International Journal of Biomaterials

WILEY

REVIEW ARTICLE OPEN ACCESS

Collagen Biomaterials: From Traditional Animal Sources to Marine and Recombinant Alternatives

Noushin Rezaeivandchali[1] | Lionel Hebbard[1,2,3] | Craig McFarlane[1,2]

[1]Discipline of Biomedical Sciences and Molecular Biology, College of Medicine and Dentistry, James Cook University, Townsville 4811, Queensland, Australia | [2]Australian Institute of Tropical Medicine and Health, Centre for Molecular Therapeutics, Centre for Tropical Bioinformatics and Molecular Biology, James Cook University, Townsville 4811, Queensland, Australia | [3]Storr Liver Centre, Westmead Institute for Medical Research, Westmead Hospital and University of Sydney, Westmead 2145, New South Wales, Australia

Correspondence: Craig McFarlane (craig.mcfarlane@jcu.edu.au)

Received: 9 November 2025 | **Revised:** 6 February 2026 | **Accepted:** 20 February 2026

Academic Editor: Kai-Chiang Yang

Keywords: biomaterials | biomedical | collagen | cosmetics | food and beverage | land animal collagen | marine collagen | recombinant collagen

ABSTRACT

Collagen is the most abundant structural protein in animals and a key biomaterial due to its biocompatibility, biodegradability, and versatile functional properties. Traditionally, collagen has been obtained from land animal tissues such as bovine, porcine, and donkey skin, tendon, and bone. However, concerns regarding disease transmission, immunogenicity, and cultural restrictions have driven the exploration of alternative sources. Marine organisms, including fish, jellyfish, and sea cucumber, provide collagens that are widely reported to exhibit lower immunogenic responses compared with mammalian sources, alongside reduced zoonotic and prion-related safety concerns, although these observations are context-dependent and influenced by species origin, processing methods, and intended application. More recently, recombinant technologies using microbial and eukaryotic expression systems have emerged as innovative strategies to produce human-like collagens with tailored properties and improved safety. Together, these diverse sources expand the availability of collagen for a wide range of applications, from food and beverage systems to biomedical uses in tissue engineering, wound healing, and cosmetics. By outlining the advantages and limitations of land animal, marine, and recombinant collagen sources, this review highlights the growing importance of collagen as a multifunctional biomaterial and underscores the potential of emerging sustainable alternatives.

1 | Introduction

Biomaterials serve as substitutes for biological tissues in the human body and have the ability to interact with biological systems. They can be broadly classified into natural and synthetic, both of which have been extensively developed for therapeutic applications over the past 5 decades [1]. Traditionally, biomaterials were primarily composed of synthetic polymers designed to replicate the mechanical properties of native tissues. However, these often fail to achieve the same level of biocompatibility and bioactivity as naturally derived alternatives. In response, researchers have increasingly focused on extracellular matrix (ECM)-based biomaterials, which preserve the biochemical and structural framework needed to support cell adhesion, proliferation, and tissue remodeling [2, 3]. Moreover, natural ECM-based biomaterials can modulate the immune system, making them more suitable for clinical applications such as tissue regeneration [4]. Additionally, the ability to modify ECM biomaterials with functional additives, such as antimicrobial agents or growth factors, expands their potential in biomedical and therapeutic applications [5, 6]. Among natural ECM-derived biomaterials, collagen is one of the most widely studied due to its biocompatibility, biodegradability, and widespread availability [7]. As the primary structural protein in the

