Life Sciences Student Journal

2025 Vol.3 No.3, pp: 45-55

DOI: 10.22034/LSSJ.2025.173

Different form of Collagen Type I and Its Applications in Biomedicine, Nutrition, and Industry

Mohammad Hamed Rashidi[1] ,Mostafa Eslami[2,], Soheila Naderi Gharahgheshlagh[3] and Mohammad Reza Nourani [4,5, *]

1. School of Pharmacology, Baqiyatallah University of Medical Sciences, Tehran, Iran
2. School of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran
3. Burn Research Center, Iran University of Medical Sciences, Tehran, Iran
4. Research and Development Dept. Exir Health Technology Pioneers Company, Tehran, Iran
5. Tissue Engineering and Regenerative Medicine Research Center, New Health Technology Institute, Baqiyatallah university of Medical Sciences, Tehran, Iran

*. Corresponding Author: Mohammad Reza Nourani, r.nourani@yahoo.com

Mohammad Hamed Rashidi

Article type: Review article

Received: 12 Oct. 2025

Revised: 30 Oct. 2025

Accepted: 19 Nov. 2025

Abstract:

Collagen, the most abundant protein in the extracellular matrix, is essential for the strength and function of connective tissues. Of its 28 types, Type I collagen is the most prevalent and widely studied, with applications spanning biomedicine, nutrition, and industry. This review highlights its molecular structure, hierarchical organization, and processed forms: native collagen, atelocollagen, and hydrolyzed collagen peptides. Each form offers distinct properties—native collagen provides mechanical strength, atelocollagen reduces immunogenicity while retaining biocompatibility, and hydrolyzed peptides enhance bioavailability for nutritional and cosmetic use. Special attention is given to fish-derived collagen, a sustainable alternative to mammalian sources, offering lower immunogenicity, reduced zoonotic risk, and compatibility with halal and kosher standards. Extraction protocols, including acid treatment, enzymatic digestion, and hydrolysis, are outlined with emphasis on yield optimization and molecular control. Ultimately, the choice of collagen form depends on structural integrity, immunogenicity, bioavailability, and application-specific requirements, guiding rational use across biomedical and industrial domains.

Keywords: Collagen Type I, Native collagen, Atelocollagen, Hydrolyzed collagen peptides

Introduction

Collagen is the most abundant structural protein in the extracellular matrix of animal tissues, accounting for approximately 30% of total protein content in the human body(1).

It plays a fundamental role in maintaining the structural integrity, mechanical strength, and biological function of connective tissues such as skin, bones, tendons, ligaments, cartilage, and blood vessels. Collagen molecules contribute to tissue architecture by forming fibrous networks that support cellular adhesion, migration, and differentiation, making them indispensable in both physiological and pathological processes (2–4). Among the 28 distinct types of collagens identified to date, Type I collagen is the most prevalent and extensively studied. It is primarily found in dermis, bone, cornea, and tendons, where it provides tensile strength and resistance to mechanical stress (1). Structurally, Type I collagen consists of two α1(I) chains and one α2(I) chain, which assemble into a right-handed triple helix stabilized by hydrogen bonds and hydrophobic interactions. These helices further aggregate into fibrils and fibers, forming the backbone of connective tissue matrices (2,5).

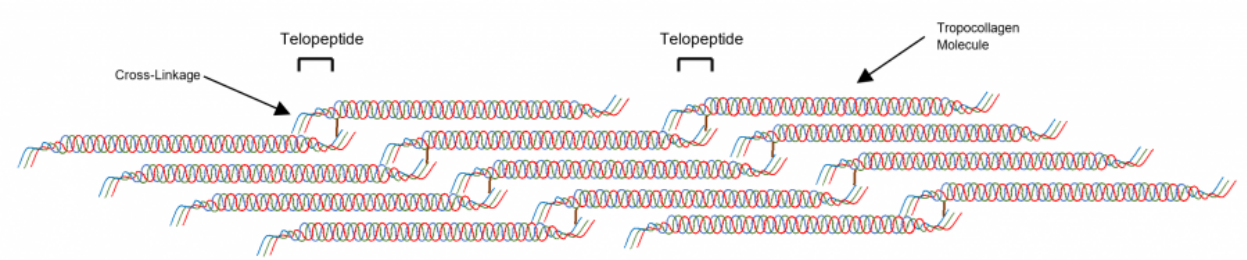

Figure 1. Structure of a collagen fibril. Tropocollagen molecules are cross-linked by bonds at their telopeptide sequences, forming collagen fibrils. Collagen fibrils provide structural support in the ECM. The cross-linkages between telopeptide sequences of α-chains increase the strength of collagen fibers(6).

