10.21486/RECREATION.2025.15.4.1

Bioactive collagen peptides and fibroblast-mediated matrix regeneration: From peptide absorption to tissue remodeling

Bioaktív kollagén peptidek és fibroblaszt-mediált mátrixregeneráció: A peptidfelszívódástól a szöveti átépülésig

Szerzők: **Péter Fritz [1], Annamária Maszlag [2], Lívia Mayer-Sopronyi [3]**

Benyújtva: 2025. november 17. | Átdolgozva: 2025. december 5. | Elfogadva: 2025. december 16. | Megjelent: 2025. december 30.

Rovatszerkesztő:
Fritz Réka
Szegedi Tudományegyetem,
Fül-Orr-Gégészeti és Fej-Nyaksebészeti Klinika
fritz.reka@med.u-szeged.hu

Péter Fritz [1]
Károli Gáspár University of the Reformed Church in Hungary
Faculty of Economics, Health Sciences and Social Studies
Lifestyle and Physical Culture Institute
fritz.peter@kre.hu

Annamária Maszlag [2]
SuperFoods Ltd.
annamaria.maszlag@gmail.com

Lívia Mayer-Sopronyi [3]
SuperFoods Ltd.
s.mayer.livia@gmail.com

Absztrakt:
A kollagén peptidek olyan bioaktív tápanyag-összetevőkké váltak, amelyek képesek befolyásolni a sejtszintű jelátviteli folyamatokat és az extracelluláris mátrix (ECM) átépülését. A korai vizsgálatok (2003–2017) igazolták a **prolil-hidroxiprolin (Pro-Hyp) és hidroxiprolil-glicin (Hyp-Gly)** di-/tripeptidek felszívódását és fibroblasztokat serkentő hatását, a legújabb bizonyítékok (2020–2024) ezt a modellt klinikailag is releváns eredményekkel bővítették: időskori szöveti változások, sportrehabilitáció, ízületi funkció és bőrre-generáció területén egyaránt
Szájon át történő bevitel után a hidrolizált kollagén enzimatikus emésztésen megy keresztül, amelynek során kis molekulatömegű peptidek keletkeznek, és a PEPT1 transzporter közvetítésével jutnak át a bélfalon. Ezek a peptidek felhalmozódnak a kötőszövetekben, modulálják a TGF-β/SMAD és MAPK jelátviteli útvonalakat, fokozzák a COL1A1/COL3A1 génexpressziót, miközben csökkentik a mátrix-metalloproteinázok (MMP) aktivitását.
Modern, randomizált kontrollált vizsgálatok és metaanalízisek igazolják a bőrrugalmasság javulását, az ínszöveti regeneráció javulását, a fájdalom csökkenését, valamint a funkcionális teljesítmény növekedését az idősebb és sportoló populációkban.
A jelen áttekintés integrálja a molekuláris mechanizmusokat a humán klinikai eredményekkel, és kritikai elemzésben vizsgálja a jelenlegi kutatások korlátait (módszertani heterogenitás, adagolási eltérések). A kollagén–fibroblaszt–ECM tengely mélyebb megértése új transzlációs lehetőségeket nyit a regeneratív medicina, az életmódbeli intervenciók és a mozgásszervi egészség területén. Továbbá ezen mechanizmusokra építve jelen áttekintés megkísérel gyakorlati útmutatót kínálni a rekreáció és az életmódorvoslás területén dolgozó szakemberek számára.
Kulcsszavak: kollagén peptidek, fibroblaszt-aktiváció, extracelluláris mátrix, szöveti regeneráció, TGF-β/SMAD, MAPK, Pro-Hyp, mozgásszervi egészség, egészséges öregedés