ECM, collagen plays a crucial role in maintaining biological and structural integrity. It is a highly dynamic molecule, continuously undergoing remodeling in response to physiological processes. In humans, collagen constitutes approximately 30% of the total body protein content [8] and interacts with cells through multiple receptor families, such as integrins and discoidin domain receptors (DDRs) [9, 10]. These interactions influence critical cellular functions, including proliferation, migration, and differentiation, which are essential for tissue regeneration [11]. Due to its versatile structural properties, collagen can be processed into various biomaterial forms for diverse biomedical applications. These include hydrogels, membranes, films, scaffolds, sponges, and microspheres, each designed to support specific therapeutics (Table 1). The performance of collagen-based biomaterials is strongly influenced by their source. Land animal, marine, and recombinant collagens each present unique advantages and limitations in terms of stability, functionality, sustainability, and acceptability. Importantly, these material attributes determine collagen performance not only in regenerative and tissue-interfacing biomaterials but also in cosmetic and food-related systems, where collagen acts as a bioactive, degradable material that interacts with biological tissues or cells. Therefore, this review evaluates collagen derived from diverse sources through a biomaterials-oriented perspective, emphasizing how source- and processing-dependent properties influence suitability for applications ranging from wound healing and tissue engineering to cosmetic formulations and food systems.

2 | Methods: Literature Search and Data Curation

This review was conducted as a narrative literature review with structured data curation to enable quantitative comparison of collagen sources. A comprehensive literature search was performed using PubMed, Web of Science, and Scopus databases. Titles and abstracts were screened for relevance, followed by full-text assessment of eligible studies.

Searches were conducted from December 1989 to July 2025 to capture both foundational studies on collagen structure and extraction, as well as recent advances in marine and recombinant collagen technologies, covering articles published in English. Search terms included combinations of keywords related to collagen source, extraction, and properties, such as “collagen extraction,” “marine collagen,” “land animal collagen,” “recombinant collagen,” “yield,” “imino acid content,” “denaturation temperature,” “thermal stability,” “biomedical collagen,” and “collagen applications.” Reference lists of relevant reviews were also manually screened to identify additional original studies. Studies were included if they reported original experimental data on collagen isolated from land animal, marine, or recombinant sources and provided quantitative measurements relevant to comparison, including extraction yield, imino acid content, and/or denaturation temperature. Conference abstracts and studies lacking quantitative data were excluded. For quantitative data, reported values were harmonized to common units (e.g., percentage yield, residues per 1000 amino acids, and temperature in °C). When multiple values were reported for the same source due to different tissues or extraction methods, each value was retained and reported separately to reflect methodological variability rather than averaged.

3 | Characteristics of Collagen

The collagen superfamily includes approximately 28 types formed from at least 46 different α-chains, each with distinct structures and functions in tissue integrity, and some linked to disease [37]. Collagens are grouped as fibrillar or nonfibrillar. In vertebrates, fibrillar collagens make up nearly 90% and provide the main structural framework of the ECM; the classical fibrillar Types are I, II, III, V, XI, XXIV, and XXVII [38, 39]. All collagens share a triple-helical molecule of three α-chains, built on the repeating Gly–X–Y motif (often pro and hydroxyproline), which is essential for helix stability [40]. The basic unit, tropocollagen, assembles through electrostatic and hydrophobic interactions into fibrils and fibers, with short nonhelical telopeptides at each end that enable intermolecular cross-linking and matrix binding [41, 42]. By contrast, nonfibrillar collagens contain natural interruptions in the Gly–X–Y sequence within their triple helix, adding flexibility and allowing nonfibrillar architectures, for example, network-forming Type IV in basement membranes [43]. The fibrillar collagens, including Types I, II, and III, are the dominant subgroup [44] because they form the principal scaffold of the ECM and are central to maintaining tissue structure and enabling biomedical applications [39]. The main characteristics, sources, and biomedical relevance of these fibrillar collagens are summarized in Table 2.

4 | Collagen Biosynthesis and Fibril Assembly

Collagen biosynthesis is a complex process that is essential for maintaining tissue structure and function. Beyond simply producing structural proteins, collagen biosynthesis involves multiple steps of regulation to ensure that collagen molecules are properly modified, folded, and assembled. The enzymatic hydroxylation and glycosylation of specific amino acid residues play a critical role in stabilizing the triple-helical structure and promoting intermolecular interactions. These modifications not only affect fibril formation but also influence collagen resistance to proteolytic degradation and its interaction with other matrix components. Mutations or disruptions at various stages of this pathway, whether during gene transcription, post-translational processing, or extracellular assembly, can lead to connective tissue disorders. Furthermore, the precise cleavage of propeptides by enzymes, such as a disintegrin and metalloproteinase with thrombospondin motifs (ADAMTS) and bone morphogenetic protein 1 (BMP-1), serves as a regulatory checkpoint, ensuring that correctly folded procollagen is incorporated into the ECM [69, 70]. The key steps of the collagen biosynthesis pathway are summarized in Figure 1.