The biomedical relevance of Type I collagen extends beyond its native biological function. Due to its biocompatibility, biodegradability, and ability to support cell growth, it has become a cornerstone material in tissue engineering, wound healing, drug delivery systems, and regenerative medicine(7,8). In addition, its processed forms such as atelocollagen (with reduced immunogenicity) and hydrolyzed collagen (with enhanced bioavailability) have opened new avenues in clinical, cosmetic, and nutritional applications (9). Recent advances in extraction technologies, particularly from marine sources such as fish skin and scales, have further expanded the accessibility and sustainability of collagen production. Marine-derived collagen offers advantages in terms of lower risk of zoonotic transmission, compatibility with halal and kosher markets, and reduced environmental impact (3,9,10). These developments have positioned collagen not only as a biological scaffold but also as a functional ingredient in health-promoting formulations.

This review aims to provide a comprehensive overview of Type I collagen, including its

molecular structure, processed forms, specialized applications, and extraction protocols from various forms. Emphasis is placed on the translational potential of fish-derived collagen and its alignment with industrial and biomedical standards.

Chemical Structure of Collagen

Collagen is a fibrous protein characterized by a unique triple-helical structure that distinguishes it from globular proteins. The primary building block of collagen is the tropocollagen molecule, which consists of three polypeptide chains (α-chains) wound around each other in a right-handed triple helix. In Type I collagen, the most abundant form in vertebrates, this helix is composed of two α1(I) chains and one α2(I) chain, encoded by the *COL1A1* and *COL1A2* genes, respectively (11).

Amino Acid Composition and Primary Structure

The amino acid sequence of collagen is highly repetitive, dominated by the tripeptide motif Gly–X–Y, where glycine is present at every third residue, and X and Y are frequently proline and hydroxyproline. Glycine, the smallest amino acid, allows tight packing of the three chains, while hydroxyproline contributes to thermal stability through hydrogen bonding(12). This unique sequence enables the formation of a rigid, rod-like triple helix approximately 300 nm in length and 1.5 nm in diameter. (2).

Post-Translational Modifications

Collagen biosynthesis involves extensive post-translational modifications: Hydroxylation of proline and lysine residues by prolyl and lysyl hydroxylases, requiring vitamin C as a cofactor. Glycosylation of hydroxylysine residues with galactose or glucose-galactose units. Formation of disulfide bonds in the C-terminal propeptides, which guide proper chain alignment and helix formation. These modifications are essential for triple helix stability and fibril assembly. Defects in hydroxylation, as seen in scurvy, lead to impaired collagen synthesis and tissue fragility(11).

Triple Helix and Quaternary Structure

Once synthesized, the three α-chains align and fold into a triple helix in the endoplasmic reticulum. The helix is stabilized by interchain hydrogen bonds, particularly involving hydroxyproline residues. The C-terminal region initiates folding, while the N-terminal region completes it. After secretion into the extracellular space, propeptides are cleaved, and tropocollagen molecules spontaneously assemble into fibrils through staggered alignment and lateral interactions(12).

These fibrils are further stabilized by covalent crosslinks formed by lysyl oxidase-mediated deamination of lysine and hydroxylysine residues. The resulting mature collagen fibers exhibit remarkable tensile strength and durability, essential for load-bearing tissues such as bone and tendon(13).

Hierarchical Organization

Collagen exhibits a hierarchical structure

Molecular level: Triple helix of tropocollagen. Supramolecular level: Fibrils formed by staggered tropocollagen units and Macroscopic level: Fibers and bundles integrated into connective tissues This multiscale organization allows collagen to function as both a structural

scaffold and a dynamic signaling matrix, influencing cell behavior, migration, and differentiation(14,15).

Different Forms of Type I Collagen: Structure, Processing, and Applications

Type I collagen can be processed into distinct forms depending on its intended biomedical, cosmetic, or nutritional application (Table 1) (Fig2). The three most widely used forms are:

Native Type I Collagen

Structure: Native collagen retains its full triple-helical structure along with intact terminal regions known as telopeptides. These telopeptides are essential for natural fibril formation and crosslinking, mimicking the physiological architecture of connective tissues (11). Processing: Extracted using acidic solutions (e.g., acetic acid) without enzymatic treatment. The preservation of telopeptides results in higher immunogenic potential but also superior mechanical strength.