Abstract:
Collagen peptides have emerged as bioactive nutritional compounds capable of influencing cellular signaling and extracellular matrix (ECM) remodeling. While classical studies (2003–2017) established the absorption of **prolyl-hydroxyproline (Pro-Hyp) and hydroxyprolyl-glycine (Hyp-Gly)** di-/tripeptides and their stimulatory effects on fibroblasts, recent evidence (2020–2024) has expanded this model with clinically relevant outcomes across aging, sports recovery, joint health, and dermal regeneration.
Following oral ingestion, hydrolyzed collagen undergoes enzymatic digestion, producing low-molecular-weight peptides that are transported across the intestinal barrier via PEPT1. These fragments accumulate in connective tissues, modulate TGF-β/SMAD and MAPK signaling pathways, and enhance COL1A1/COL3A1 transcription while reducing matrix metalloproteinase (MMP) activity. Modern randomized controlled trials and meta-analyses confirm improvements in skin elasticity, tendon remodeling, pain reduction, and functional performance in elderly and athletic populations. This review integrates molecular mechanisms with human clinical evidence and critically evaluates the limitations of current research, including methodological heterogeneity and dosage inconsistency. Understanding the collagen–fibroblast–ECM axis offers translational insights for regenerative medicine, lifestyle interventions, and musculoskeletal health, and this overview builds on these mechanisms by translating them into everyday recreational practice, providing a practical guide for specialists in recreation and lifestyle medicine.
Keywords: collagen peptides, fibroblast activation, extracellular matrix, tissue regeneration, TGF-β/SMAD, MAPK, Pro-Hyp, musculoskeletal health, healthy aging

Introduction

Collagen is the most abundant structural protein in the human body, accounting for nearly 30% of total protein mass. It forms the molecular scaffold of connective tissues such as skin, bone, tendons, cartilage, and fascia. Its unique triple-helical structure, composed of repeating sequences of glycine, proline, and hydroxyproline, provides mechanical stability, tensile strength, and resilience to tissues under constant stress and repair.

With aging, mechanical strain, and oxidative stress, collagen metabolism gradually shifts toward degradation rather than synthesis. Fibroblast activity declines, reactive oxygen species (ROS) accumulate, and matrix metalloproteinase (MMP) activity increases, leading to fragmentation of collagen fibers and loss of tissue elasticity (Ghosh & Ingber, 2007). This imbalance contributes to visible signs of aging, slower recovery from physical activity, and the progression of degenerative musculoskeletal disorders.

Nutritional science and molecular physiology have increasingly recognized that collagen peptides act not merely as structural substrates but also as signaling molecules. Once digested and absorbed, specific collagen-derived peptides interact with fibroblast receptors, upregulating the expression of genes such as COL1A1, COL3A1, and ELN while concurrently inhibiting MMP activity (Iwai et al., 2005; Oesser & Seifert, 2003). These findings position hydrolyzed collagen as a unique category of bioactive protein with the ability to influence cell behavior, not only to supply amino acids. Emerging evidence demonstrates that oral collagen supplementation can enhance skin elasticity, improve joint function, and support injury recovery in both clinical and athletic populations (Shaw et al., 2017; Shigemura et al., 2009; Zdzieblik et al., 2017). From a physiological standpoint, collagen metabolism represents an integrative "collagen – fibroblast – ECM axis" linking nutrient intake, cellular signaling, and tissue remodeling. Understanding this axis provides mechanistic insight into how dietary interventions may influence regenerative capacity and overall healthspan.

Collagen digestion and absorption

Collagen bioavailability depends largely on its molecular size and structural complexity. Native collagen molecules are approximately 300 kDa and composed of tightly packed triple helices stabilized by hydrogen bonds. Such macromolecules resist enzymatic degradation and cannot be absorbed intact. In contrast, hydrolyzed collagen – also known as collagen peptides – is pre-digested into smaller peptide chains (around 0.3–6 kDa) that exhibit high solubility and intestinal permeability (Daneault et al., 2017).

Following oral ingestion, hydrolyzed collagen undergoes sequential enzymatic hydrolysis in the gastrointestinal tract. Pepsin initiates cleavage in the stomach under acidic conditions, while trypsin and chymotrypsin further fragment the peptides in the small intestine. This process yields a mixture of di- and tripeptides such as prolyl-hydroxyproline (Pro-Hyp) and hydroxyprolyl-glycine (Hyp-Gly), which are considered key bioactive fragments (Iwai et al., 2005; Ohara et al., 2007). Approximately 1–10% of these low-molecular-weight peptides cross the intestinal barrier intact via proton-coupled oligopeptide transporter PEPT1, while the remainder is degraded into free amino acids – predominantly glycine, proline, and hydroxyproline. These amino acids are essential building blocks for new collagen synthesis and help maintain the stability of the collagen triple helix (Oesser & Seifert, 2003).

Once absorbed, collagen peptides appear in human plasma within 1–2 hours and are distributed via the bloodstream to target tissues such as skin, cartilage, and tendons. Experimental tracing studies have shown that specific peptide fragments can accumulate preferentially in connective tissues, suggesting a tropism toward fibroblast-rich regions (Ohara et al., 2007). Within these sites, the bioactive peptides serve as both metabolic substrates and signaling molecules, activating cellular pathways responsible for extracellular matrix (ECM) renewal. In this way, digestion and absorption are not merely nutritional processes but the first regulatory steps in a biochemical cascade linking oral collagen intake to tissue-level remodeling.