5 | Collagen-Mediated Regulation of Cellular Behavior

Collagen fibrils not only provide structural support but also regulate cellular behavior through receptor-mediated signaling [71]. Cells interact with collagen through a diverse range of surface receptors, including integrins, DDRs, glycoprotein VI (GPVI), leukocyte-associated immunoglobulin-like receptor-1 (LAIR-1), osteoclast-associated receptor (OSCAR), and uPARAP/Endo180. These receptors recognize specific collagen motifs and initiate intracellular signaling pathways that regulate cytoskeletal organization and gene expression and ultimately

TABLE 1 | Summary of collagen-based biomaterials and their applications.

Collagen biomaterial	Description	Applications	Refs.
Hydrogels	Hydrophilic polymer networks capable of absorbing significant amounts of water, allowing cells to adhere, proliferate, and differentiate	• Vascular grafts • Wound dressing • Skin tissue engineering • Corneal tissue engineering • Dermal fillers • Drug delivery systems	[12–19]
Membranes	A thin biodegradable collagen structure designed as a barrier	• Guided bone regeneration • Oral tissue healing • Burn wound healing	[20–22]
Films	A thin transparent, and elastomeric polymer sheet	• Wound healing • Bone tissue engineering • Food packaging	[23–25]
Scaffolds	A three-dimensional, highly porous, and interconnected structure	• Bone tissue engineering • Vascular tissue engineering	[26–29]
Sponges	A three-dimensional, highly porous, and interconnected structure providing temporary or permanent coverage	• Acute wound healing • Oral tissue healing	[30–34]
Microspheres	Spherical biodegradable polymeric particles with tunable size and surface properties	• Drug delivery • Bone tissue engineering	[35, 36]

Note: This table summarizes the primary forms of collagen-based biomaterials, describing their physical characteristics and typical biomedical applications. Each entry highlights how specific formats such as hydrogels, membranes, films, scaffolds, sponges, and microspheres are engineered to support various therapeutic outcomes, including tissue repair, drug delivery, and regenerative medicine. Relevant references are provided.

TABLE 2 | Fibrillar collagen types: sources, applications, and biomedical relevance.

Collagen type	Fibrillar collagen α chains	Primary sources	Applications	Refs.
I	α1(I), α2(I)	Skin, tendon, bone, ligament, cornea	• Skin smoothness • Regenerative medicine therapies • Chronic wound healing • Drug delivery systems • Food and nutrition	[45–50]
II	α1(II)	Cartilage	• Joint protection • Cartilage preservation	[51–54]
III	α1(III)	Skin, blood vessels, cornea	• Skin smoothness • Corneal tissue engineering • Collagen fibrillogenesis	[45, 55, 56]
V	α1(V), α2(V), α3(V)	Skin, tendon, bone, ligament, cornea	• Collagen fibrillogenesis • Cardiac repair • Wound healing	[57–59]
XI	α1(XI), α2(XI), α3(XI)	Cartilage, tendon	• Tendon matrix organization • Cartilage matrix organization • Predictive biomarker for early malignant transformation in breast lesions	[60–63]
XXIV	α1(XXIV)	Bone, cornea, cartilage	• Bone matrix mineralization • Osteoblast differentiation • Collagen fibrillogenesis	[64–66]
XXVII	α1(XXVII)	Cartilage, bone	• Cartilage calcification • Bone formation • Cartilage matrix organization	[67, 68]

Note: This table presents the major types of fibrillar collagen, detailing their α-chain composition, primary tissue sources, and key biomedical applications. Each collagen type is associated with specific structural and functional roles relevant to tissue engineering and regenerative medicine. Relevant references are provided.