Applications: biomedical scaffolds for tissue engineering, wound dressings and skin regeneration matrices and bone grafts and orthopedic implants

Advantages: High tensile strength, natural fibril formation Limitations: Low solubility, potential immunogenicity

Atelocollagen

Structure: Atelocollagen is derived from native collagen by enzymatic removal of telopeptides, typically using pepsin. This modification reduces antigenicity while preserving the triple-helical core(2).

Processing: Pepsin digestion under acidic conditions selectively cleaves telopeptides, yielding a more biocompatible form. It remains soluble in acidic environments and can be reconstituted into gels or membranes.

Applications: Injectable biomaterials for soft tissue augmentation, drug delivery systems and cell culture substrates for 3D scaffolding.

Advantages: Reduced immunogenicity, improved biocompatibility
Limitations: Requires precise purification, higher cost

Hydrolyzed Collagen (Collagen Peptides)

Structure: Hydrolyzed collagen consists of short-chain peptides (<5 kDa) resulting from enzymatic or chemical breakdown of the triple helix. It lacks the native structure and does not form fibrils (7).

Processing: Hydrolysis is performed using proteolytic enzymes such as alcalase, papain, or trypsin. The resulting peptides are water-soluble and highly bioavailable.

Applications: Oral supplements for joint, skin, and bone health, functional foods and beverages, cosmetic formulations for anti-aging and hydration.

Advantages: High absorption, low allergenicity
Limitations: No structural integrity, unsuitable for scaffolding(10)

Table 1: Comparative Forms of Type I Collagen

Form	Structure	Processing Method	Key Applications	Advantages	Limitations	Ref.
Native Collagen	Triple helix + intact telopeptides	Acid extraction	Scaffolds, wound healing, bone grafts	High strength, natural fibrils	Immunogenicity, low solubility	(11)
Atelocollagen	Triple helix – telopeptides removed	Pepsin digestion	Injectable gels, drug delivery, cell scaffolds	Biocompatible, reduced antigenicity	Costly, needs purification	(2)
Hydrolyzed Collagen	Short peptides (<5 kDa), no helix	Enzymatic hydrolysis	Supplements, cosmetics, functional foods	High bioavailability, soluble	No fibril formation, no mechanical use	(7)

