicates that collagen supplementation, particularly types I, II, and III, offers notable benefits for knee joint health. In patients with osteoarthritis and early joint degeneration, undenatured type II collagen and collagen peptides significantly reduced pain, stiffness, and improved mobility, as measured by standardized tools like WOMAC, KOOS, and VAS. Similar improvements were noted in athletes and active individuals experiencing activity-related knee discomfort, with reported reductions in joint pain and decreased reliance on additional treatment. Certain collagen formulations also improved range of motion and flexibility in both healthy subjects and those with minor joint issues. Additionally, recent studies show that collagen can help those with meniscal injuries by reducing pain, boosting leg strength, and enhancing quality of life.
Conclusion: Collagen supplements appear to be a safe and effective option for improving knee joint health, particularly in cases of osteoarthritis and functional joint discomfort. While outcomes vary depending on the collagen type and dosage, overall evidence supports their potential in reducing pain and enhancing joint function across a range of populations.

KEYWORDS

Osteoarthritis, Knee Joint, Supplementation, Collagen

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Introduction and purpose

Collagen is the most abundant structural protein in the human body, making up approximately 25-30% of total protein content. It is a key component of connective tissues, including skin, tendons, ligaments, cartilage, and bones. Collagen molecules are composed of amino acids (mainly glycine, proline, and hydroxyproline) arranged in a triple helix structure that provides tensile strength and structural integrity.

Collagen supplementation—typically in the form of hydrolyzed collagen peptides or gelatin—has gained popularity due to growing interest in its potential benefits for joint health, skin elasticity, bone strength, and overall connective tissue repair.

Collagen supplementation has gained attention for its potential to support knee joint health by reducing pain, improving mobility, and promoting cartilage integrity. Clinical studies suggest it may be beneficial for individuals with osteoarthritis or joint stress, offering a safe, non-pharmacological option to support joint function.

This review synthesizes the latest evidence to evaluate current ventilatory and pharmacological strategies, address persistent challenges in implementation, and explore the paradigm shift toward precision medicine approaches in ARDS management.

This review synthesizes the latest evidence to evaluate the efficacy of collagen supplementation in knee joint health, examine ongoing challenges in clinical application, and explore its emerging role within personalized approaches to musculoskeletal care.

Material and methods

A comprehensive literature review was conducted using two primary databases: PubMed and Google Scholar. The search focused on articles related to collagen supplementation, published from 2016 onwards. Key search terms included "collagen" "knee joint ," "supplementation," "osteoarthritis," .

Collagen supplementation in knee joint osteoarthritis

Osteoarthritis (OA) is a progressive joint disorder characterized by cartilage degradation, inflammation, and impaired joint function—processes closely tied to the decline of collagen, a key structural protein in articular cartilage. Growing interest in collagen supplementation has prompted clinical research into its potential to alleviate OA symptoms, improve joint mobility, and support cartilage integrity. The following section reviews three recent clinical studies evaluating various forms of collagen supplementation in the management of knee osteoarthritis.

The 2024 double-blind, randomized, placebo-controlled study titled "Effect of supplementation with type 1 and type 3 collagen peptide and type 2 hydrolyzed collagen on osteoarthritis-related pain, quality of life, and physical function" provides valuable insights into the clinical efficacy of multi-type collagen supplementation in managing symptoms associated with osteoarthritis. In this 2024 double-blind, randomized, placebo-controlled study, 31 patients (mean age 53.5) with Grade 2–3 knee osteoarthritis were assigned to either a collagen (n=16) or placebo group (n=15). Over eight weeks, participants were assessed using a comprehensive set of pain, quality of life, and functional outcome measures. Collagen supplementation led to significant improvements in pain and quality of life scores (VAS, WOMAC, KOOS-PS, OKS, TSK, SF-12, FFI; $p<0.05$) and enhanced performance on the Berg Balance Scale and 6-Minute Walk Test ($p<0.05$). No significant differences were observed in TUG, 5STS, or SCT outcomes ($p>0.05$).