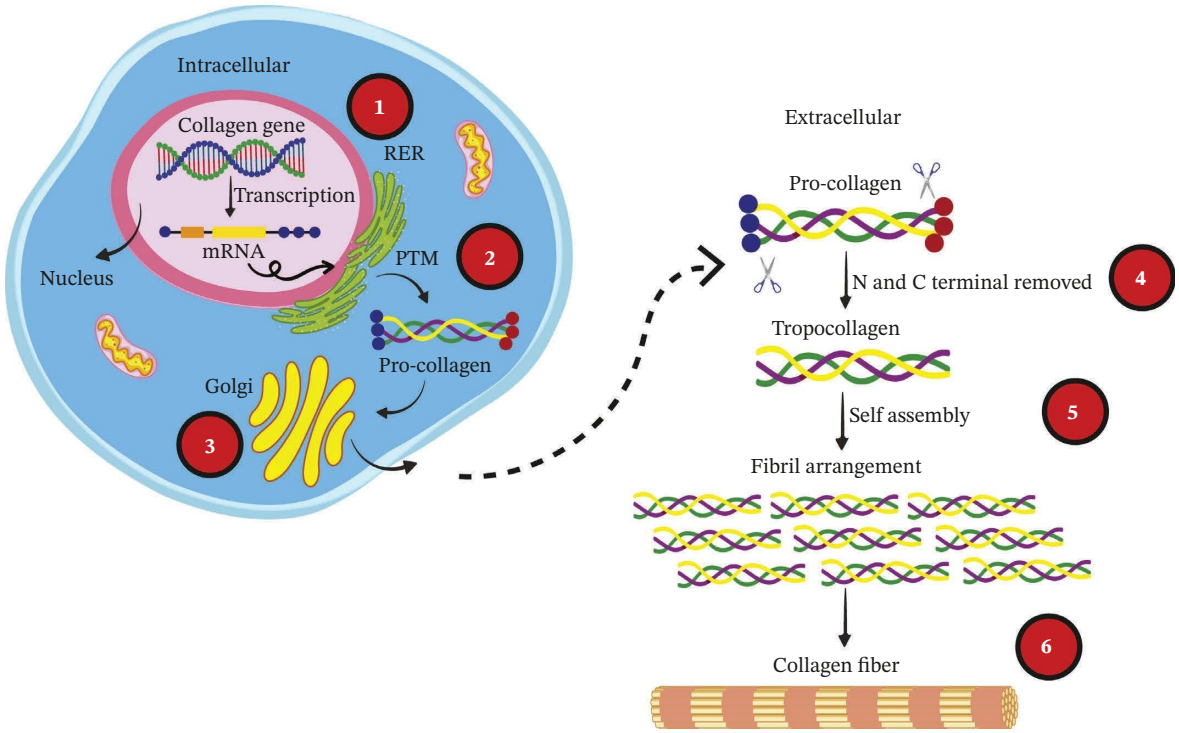

FIGURE 1 | Overview of collagen biosynthesis. This process occurs in both intracellular and extracellular regions. (1) In the nucleus, the collagen gene is transcribed into mRNA. (2) The mRNA is translated on the rough endoplasmic reticulum (RER), where post-translational modifications (PTMs) such as hydroxylation and glycosylation produce pro-collagen. (3) Pro-collagen is then transported to the Golgi apparatus for further processing and packaging into vesicles. (4) After secretion into the extracellular space, N- and C-terminal propeptides are cleaved, generating tropocollagen. (5) Tropocollagen self-assembles into collagen fibrils, which subsequently arrange into mature collagen fibers (6), contributing to the extracellular matrix structure.