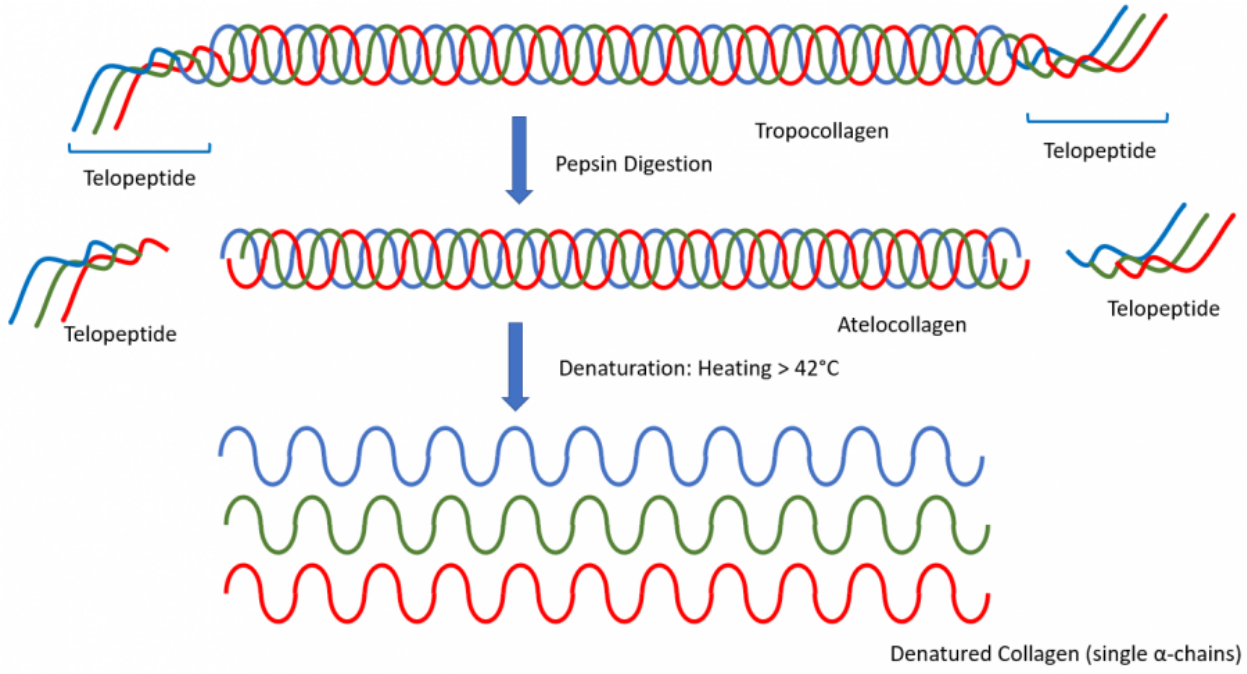

Figure 2. Pepsin digestion will cleave the telopeptide sections of the tropocollagen molecules, resulting in atelocollagen. When atelocollagen is exposed to temperatures above 42°C, it loses its triple-helix structure, resulting in three individual α-chains(6).

Different forms of Collagen type 1 Extraction Protocols from fish skin

Fish-derived collagen is gaining popularity due to its sustainability, low immunogenic risk, and compatibility with halal markets (8,9). Bovine and porcine sources are widely used but raise concerns about zoonotic diseases and religious restrictions.

Native Collagen type 1 Extraction Protocols from fish skin

Native collagen refers to the unmodified, naturally occurring form of collagen that preserves its characteristic triple-helical conformation and complete polypeptide chains. This structural integrity is essential for maintaining the biological and mechanical properties of collagen, such as tensile strength, thermal stability, and its ability to support cell adhesion and tissue scaffolding. Native collagen is typically found in connective tissues like skin, tendon, cartilage, nerve and bone, where it plays a critical role in maintaining structural integrity and facilitating cellular interactions(16). Its intact molecular architecture makes it particularly valuable for biomedical applications that require high biocompatibility and functional mimicry of the extracellular matrix. One notable application is in corneal tissue engineering, where native collagen scaffolds are used to support epithelial cell growth and restore vision in patients with corneal damage.

The collagen extraction process has already been completed by our team and is summarized (8) and by Ampitiya, A.G.D.M and their colleagues(17) as below (Fig 2):

Pre-treatment: Washing, defatting, demineralization, Extraction: Acidic (e.g., acetic acid) for native collagen, Purification: Dialysis, filtration, freeze-drying or spray-drying. Optimization of pH, temperature is critical for yield and molecular weight control (5).

Atelocollagen extraction

Atelocollagen is a purified form of collagen in which the non-helical terminal regions, known as telopeptides, have been enzymatically removed. These telopeptides are primarily responsible for intermolecular cross-linking and are known to contribute to immunogenic responses when collagen is introduced into biological systems. By eliminating these regions, typically through pepsin digestion, atelocollagen exhibits significantly reduced antigenicity while retaining the structural integrity of the triple helix. This enhances its biocompatibility and makes it particularly suitable for biomedical applications such as tissue engineering, wound healing, and injectable formulations. In addition to medical use, atelocollagen is increasingly applied in cosmetic products for skin regeneration and anti-aging treatments due to its excellent dermal absorption and bioactivity (Fig3).

Atelocollagen extraction

Atelocollagen is a purified form of collagen in which the non-helical terminal regions, known as telopeptides, have been enzymatically removed.