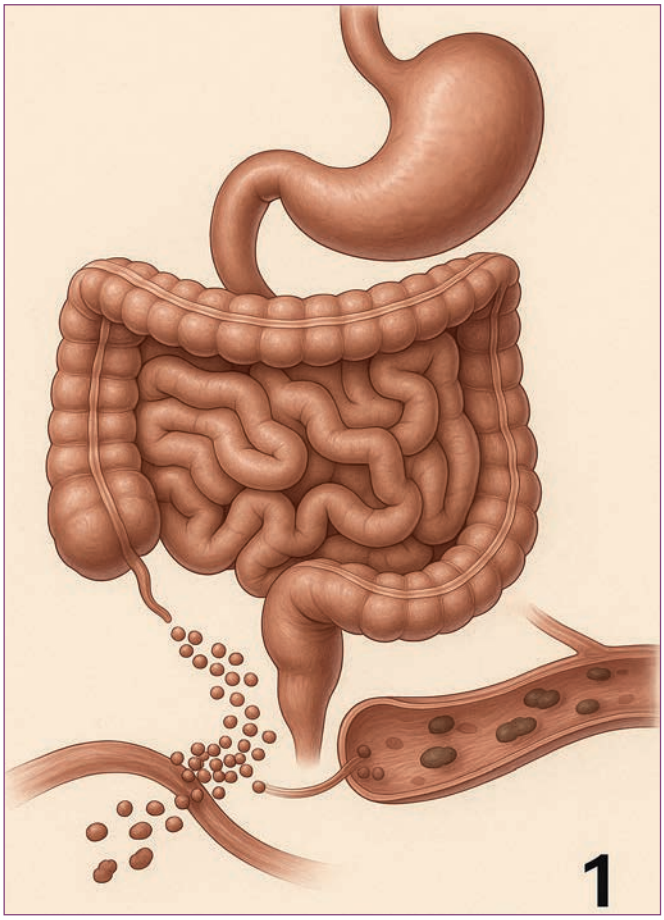

Figure 1. Collagen digestion and intestinal absorption following oral ingestion of hydrolyzed collagen peptides.
Hydrolyzed collagen undergoes stepwise enzymatic degradation in the stomach and small intestine, producing low–molecular-weight di- and tripeptides (e.g., Pro-Hyp, Hyp-Gly). A fraction of these bioactive peptides is absorbed via PEPT1 transporters into the bloodstream, while non-absorbed residues continue toward the large intestine.
Source: Own editing with ChatGPT version 5.2.

Fibroblast activation and collagen biosynthesis

Fibroblasts are the principal cells responsible for maintaining and regenerating the ECM. They synthesize and secrete a wide range of structural proteins – most notably collagen types I and III – as well as elastin, fibronectin, and glycosaminoglycans. Within connective tissues such as the dermis, tendons, and ligaments, fibroblasts respond dynamically to biochemical and mechanical stimuli, allowing continuous turnover of ECM components in response to local demands (Ghosh & Ingber, 2007).

Bioactive peptide signaling

Recent findings demonstrate that specific collagen-derived di- and tripeptides can act as molecular messengers that directly influence fibroblast function. After intestinal absorption, peptides like Pro-Hyp and Hyp-Gly circulate through the bloodstream and reach fibroblast-rich tissues. These fragments bind to cell surface receptors associated with integrin and transforming growth factor-β (TGF-β) signaling pathways, initiating downstream cascades that activate collagen-related genes such as COL1A1, COL1A2, and COL3A1 (Iwai et al., 2005; Oesser & Seifert, 2003). Once activated by these signals, fibroblasts increase their synthesis of collagen, elastin, and other matrix proteins while simultaneously reducing MMP expression. This dual effect – enhancing new matrix production and decreasing matrix degradation – creates a net anabolic environment in the ECM, thereby promoting tissue regeneration and structural integrity.

Collagen biosynthesis in fibroblasts

Collagen synthesis is an intricate, multistage intracellular process. It begins in the rough endoplasmic reticulum (RER), where ribosomes translate collagen mRNAs into pre-pro-α chains of procollagen. Within the RER lumen, post-translational modifications occur: proline and lysine residues are hydroxylated (a reaction requiring vitamin C as a cofactor) and specific hydroxylysines are glycosylated, steps that stabilize the developing triple-helix structure. The modified polypeptide chains then align to form the procollagen triple helix (Shigemura et al., 2009).