influence processes such as cell proliferation, migration, differentiation, and apoptosis [10]. Among the most important are integrins ($\alpha1\beta1$, $\alpha2\beta1$, $\alpha10\beta1$, and $\alpha11\beta1$), which control adhesion, migration, survival, and differentiation and are therefore central to processes such as wound healing and tissue regeneration [72, 73]. DDR1 and DDR2 transmit matrix-to-cell signals that promote cell migration, adhesion [9], and epithelial–mesenchymal transition (EMT), linking collagens to tissue repair as well as pro-survival and anti-apoptotic signaling [74]. GPVI is a platelet collagen receptor that activates signaling cascades leading to platelet aggregation and thrombus formation. This activity forms the basis for using collagen in hemostatic dressings and as a vascular graft material, where rapid clot formation and vascular repair are required [75]. OSCAR enhances osteoclast differentiation and bone resorption, highlighting the role of collagen in bone turnover and in biomaterials designed for skeletal repair [76]. In contrast, LAIR-1 acts as an inhibitory receptor on immune cells, suppressing inflammatory signaling and contributing to immune tolerance, which is particularly relevant for biomaterials where reduced immunogenicity is desired [77]. Finally, uPARAP/Endo180 mediates the uptake and degradation of collagen fragments, a process important for ECM remodeling and therefore for the integration and controlled degradation of collagen-based implants [78]. Together, these receptor-mediated interactions illustrate how collagen directs key biological responses. In practice, the specific collagen type and source, such as land animal, marine, or recombinantly derived collagen, can shape these outcomes, influencing how effectively biomaterials support wound healing, promote bone and cartilage regeneration, enable hemostasis, or reduce inflammatory responses. This highlights the importance of source selection in designing collagen-based dressings, scaffolds, vascular grafts, and immune-modulating biomaterials. These mechanisms are illustrated in Figure 2, which summarizes the major collagen-binding receptors and their downstream effects.

6 | Collagen Sources

Collagen is obtained from a variety of biological and engineered systems that can be grouped into three major categories: land animal, marine, and recombinant sources. Each unique source has specific advantages and limitations in terms of availability, extraction efficiency, biochemical composition, and suitability for end-use applications. Tissues from land animals, such as skin, bone, tendon, and cartilage, are rich in fibrillar collagens, with Type I being the most abundant, Type II being predominantly in cartilage, Type III being commonly present in skin and vascular tissues, and Type V occurring in nails and hair. In contrast, Type IV, a nonfibrillar collagen, is a major structural component of basement membranes [79]. Similarly, marine organisms provide important alternative sources of collagen; for example, fish skin, scales, and bones are particularly rich in fibrillar Type I collagen, the predominant form in most marine vertebrates. Sea cucumber body walls also represent a notable source of Type I collagen [80]. In contrast, Type II collagen is mainly present in fish cartilage, such as found in sharks [81]. Marine invertebrates also represent a valuable source of collagen. Jellyfish are particularly rich in