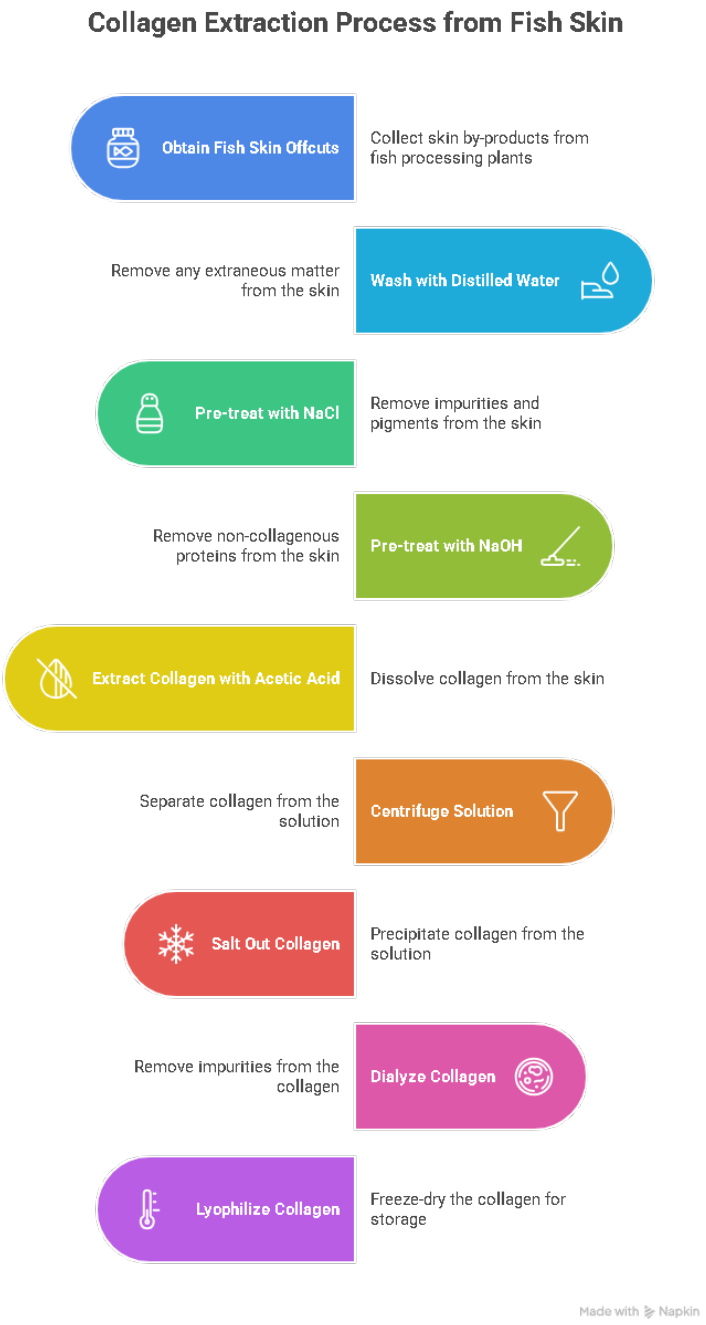

Figure 3: Collagen extraction processes from fish skin

These telopeptides are primarily responsible for intermolecular cross-linking and are known to contribute to immunogenic responses when collagen is introduced into biological systems. By eliminating these regions, typically through pepsin digestion, atelocollagen exhibits significantly reduced antigenicity while retaining the structural integrity of the triple helix. This enhances its biocompatibility and makes it particularly suitable for biomedical

applications such as tissue engineering, wound healing, and injectable formulations. In addition to medical use, atelocollagen is increasingly applied in cosmetic products for skin regeneration and anti-aging treatments due to its excellent dermal absorption and bioactivity.

The following protocol is adapted from recent advancements in marine collagen extraction, with a focus on fish skin as a sustainable and collagen-rich source. Fish skin offers several advantages over terrestrial sources, including lower risk of zoonotic disease transmission, high collagen content, and favorable amino acid profiles. The method integrates alkali pretreatment, acid extraction, enzymatic digestion, and purification steps to yield high-quality atelocollagen suitable for downstream characterization and application(18)(Fig4).