Subsequently, the Golgi apparatus packages these procollagen molecules into secretory vesicles and exports them to the extracellular space. Once secreted, specialized procollagen peptidases remove the N- and C-terminal propeptides, converting procollagen into mature tropocollagen molecules capable of self-assembly into fibrils. These collagen fibrils spontaneously aggregate into larger fibers, forming the load-bearing architecture of connective tissues (Ghosh & Ingber, 2007).

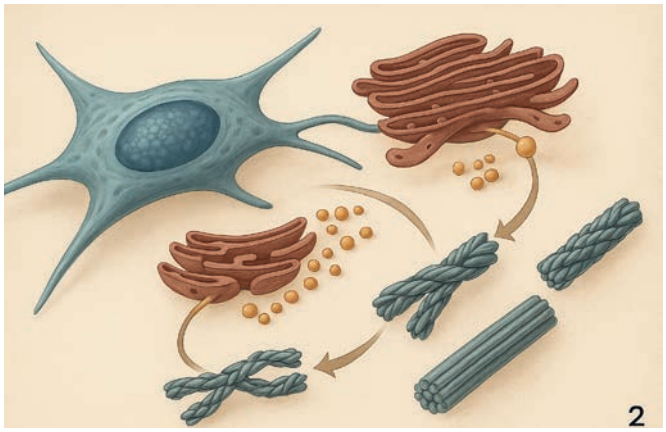

Figure 2. Fibroblast activation by collagen-derived peptides and intracellular collagen biosynthesis.
Collagen-derived di- and tripeptides reaching connective tissues bind to fibroblast receptors and activate intracellular signaling pathways, including integrin- and TGF-β-mediated cascades. The activated fibroblast initiates collagen biosynthesis in the rough endoplasmic reticulum through translation, hydroxylation, glycosylation, and triple-helix formation, followed by Golgi-mediated packaging and secretion of procollagen.
Source: Own editing with ChatGPT version 5.2.

Regulation and mechanical integration

Fibroblast activity is finely tuned by both chemical and mechanical factors. Mechanical stretch or tissue deformation activates mechanotransduction pathways (via integrins and focal adhesion kinase), which in turn stimulate ECM gene expression and collagen production. Conversely, chronic physical inactivity or oxidative stress can shift fibroblasts toward a catabolic phenotype, resulting in weaker collagen networks. Adequate nutrient availability – including a steady supply of collagen peptides – helps maintain the balance between synthesis and degradation, supporting ECM resilience and repair. Overall, fibroblasts act as the cellular nexus between molecular signaling and macroscopic tissue regeneration. Through their coordinated synthetic and remodeling functions, they ensure dynamic renewal of connective tissue structures, sustaining both mechanical strength and biological vitality throughout the lifespan.

Extracellular matrix remodeling and functional integration

The extracellular matrix is a dynamic, multifunctional network that not only provides structural support to tissues but also regulates cellular communication, proliferation, and differentiation. The ECM is composed primarily of fibrous proteins (collagen, elastin, fibronectin) embedded in a hydrated ground substance of proteoglycans and glycosaminoglycans. In connective tissues, ECM remodeling is a continuous and tightly regulated process that ensures both mechanical stability and regenerative potential (Ghosh & Ingber, 2007).

Collagen fibril organization and cross-linking

After secretion from fibroblasts, collagen molecules spontaneously align and assemble into fibrils, which then organize into larger fiber bundles. The hierarchical architecture of collagen fibrils is fundamental to tissue tensile strength and elasticity. Covalent cross-links formed between lysine and hydroxylysine residues stabilize the collagen network, improving its mechanical resistance and durability (Oesser & Seifert, 2003). When peptide supply and fibroblast activity are optimal, newly synthesized collagen fibrils integrate efficiently into the existing matrix, enhancing the biomechanical competence of tissues such as tendons, cartilage, and dermis. By contrast, in states of nutrient deficiency, physical inactivity, or oxidative stress, collagen degradation can exceed synthesis, leading to disorganized fibril networks and structural fragility (Ghosh & Ingber, 2007). Continuous collagen peptide intake helps restore homeostasis by balancing collagen turnover and promoting tissue resilience.