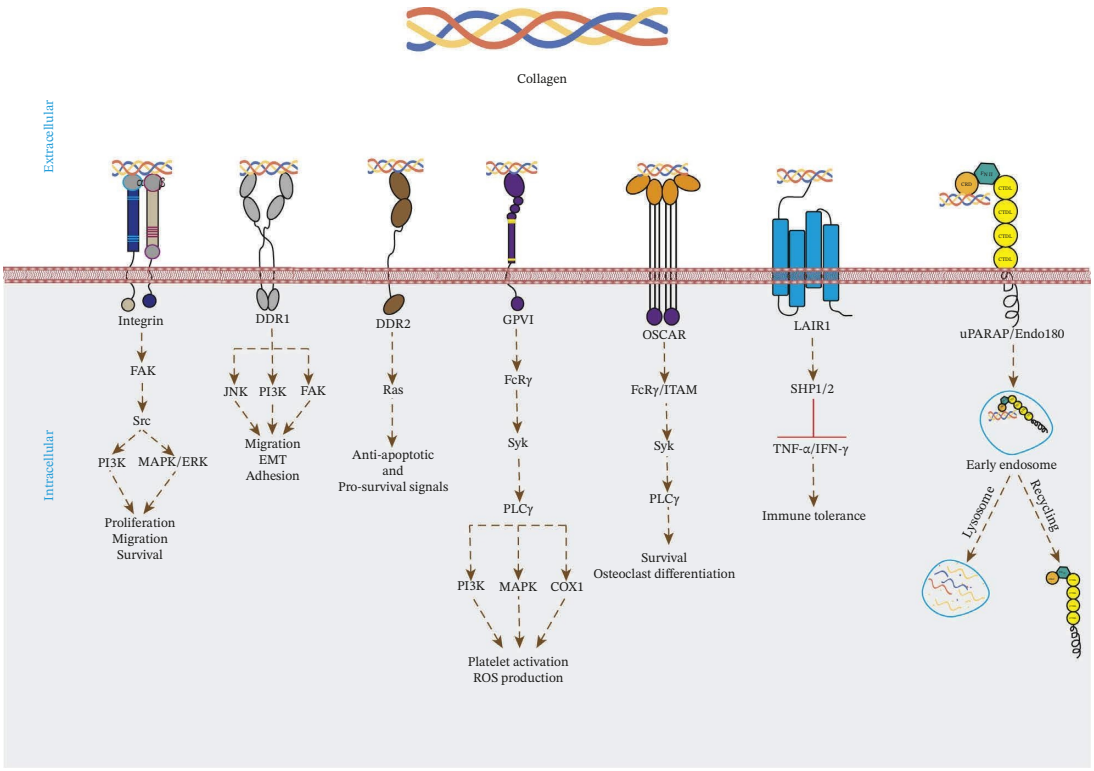

FIGURE 2 | Collagen receptors and their downstream signaling pathways. Illustration of key collagen-binding receptors at the cell surface and the intracellular signaling cascades they activate. These regulate diverse cellular functions, including migration, survival, immune tolerance, and matrix remodeling.

fibrillar Type I collagen, which has attracted attention for biomedical and cosmetic applications [82], while sponges contain both fibrillar collagens and nonfibrillar forms, such as Type IV collagen, contributing to their basement membrane-like structures [83]. For both land animal and marine sources, the most common extraction methods are acid solubilization and enzyme-assisted hydrolysis. Acid extraction employs organic or inorganic acids, for example, acetic acid, hydrochloric acid, or citric acid, to disrupt cross-linking and to solubilize the collagen. In land animal tissues, such as skin and tendons, this method provides high solubility and preserves telopeptides, which supports natural fibril formation. Similarly, in marine tissues, such as fish skin and scales, acid extraction is highly effective because of their lower cross-link density, often resulting in comparatively higher yields. However, in highly cross-linked or mineralized tissues such as bone and cartilage from land animals, yields remain low, which limits the scalability of this approach for industrial applications [84, 85].

Enzyme-assisted hydrolysis, typically using proteolytic enzymes such as pepsin or trypsin, is also widely applied to both land animal and marine tissues. This method provides higher selectivity, allowing greater recovery of intact collagen molecules, while gentle conditions preserve the triple-helix structure. It also minimizes equipment damage, reduces energy requirements, and contributes to environmentally sustainable processing. In marine sources such as fish skin, enzymatic extraction is particularly advantageous for achieving high yields, while in land animal tissues it is essential for solubilizing dense, cross-linked structures such as tendon and bone, where acid extraction alone is insufficient. Nonetheless, enzymatic extraction has disadvantages, including higher processing costs and sensitivity to over-crosslinking, which can reduce enzyme accessibility and limit overall yield in certain land animal tissues [86, 87]. Beyond conventional methods, ultrasound-assisted extraction has increasingly been explored for marine collagen sources. This approach enhances extraction efficiency by increasing collagen recovery while maintaining the stability of its triple-helical structure, offering a promising alternative to improve yield and functionality [88, 89].

These approaches result in different extraction efficiencies, with yields strongly influenced by species, tissue type, and processing conditions. The yields and methodological differences for land animal sources are presented in Table 3, while those for marine sources are summarized in Table 4.

6.1 | Bovine Collagen

Bovine collagen is predominantly extracted from cowhides, bones, and tendons and is composed mainly of Type I collagen, particularly when derived from dense connective tissues such as the Achilles tendon. Other collagen types can also be obtained from specific bovine tissues, such as Type II from articular cartilage and Type IV from placental tissue [120]. Extraction typically relies on acid solubilization, pepsin digestion, or modified combined protocols, with yields varying considerably depending on tissue and method; for example, tendon collagen shows yields of 64.91% with acid or 56.78% with enzyme methods, while bovine hides yield approximately 5.62%–20.15% depending on whether acid, acid-enzyme, or modified acid-enzyme protocols are used [90, 91]. Importantly, bovine

TABLE 3 | Collagen extraction from land animal sources.