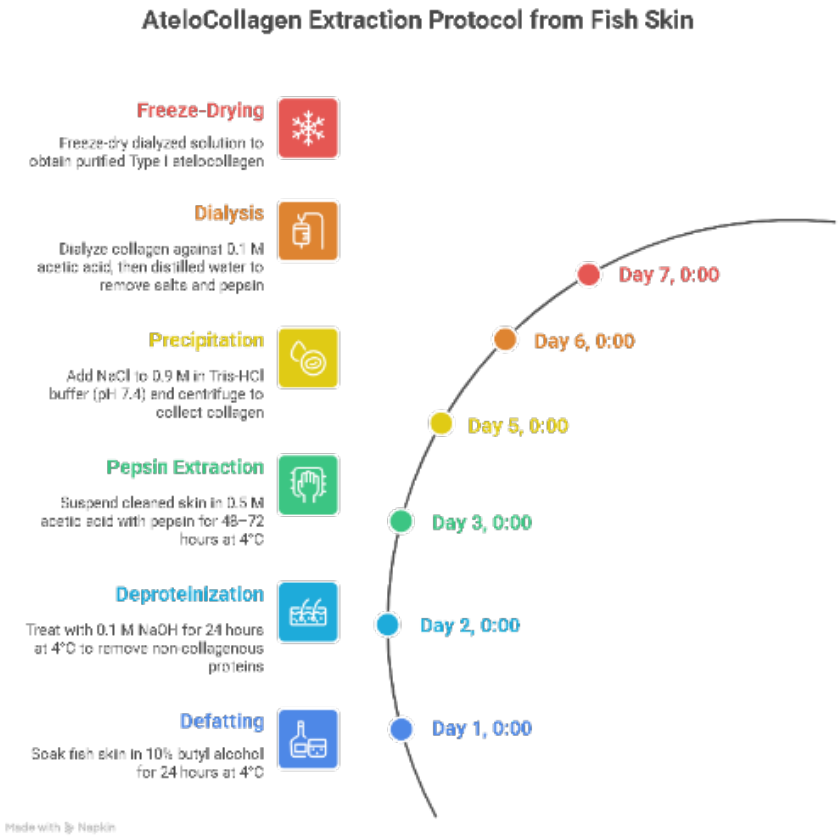

Figure 4: AteloCollagen extraction processes from fish skin

Hydrolyzed (peptide) collagen extraction

Collagen peptides from marine organisms have drawn great attention in food, cosmetics and medicine owing to their multiple functions including antioxidant, anticancer, cardioprotection, skin protection, and wound healing effects(19).

Comparative Market Perspective

In the global collagen market, bovine and porcine sources have traditionally dominated due to high yield and established supply chains. However, fish-derived collagen is gaining traction as a sustainable and ethically favorable alternative. Fish collagen offers superior bioavailability and lower immunogenicity, making it attractive for biomedical and cosmetic applications(20). Importantly, fish collagen is widely accepted in halal and kosher markets, whereas bovine and porcine sources face religious and cultural restrictions(21). Although fish collagen extraction yields are generally lower and production costs higher, its compatibility with diverse dietary standards and reduced zoonotic risk justify its growing(20).The collagen peptide supplement market is expanding rapidly, driven by consumer interest in skin health, joint support, and anti-aging benefits. As of 2025, collagen peptides represent a multi-billion-dollar segment, with fish collagen increasingly featured in functional foods, nutricosmetics, and dermal formulations. This shift reflects a broader industry trend toward clean-label, bioactive ingredients that align with health, sustainability, and ethical sourcing priorities(22).

Conclusion

Type I collagen remains a cornerstone biomaterial due to its structural versatility, biocompatibility, and broad applicability. Its processed forms native collagen, atelocollagen, and hydrolyzed peptides offer tailored solutions for medical, cosmetic, and nutritional needs. Marine-derived collagen, particularly from fish skin, has emerged as a sustainable and effective source, aligning with global health and ethical standards. Optimized extraction and purification protocols enhance yield, reduce immunogenicity, and improve functional performance. As research advances, collagen's role in regenerative medicine, functional foods, and industrial formulations will continue to expand, reinforcing its value across disciplines

Aknowlegement:

The author gratefully acknowledges the use of Napkin for figure design and Copilot for assistance with paraphrasing, as well as the support provided by the Research and Development Department of Exir Health Technology Pioneers Company, Tehran, Iran.

References

1. Shoulders MD, Raines RT. Collagen Structure and Stability. Annu Rev Biochem. 2009 Jun 1;78(1):929–58.
2. Ricard-Blum S. The Collagen Family. Cold Spring Harb Perspect Biol. 2011 Jan 1;3(1):a004978–a004978.
3. Maboud AlizadehNodeh, Zahra Moradi, Mohammad Reza Nourani. Isolation and Purification of Collagen from the Skin of Black Pomfret (Parastromateus Niger) for Tissue Engineering Purpose. The Journal of Applied Tissue Engineering. 2014;1(1):18–21.

4. Aazam Rahimi ANJANGREBSEB. Motor neurons differentiation of encapsulated human endometrial stem cells in collagen without HLA-DR expression. Journal of Applied Tissue Engineering. 2019 Dec 4;6(1).

5. Canelón SP, Wallace JM. β-Aminopropionitrile-Induced Reduction in Enzymatic Crosslinking Causes In Vitro Changes in Collagen Morphology and Molecular Composition. PLoS One. 2016 Nov 9;11(11):e0166392.

6. https://www.chondrex.com/blog/type-i-type-ii-collagen-structure-influences-staining-patterns. Chondrex, Inc. Type I & Type II Collagen: Structure Influences Staining Patterns.