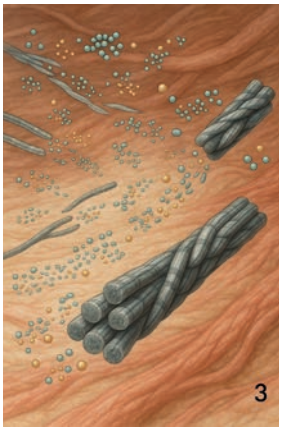

Figure 3. Extracellular processing of procollagen and collagen fibrillogenesis within the extracellular matrix.
Secreted procollagen is cleaved by extracellular procollagen peptidases to form mature collagen molecules, which spontaneously assemble into fibrils. These fibrils undergo lateral aggregation and enzymatic cross-linking, enabling the formation of mechanically resilient collagen fibers in the extracellular matrix.
Source: Own editing with ChatGPT version 5.2.

ECM–cell communication and remodeling dynamics

The ECM functions as an active signaling interface that transmits information between cells and their surrounding microenvironment. Fibroblasts and other ECM-producing cells interact with the matrix via integrin receptors and focal adhesion complexes. These structures sense and transduce mechanical and biochemical stimuli into intracellular responses – a phenomenon known as mechanotransduction. Mechanical loading (such as stretching, compression, or shear stress) activates intracellular cascades (e.g. MAPK and PI3K/Akt pathways) that regulate fibroblast proliferation and collagen synthesis. Collagen peptides can indirectly support this remodeling process by sustaining fibroblast viability and reducing pro-inflammatory cytokine production. Over time, adequate peptide availability ensures a stable equilibrium between ECM synthesis and degradation, allowing adaptive remodeling of the matrix according to tissue demands (Shigemura et al., 2009).

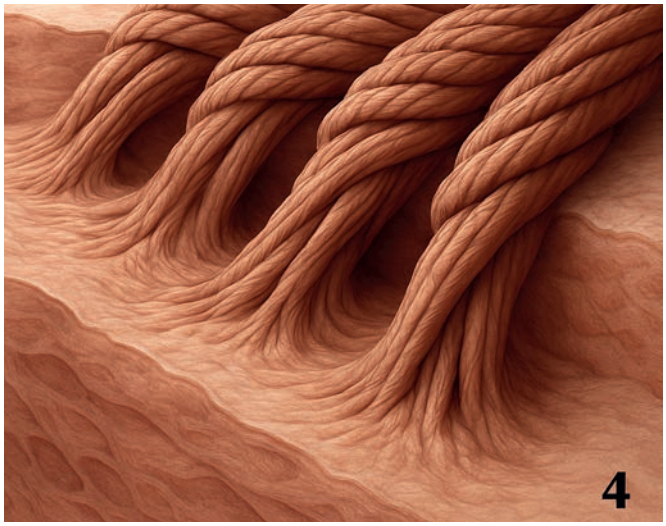

Figure 4. Tissue-level integration of newly synthesized collagen fibers into the extracellular matrix.
Mature collagen fibrils integrate into existing ECM structures, forming higher-order bundles that contribute to the tensile strength, elasticity, and durability of connective tissues. This process underlies improved structural integrity during tissue repair and remodeling.
Source: Own editing with ChatGPT version 5.2.

Functional outcomes and regenerative physiology

At the tissue and organismal level, the molecular and cellular effects of collagen peptides translate into measurable physiological benefits. Studies indicate that regular collagen peptide intake can improve skin elasticity (Shigemura et al., 2009), enhance joint mobility while reducing activity-related joint pain (Zdzieblik et al., 2017), and even strengthen the mechanical properties of tendons and ligaments (Shaw et al., 2017). There is also emerging evidence of benefits to bone health, as collagen supplementation may help maintain bone mineral density in osteopenic individuals (Daneault et al., 2017).

This integrative model highlights how nutrition, cellular signaling, and mechanical activity converge to sustain connective tissue health. The collagen–fibroblast–ECM axis provides a unifying biological framework linking molecular nutrition with regenerative physiology. Within the context of lifestyle and preventive medicine, this axis illustrates how targeted collagen peptide intake, combined with regular physical activity and proper micronutrient support, can support healthy aging, functional recovery, and structural resilience of the musculoskeletal system.

Practical recommendations for recreational and lifestyle professionals

The growing body of evidence supporting collagen peptide supplementation has clear translational relevance for recreational health promotion, rehabilitation, and preventive exercise programs. While molecular mechanisms (e.g., fibroblast signaling and ECM remodeling) form the basis for understanding efficacy, professionals working in the fields of recreational therapy, active aging, and lifestyle medicine require actionable guidance on how to apply these findings in real-world settings. This section outlines evidence-based recommendations on dosing, timing, combination with exercise, and population-specific applications for recreational practice.