A 2016 multicenter, randomized, double-blind, placebo-controlled trial titled "Efficacy and tolerability of an undenatured type II collagen supplement in modulating knee osteoarthritis symptoms" investigated the therapeutic potential of undenatured type II collagen (UC-II), derived from chicken sternum cartilage, by comparing its effects on knee osteoarthritis symptoms to both placebo and a combination of glucosamine hydrochloride with chondroitin sulfate. In this study, 191 participants with knee osteoarthritis were randomly assigned to receive either undenatured type II collagen (UC-II, 40 mg), glucosamine plus chondroitin (GC), or placebo daily for 180 days. The primary outcome was change in total WOMAC score, with secondary endpoints including the Lequesne Index, VAS pain scale, and WOMAC subscales. By day 180, the UC-II group showed a statistically significant reduction in overall WOMAC scores compared to both placebo ($p = 0.002$) and GC ($p = 0.04$). Improvements were also observed in WOMAC subdomains—pain, stiffness, and physical function—with UC-II outperforming both comparators. No differences in safety profiles were noted among groups.

A 2024 double-blind, multicenter, randomized, placebo- and active-controlled clinical trial titled "Management and Amelioration of Knee Joint Osteoarthritis in Adults Using a Novel High-Functional Bovine Collagen Peptide as a Nutritional Therapy" explored the therapeutic potential of a new collagen formulation, "Wellnex" Type J, in alleviating symptoms of knee osteoarthritis. In this five-arm study involving 100 participants, subjects received daily doses of either 2.5 g, 5.0 g, or 10.0 g of Type J collagen, 10.0 g of conventional collagen peptides, or 10.0 g of placebo over 90 days. Key outcomes included WOMAC scores, pain scales, quality of life (QoL), physician assessments (PICS), serum CTX-II levels, and MRI-based MOAKS parameters. The 2.5 g Type J group showed significant improvements across WOMAC, QoL, CTX-II, and MOAKS measures, demonstrating comparable efficacy to 10 g of standard collagen peptides, while also confirming safety and tolerability.

Type of Collagen	Sample Size / Duration	Outcome Measures	Key Results	Significance
Type I & III collagen peptides + Type II hydrolyzed collagen	31 patients / 8 weeks	VAS, WOMAC, KOOS-PS, OKS, TSK, SF-12, FFI, BBS, TUG, 6MWT, 5STS, SCT	Significant improvement in pain and QoL scores (VAS, WOMAC, KOOS-PS, etc.), improved BBS & 6MWT; no difference in TUG, 5STS, SCT	$p < 0.05$ for most outcomes
Undenatured Type II collagen (UC-II)	191 patients / 180 days	WOMAC, VAS, LFI, WOMAC subscales	Significant reductions in total WOMAC and all subscales vs. placebo and GC	$p = 0.002$ (vs placebo), $p = 0.04$ (vs GC); subscales $p < 0.05$
High-functional Type J bovine	100 patients / 90 days	WOMAC, QoL, PICS, CTX-II, MOAKS	2.5 g Type J collagen improved WOMAC, QoL, CTX-II, MOAKS; efficacy comparable to 10 g conventional collagen	Statistically significant (exact p-values not specified)

Early knee arthritis, particularly in physically active individuals, can represent the initial stages of osteoarthritic degeneration, making timely intervention crucial for preventing long-term joint damage. In this context, the study titled "Comparison of Single and Combined Treatment with Exercise Therapy and Collagen Supplementation on Early Knee Arthritis among Athletes—A Quasi-Randomized Trial" investigated the effects of collagen supplementation, both alone and in combination with exercise therapy, offering insight into integrated strategies for mitigating symptoms and supporting joint function in the early phases of disease progression. In this quasi-randomized trial, 48 recreational athletes diagnosed with early osteoarthritis (EOA) were allocated into three intervention groups: collagen supplementation alone (Col), exercise therapy alone (Ex), and a combined approach (ColEx). Over a 12-week period, participants were evaluated using the Visual Analog Scale (VAS), knee flexion range of motion (ROM), muscle strength assessments, and the Knee injury and Osteoarthritis Outcome Score (KOOS). While all groups showed improvements in activity-related pain, significant gains in knee ROM were observed particularly in the Col group compared to Ex. Notably, the Ex and ColEx groups demonstrated marked improvements in muscle strength and KOOS scores. These findings suggest that while exercise therapy alone benefits pain and function in EOA, its combination with collagen supplementation may amplify clinical outcomes.

Collagen supplementation in general knee pain

Knee pain, whether due to early joint degeneration, overuse, or mechanical stress, is a common concern affecting quality of life and physical function across diverse populations. Collagen, as a fundamental component of connective tissue, plays a vital role in maintaining the structural integrity and resilience of the knee joint. Emerging evidence supports the use of collagen supplementation not only in osteoarthritis but also in mitigating general knee pain and enhancing joint performance in both clinical and athletic settings. In this section, we present three additional clinical studies that explore the effects of collagen supplementation on general knee pain, focusing on its impact in physically active individuals and non-OA populations.