7. Bello AE, Oesser S. Collagen hydrolysate for the treatment of osteoarthritis and other joint disorders:a review of the literature. Curr Med Res Opin. 2006 Nov 10;22(11):2221–32.

8. Maboud AlizadehNodeh, Zahra Moradi, Mohammad Reza Nourani. Isolation and Purification of Collagen from the Skin of Black Pomfret (Parastromateus Niger) for Tissue Engineering Purpose. The Journal of Applied Tissue Engineering. 2014;1(1):18–21.

9. Jafari H, Lista A, Siekapen MM, Ghaffari-Bohlouli P, Nie L, Alimoradi H, et al. Fish Collagen: Extraction, Characterization, and Applications for Biomaterials Engineering. Polymers (Basel). 2020 Sep 28;12(10):2230.

10. Hema GS, Joshy CG, Shyni K, Chatterjee NS, Ninan G, Mathew S. Optimization of process parameters for the production of collagen peptides from fish skin (Epinephelus malabaricus) using response surface methodology and its characterization. J Food Sci Technol. 2017 Feb 31;54(2):488–96.

11. Shoulders MD, Raines RT. Collagen Structure and Stability. Annu Rev Biochem. 2009 Jun 1;78(1):929–58.

12. Ramshaw JAM, Shah NK, Brodsky B. Gly-X-Y Tripeptide Frequencies in Collagen: A Context for Host–Guest Triple-Helical Peptides. J Struct Biol. 1998;122(1–2):86–91.

13. Herchenhan A, Uhlenbrock F, Eliasson P, Weis M, Eyre D, Kadler KE, et al. Lysyl Oxidase Activity Is Required for Ordered Collagen Fibrillogenesis by Tendon Cells. Journal of Biological Chemistry. 2015 Jun;290(26):16440–50.

14. Fratzl P. Collagen: Structure and mechanics. Springer Science & Business Media.; 2008.

15. KOKEN. KOKEN CO., LTD 1-4-14 Koraku,Bunkyo-ku Tokyo 112-0004, Japan. Atelocollagen/Native Collagen Acidic Solutions.

16. Navid Dehnavi, Kazem Parivar, Vahabodin Goodarzi, Ali Salimi MRN. Systematically engineered electrospun conduit based on PGA/collagen/bioglass nanocomposites: The evaluation of morphological, mechanical, and bio-properties.

17. Ampitiya AGDM, Gonapinuwala ST, Fernando CAN, de Croos MDST. Extraction and characterisation of type I collagen from the skin offcuts generated at the commercial fish processing centres. J Food Sci Technol. 2023 Feb 9;60(2):484–93.

18. Hsieh DJ, Srinivasan P. Protocols for Accelerated Production and Purification of Collagen Scaffold and Atelocollagen from Animal Tissues. Biotechniques. 2020 Sep 3;69(3):220–5.

19. Hou NT, Chen BH. Extraction, purification and characterization of collagen peptide prepared from skin hydrolysate of sturgeon fish. Food Quality and Safety. 2023 Jan 1;7.

20. Abu-Al-Basal MA. Healing potential of Rosmarinus officinalis L. on full-thickness excision cutaneous wounds in alloxan-induced-diabetic BALB/c mice. J Ethnopharmacol. 2010 Sep;131(2):443–50.

21. Baradwan S, AlJaroudi D, Agdi M, Hafedh B, Abduljabbar HH, Sabban H, et al. Calcium versus cabergoline for prevention of ovarian hyperstimulation syndrome: A systematic review and meta-analysis. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2024 Oct; 301:1–11.

22. Abuine R, Rathnayake AU, Byun HG. Biological activity of peptides purified from fish skin hydrolysates. Fish Aquatic Sci. 2019 Dec 23;22(1):10.

23. ETprotein R&D team. https://www.etprotein.com/bovine-collagen-vs-fish-collagen-a-complete-comparison/. 2025. https://www.etprotein.com/bovine-collagen-vs-fish-collagen-a-complete-comparison/.

24. Karim Banna. https://fishingandfish.com/is-fish-collagen-better-than-bovine/. 2025. Fish Collagen vs. Bovine: Key Benefits, Differences, and Which is Better?

25. Choosing the Right Collagen for Your Product Line: Fish, Bovine, or Porcine. https://www.champion-bio.com/news-detail/choosing-right-collagen-for-products/ [Internet]. 2025.