Older adults

In aging populations, collagen peptide supplementation has been shown to improve joint health, skin elasticity, muscle mass, and even bone mineral density (König et al., 2018; Zdzieblik et al., 2017). In a 12-week study, daily supplementation with 15 g of specific collagen peptides combined with resistance training led to greater gains in fat-free mass and leg strength compared to exercise alone (Zdzieblik et al., 2017). Similarly, postmenopausal women taking 5 g of collagen peptides daily for 12 months showed significant increases in bone mineral density at the spine and femoral neck (König et al., 2018). Additionally, randomized trials have reported improved skin hydration and elasticity in older adults after 8–12 weeks of daily supplementation (Proksch et al., 2014).

Recommendation: For older adults, a dose of 5–10 g/day of hydrolyzed collagen peptides is appropriate, ideally for a period of 3–6 months to observe structural improvements (Daneault et al., 2017). Co-ingestion with vitamin C (at least 50–100 mg) is strongly recommended to facilitate collagen cross-linking and tissue incorporation (Shaw et al., 2017). Collagen can be incorporated into the morning routine (e.g., in tea or smoothies) and paired with low-impact aerobic exercise (e.g., walking, swimming) and moderate resistance training, which jointly promote ECM remodeling and fibroblast activation (Ghosh & Ingber, 2007).

Recreational athletes

For recreationally active individuals, collagen supplementation primarily aims to reduce activity-induced joint discomfort and enhance tissue recovery. In a randomized controlled trial, 10 g/day of collagen hydrolysate over 24 weeks significantly reduced joint pain during activity in young adults (Clark et al., 2008). A separate study demonstrated that 5 g/day for 12 weeks decreased knee joint discomfort in active individuals, with improved mobility and reduced inflammation (Zdzieblik et al., 2017). Furthermore, collagen peptides taken 30–60 minutes before exercise – particularly when combined with vitamin C – have been shown to significantly elevate markers of collagen synthesis (Shaw et al., 2017).

Recommendation: A 5–10 g/day dose of collagen peptides is suitable for recreational athletes. Timing 10–15 g of collagen with ~50 mg vitamin C about 1 hour before physical activity may further optimize tendon or ligament repair in high-stress areas (Shaw et al., 2017). While collagen is not a complete protein, it complements a protein-rich diet and can be used in addition to whey or plant-based proteins, focusing specifically on connective tissue support. It pairs well with joint-friendly strength training, mobility work, and eccentric loading protocols aimed at injury prevention.

Individuals in rehabilitation

Rehabilitation programs benefit from supporting tissue healing and reducing inflammation. Several studies have shown that collagen peptide supplementation improves functional recovery in joint instability and tendon pathologies (Dressler et al., 2018; Praet et al., 2019). For example, in a six-month intervention among athletes with chronic ankle instability, specific collagen peptide intake improved subjective joint function and reduced re-injury risk (Dressler et al., 2018). In Achilles tendinopathy, collagen combined with eccentric training supported faster return to activity, although not necessarily a shorter recovery time (Praet et al., 2019).
Recommendation: In rehabilitative contexts, 10–15 g/day of collagen peptides is suggested, especially in the early or high-demand phase of recovery. Co-supplementation with vitamin C (100–200 mg/day) ensures proper collagen fiber assembly (Shaw et al., 2017). Ideally, collagen should be consumed 30–60 minutes before physical therapy or active rehab sessions to align with increased blood flow and mechanical signaling. As part of a multidisciplinary rehabilitation strategy, collagen supplementation may promote tissue regeneration, reduce inflammation, and accelerate functional recovery without adverse effects (Daneault et al., 2017; Shigemura et al., 200).

Summary

Across populations – whether aging individuals, physically active adults, or those undergoing rehabilitation–collagen peptides offer a safe, evidence-based adjunct to support connective tissue health. Their effectiveness is maximized when combined with mechanical stimuli (i.e., exercise) and co-factors such as vitamin C. In recreational programming, collagen can be strategically integrated into lifestyle counseling, injury-prevention protocols, or active-aging programs. Its role is not to replace general protein needs but to target fibroblast-mediated ECM remodeling, which underlies musculoskeletal resilience. Thus, collagen peptide supplementation represents a valuable tool in the toolkit of recreational and lifestyle health professionals.