A 2023 study titled "Oral supplementation with fish cartilage hydrolysate in an adult population suffering from knee pain and function discomfort" investigated the effects of fish cartilage hydrolysate on knee pain and function. This innovative approach combined both clinical and ex vivo investigations to explore the potential of collagen-based supplementation in alleviating knee discomfort and improving joint function in individuals without a specific osteoarthritis diagnosis.

In this exploratory, non-comparative, multicenter clinical trial, 33 adults with moderate knee discomfort and functional limitations received oral supplementation with fish cartilage hydrolysate (FCH). Over the course of the study, participants reported significant improvements in knee pain and function, as measured by KOOS, VAS, PGA, and SF-36 quality of life scores. Complementing the clinical findings, an ex vivo

component demonstrated that FCH metabolites reduced inflammatory markers (NO, PGE2) and catabolic enzymes (MMP-13) in human chondrocytes, while preserving cartilage matrix synthesis in the presence of IL-1β. These results suggest FCH may provide both symptomatic relief and protective effects at the cellular level.

A 2020 randomized controlled trial titled "Effectiveness of collagen supplementation on pain scores in healthy individuals with self-reported knee pain" evaluated the impact of collagen peptides on knee discomfort in a non-clinical population, focusing on healthy individuals experiencing activity-related knee pain without underlying osteoarthritis. In this randomized controlled trial, 167 healthy, physically active individuals with self-reported knee pain were assigned to receive either 10 g/day of collagen peptides (CP) or a placebo for 12 weeks. Pain and function were assessed using the VAS, KOOS, and Lysholm scores, while biochemical markers of inflammation, cartilage, and bone turnover were also measured. Although both groups showed significant improvements in pain and function scores, there were no statistically significant differences between the CP and placebo groups in any of the clinical or biomarker outcomes. These findings suggest that CP supplementation did not offer additional benefit over placebo in reducing knee pain or modulating joint-related biomarkers in this population.

A 2017 randomized, double-blind, placebo-controlled trial titled "Improvement of activity-related knee joint discomfort following supplementation of specific collagen peptides" investigated whether targeted collagen supplementation could reduce knee joint discomfort associated with physical activity in healthy, physically active adults. In this 12-week randomized, double-blind, placebo-controlled trial, 139 athletic individuals with activity-related knee pain received either 5 g of bioactive collagen peptides (BCP) or placebo daily. The primary outcome—pain intensity during activity—was significantly reduced in the BCP group compared to placebo, as assessed by both participants and physicians ($p = 0.046$ and $p = 0.021$, respectively). While resting pain also improved, the difference was not statistically significant. No notable changes in knee range of motion were observed, but the BCP group showed a significant reduction in the need for additional treatments. These findings support the use of BCP for alleviating activity-induced knee discomfort in physically active populations.

Type of Collagen	Population / Duration	Outcome Measures	Key Results	Significance
Fish cartilage hydrolysate (FCH)	33 adults with moderate knee discomfort / exploratory clinical & ex vivo study	KOOS, VAS, PGA, SF-36; Ex vivo: MMP-13, NO, PGE2, GAG, collagen	Improved pain and function; reduced pro-inflammatory and catabolic markers in vitro	Clinically and biologically significant (exact p-values not stated)
10 g/day collagen peptides	167 healthy, active adults with self-reported knee pain / 12 weeks	VAS, KOOS, Lysholm; inflammatory and cartilage biomarkers	No significant differences between CP and placebo in pain/function or biomarkers	$p > 0.05$ for all group comparisons
5 g/day bioactive collagen peptides (BCP)	139 athletic adults with functional knee pain / 12 weeks	VAS (activity & rest), ROM, need for additional therapy	Significant improvement in activity-related pain ($p = 0.046$); reduced additional treatments	Statistically significant for primary outcomes

Collagen supplementation in knee joint flexibility

Beyond pain relief, joint flexibility is a critical factor in maintaining functional mobility and preventing long-term joint degeneration. Collagen's role in preserving the structural integrity and elasticity of connective tissues suggests it may contribute to improved joint flexibility. The following section explores clinical evidence examining the effects of collagen supplementation on knee joint range of motion and flexibility-related outcomes. In addition to its impact on pain, collagen supplementation may influence joint flexibility by supporting the elasticity and structural integrity of connective tissues. The following study investigates how collagen intake affects knee joint range of motion and flexibility-related outcomes in adults experiencing joint discomfort.

A 2022 multicenter, randomized, double-blind, placebo-controlled study titled "UC-II Undenatured Type II Collagen for Knee Joint Flexibility" examined whether daily supplementation with UC-II could enhance knee joint flexibility and mobility in adults experiencing joint stiffness and limited range of motion. In this 24-week randomized, double-blind, placebo-controlled trial, 96 healthy adults aged 20–55 with activity-related joint discomfort (ArJD) received either 40 mg/day of UC-II® undenatured type II collagen or placebo. Knee range of motion (ROM) was assessed using a digital goniometer. The collagen group demonstrated a statistically significant improvement in knee flexion compared to placebo (3.23° vs. 0.21°, $p = 0.025$), along with a meaningful increase in extension over time (2.21°, $p = 0.0061$). Subgroup analysis revealed even greater benefits in participants over 35 years of age, with a 6.79° gain in flexion versus just 0.30° in the placebo group ($p = 0.0092$). These findings support UC-II supplementation as a promising intervention to improve knee joint flexibility in physically active individuals experiencing mild joint stress.

These findings indicate that a daily dose of 40 mg undenatured collagen can enhance knee joint range of motion and flexibility in healthy individuals experiencing activity-related joint discomfort.

Collagen supplementation in meniscal function

The menisci are critical structures within the knee joint, essential for distributing load, enhancing stability, absorbing shock, preserving articular cartilage, and supporting proprioceptive function. Comprised primarily of type I collagen, along with contributions from type II fibers, their structural integrity is closely tied to knee joint stability. In light of this, the study under review explored the impact of Naturagen® 4 Joint, a supplement containing type I, II, and III collagen, on pain, quality of life, and physical function in individuals diagnosed with meniscopathy.

The 2025 study titled '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' explores the therapeutic potential of multi-type collagen supplementation in improving symptoms and functional outcomes in individuals with meniscal pathology. This randomized, double-blind, placebo-controlled clinical trial involved 32 patients with meniscopathy who received collagen supplementation or placebo over eight weeks. Participants were evaluated using a range of scales and functional tests, including VAS, WOMAC, KOOS-PS, OKS, TSK, SF-12, LEFS, FFI, and several physical performance measures. Results showed significant improvements in pain, quality of life, kinesiophobia, and foot function among those who received collagen ($p < 0.05$), along with a near-significant gain in leg strength ($p = 0.057$). However, no notable changes were observed in back strength, proprioception, balance, or most mobility-based assessments. These findings suggest that collagen supplementation may offer clinical benefits in reducing symptoms and enhancing certain aspects of physical function in patients with meniscopathy.

Conclusions

Collectively, the reviewed studies underscore the growing clinical interest in collagen supplementation as a supportive strategy in the treatment and management of knee joint pathologies. From osteoarthritis to early degenerative changes, general joint discomfort, and meniscal disorders, collagen has demonstrated positive effects on a variety of outcome measures including pain relief, functional performance, range of motion, and quality of life. Whether used alone or in combination with exercise therapy, collagen—especially in its bioactive or undenatured forms—has been shown to improve patient-reported outcomes and some objective performance measures across different age groups and activity levels. While the extent of these benefits depends on factors such as the collagen source, dosage, intervention duration, and the baseline health of participants, the findings suggest that collagen plays a meaningful role in supporting joint structure and function. Further research, particularly long-term and large-scale clinical trials, is needed to refine its therapeutic applications and determine optimal formulations and regimens. Nonetheless, collagen-based interventions appear to offer a safe, well-tolerated, and potentially effective complement to existing approaches in the preservation of knee joint health.

Disclosure

Author's contribution:

Conceptualization: BZ, MC, KM
Methodology: KM, AO, BZ
Software: BK, OJ, AO,
Check: JS
Formal analysis: BZ, MS, MM
Investigation: PS, BK, BZ
Resources: MC, BK
Data curation: MS, MM, PS
Writing –rough preparation: OJ, BZ, AO, KM
Writing –review and editing: BK, JS, BZ, MM, PS
Visualization: MS, BK
Supervision: MC, OJ, MM, MM, AO
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