Discussion and future perspectives

Recent scientific advances have transformed our understanding of collagen – from viewing it as a passive structural molecule to recognizing it as an active participant in cellular signaling and tissue homeostasis. The evidence summarized in this review underscores the dual role of hydrolyzed collagen peptides as both metabolic substrates and bioactive messengers capable of influencing fibroblast gene expression and ECM dynamics.
The mechanisms by which collagen peptides exert their effects involve a series of interlinked processes:

1. Enzymatic digestion of dietary collagen into bioavailable peptide fragments;
2. Selective absorption of these peptides through intestinal PEPT1 transporters;
3. Distribution to connective tissues followed by fibroblast activation; and
4. Stimulation of collagen gene expression and ECM remodeling in those tissues.

Together, these processes establish a nutrient-driven signaling loop that helps maintain the structure and functionality of connective tissues across the lifespan.
Although the molecular basis of collagen peptide activity is increasingly well documented, several aspects remain open for exploration. For instance, the tissue-specific distribution and retention of collagen-derived peptides are not yet fully understood. Quantitative data on peptide receptor affinities, peptide half-lives in circulation, and the influence of comorbid conditions (such as diabetes or chronic inflammation) are limited. These factors may significantly modify the bioefficacy of collagen supplementation in different individuals or clinical contexts.
Furthermore, inter-individual differences in digestive efficiency, peptide transport, and genetic regulation of collagen synthesis suggest that a personalized approach to collagen peptide intake could be optimal. Integrating multi-omics technologies – proteomics, metabolomics, and transcriptomics – will help map how collagen peptides affect fibroblast function and ECM metabolism at a systems level. Such research could identify biomarkers to predict who might benefit most from collagen supplementation or how to tailor dosing and formulation for maximal effect.
From a translational standpoint, future research should focus on combining collagen-focused molecular nutrition with lifestyle interventions. This includes structured physical activity (to provide mechanostimulation to tissues), adequate micronutrient support (e.g. vitamin C, zinc, copper, which are cofactors in collagen formation), and interventions to reduce oxidative stress. These complementary factors can synergistically enhance ECM integrity and functional recovery, particularly in populations facing age-related connective tissue decline or repetitive mechanical strain (athletes and manual workers).
The integration of collagen biology into the broader field of lifestyle medicine represents a promising avenue. As mechanistic understanding deepens, collagen peptides could become part of evidence-based strategies for preventing musculoskeletal degeneration, improving injury recovery in athletes, and supporting regenerative processes in clinical rehabilitation.

Conclusions

Hydrolyzed collagen peptides have emerged as scientifically validated bioactive compounds that bridge the gap between nutrition and cellular regeneration. Through the orchestrated processes of digestion, absorption, fibroblast activation, and ECM remodeling, collagen peptides support the renewal of connective tissues at multiple biological levels.
Notably, their biological activity extends beyond simply providing amino acids. These peptides act as signaling molecules that stimulate fibroblast gene expression, inhibit MMP-mediated collagen degradation, and enhance collagen fibril organization in the matrix. Regular intake of collagen peptides has been associated with improved tissue elasticity, greater structural strength, and enhanced recovery capacity of connective tissues.
In summary, the collagen–fibroblast–ECM axis offers a mechanistic framework linking nutrient metabolism to regenerative physiology. Applying this paradigm in preventive health and sports science may help in maintaining mobility, resilience, and healthy aging. Collagen peptide supplementation, as part of a comprehensive lifestyle approach (including exercise and adequate nutrition), exemplifies how targeted molecular nutrition can sustain the body's intrinsic capacity for repair and adaptation over the lifespan.

References

Carrillo-Norte, J. A., Gervasini-Rodríguez, G., Santiago-Triviño, M. Á., García-López, V., & Guerrero-Bonmatty, R. (2024). Oral administration of hydrolyzed collagen alleviates pain and enhances functionality in knee osteoarthritis: Results from a randomized, double-blind, placebo-controlled study. *Contemporary Clinical Trials Communications, 43*, 101424. https://doi.org/10.1016/j.conctc.2024.101424

Clark, K. L., Sebastianelli, W., Flechsenhar, K. R., Aukermann, D. F., Meza, F., Millard, R. L., Deitch, J. R., Sherbondy, P. S., & Albert, A. (2008). 24-Week study on the use of collagen hydrolysate as a dietary supplement in athletes with activity-related joint pain. *Current Medical Research and Opinion, 24*(5), 1485–1496. https://doi.org/10.1185/030079908X291967

Daneault, A., Prawitt, J., Fabien-Soulé, V., Coxam, V., & Wittrant, Y. (2017). Biological effect of hydrolyzed collagen on bone metabolism. *Critical Reviews in Food Science and Nutrition, 57*(9), 1922–1937. https://doi.org/10.1080/10408398.2015.1038377

Dressler, P., Gehring, D., Zdzieblik, D., Oesser, S., Gollhofer, A., & König, D. (2018). Improvement of functional ankle properties following supplementation with specific collagen peptides in athletes with chronic ankle instability. *Journal of Sports Science and Medicine, 17,* 298–304. https://www.jssm.org

Ghosh, K., & Ingber, D. E. (2007). Micromechanical control of cell and tissue development: implications for tissue engineering. *Advanced Drug Delivery Reviews, 59*(13), 1306–1318. https://doi.org/10.1016/j.addr.2007.08.014

Iwai, K., Hasegawa, T., Taguchi, Y., Morimatsu, F., Sato, K., Nakamura, Y., Higashi, A., Kido, Y., Nakabo, Y., & Ohtsuki, K. (2005). Identification of food-derived collagen peptides in human blood after oral ingestion of gelatin hydrolysates. *Journal of agricultural and food chemistry*, *53*(16), 6531–6536. https://doi.org/10.1021/jf050206p

König, D., Oesser, S., Scharla, S., Zdzieblik, D., & Gollhofer, A. (2018). Specific collagen peptides improve bone mineral density and bone markers in postmenopausal women–A randomized controlled study. *Nutrients, 10*(1), 97. https://doi.org/10.3390/nu10010097

Oesser, S., & Seifert, J. (2003). Stimulation of type II collagen biosynthesis and secretion in bovine chondrocytes by collagen hydrolysate. *Cell and Tissue Research, 311*(3), 393–399. https://doi.org/10.1007/s00441-003-0702-8

Ohara, H., Matsumoto, H., Ito, K., Iwai, K., & Sato, K. (2007). Comparison of quantity and structures of hydroxyproline-containing peptides in human blood after oral ingestion of gelatin hydrolysates from different sources. *Journal of Agricultural and Food Chemistry, 55*(4), 1532–1535. https://doi.org/10.1021/jf062834s

Praet, S. F. E., Purdam, C. R., Welvaert, M., Vlahovich, N., Lovell, G., Burke, L. M., ... Waddington, G. (2019). Oral supplementation of specific collagen peptides combined with calf-strengthening exercises enhances function and reduces pain in Achilles tendinopathy patients. *Nutrients, 11*(1), 76. https://doi.org/10.3390/nu11010076

Proksch, E., Schunck, M., Zague, V., Segger, D., Degwert, J., & Oesser, S. (2014). Oral intake of specific bioactive collagen peptides reduces skin wrinkles and increases dermal matrix synthesis. *Skin Pharmacology and Physiology, 27*(3), 113–119. https://doi.org/10.1159/000355523

Shaw, G., Lee-Barthel, A., Ross, M. L., Wang, B., & Baar, K. (2017). Vitamin C–enriched gelatin supplementation before intermittent activity augments collagen synthesis. *American Journal of Clinical Nutrition, 105*(1), 136–143. https://doi.org/10.3945/ajcn.116.138594

Shigemura, Y., Iwai, K., Morimatsu, F., Iwamoto, T., Mori, T., Oda, C., Taira, T., Park, E. Y., Nakamura, Y., & Sato, K. (2009). Effect of Prolyl-hydroxyproline (Pro-Hyp), a food-derived collagen peptide in human blood, on growth of fibroblasts from mouse skin. *Journal of agricultural and food chemistry*, *57*(2), 444–449. https://doi.org/10.1021/jf802785h

Zdzieblik, D., Jendricke, P., Oesser, S., Gollhofer, A., & König, D. (2021). The influence of specific bioactive collagen peptides on body composition and muscle strength in middle-aged, untrained men: A randomized controlled trial. *International Journal of Environmental Research and Public Health, 18*(9), 4837. https://doi.org/10.3390/ijerph18094837

Zdzieblik, D., Oesser, S., Gollhofer, A., & König, D. (2017). Improvement of activity-related knee joint discomfort following supplementation of specific collagen peptides. *Applied Physiology, Nutrition, and Metabolism, 40*(6), 588–595. https://doi.org/10.1139/apnm-2016-0390