Animal	Tissue origin	Collagen type (s)	Extraction techniques	Quantitative parameters			Imino acid content		Denaturation temperature (°C)	Measurement method	Ref.
				Yield (%)	Collagen content (%)	Protein content (%)	Pro + hyp (residues/1000)	Pro + hyp (g kg^{-1} collagen)			
Bovine	Tendon	I	Modified acid/enzyme	64.91/56.78	NA	NA	231/228	NA	NA	- Yield: dry weight basis. - Imino acid: automatic amino acid analyzer	[90]
Bovine	Bullhide Calf hide Cow hide Facepiece Ox hide	I	Acid/acid + enzyme/modified acid + enzyme	20.15/18.51/20.03[#] 9.84/5.85/9.14[#] 14.88/14.88/12.07[#] 5.62/5.62/5.62[#] 15.32/13.24/10.42[#]	5.30/30.20/74.45 25.70/19.50/65.72 3.80/26.90/75.13 4.90/15.40/48.86 5.20/30.10/64.52	NA	NA	NA	NA	- Yield: dry weight basis. - Collagen content: Hydroxyproline assay	[91]
Bovine	Skin	Collagen (not specified)	High pressure + ultrasound + enzyme	NA	NA	NA	NA	304.38	62.14	- Amino acid analysis: automated amino acid analyzer. - Denaturation temperature: DSC	[92]
Porcine	Skin	Collagen (not specified)	Acid	0.97	NA	NA	NA	236.36[‡]	NA	- Yield: wet weight basis (berat basah). - Amino acid analysis: HPLC + FMOC-Cl	[93]
Porcine	Skin	Collagen (not specified)	High pressure + ultrasound + enzyme	NA	NA	NA	NA	313.24	87.92	- Amino acid analysis: automated amino acid analyzer. - Denaturation temperature: DSC	[92]
Equine	Tendon	I	Commercial proprietary process (not disclosed)	NA	NA	NA	NA	NA	42.6	- Denaturation temperature: DSC	[94]
Chicken	Feet	I	Enzyme	32.16	NA	NA	NA	228.5[$]	NA	- Yield: dry weight basis. - Amino acid analysis: automated amino acid analyzer	[95]
Chicken	Skin	I and III	Acid + enzyme/ethylene diamine	38.9/25.1	NA	NA	NA	NA	NA	- Yield: Hydroxyproline colorimetric assay	[96]
Duck	Feet	I	Acid	28.37	NA	29.11	NA	179.7[$]	NA	- Yield: dry weight basis. - Protein content: AOAC standard method. - Amino acid analysis: HPLC	[97]
Donkey	Bone	Collagen (not specified)	Enzyme	NA	NA	56	NA	NA	NA	- Protein content: BCA assay	[98]

(Continues)

TABLE 3 | (Continued)

Animal	Tissue origin	Collagen type (s)	Extraction techniques	Quantitative parameters			Imino acid content		Denaturation temperature (°C)	Measurement method	Ref.
				Yield (%)	Collagen content (%)	Protein content (%)	Pro + hyp (residues/ 1000)	Pro + hyp (g kg^{-1} collagen)			
Donkey	Skin	Collagen (not specified)	High pressure + ultrasound + enzyme	NA	NA	NA	NA	323.34	96.46	- Amino acid analysis: automated amino acid analyzer. - Denaturation temperature: DSC	[92]
Sheep	Skin	Collagen (not specified)	High pressure + ultrasound + enzyme	NA	NA	NA	NA	366.82	109.61	- Amino acid analysis: automated amino acid analyzer. - Denaturation temperature: DSC	[92]
Alligator	Bone	I	Acid/enzyme	NA	NA	NA	194.1/196.1	NA	37.6–38.1/ 37.9–38.2	- Amino acid analysis: HPLC. - Denaturation temperature: circular dichroism and viscometry	[99]

Note: This table summarizes collagen extracted from land-animal sources, including animal species, tissue origin, collagen type(s), extraction techniques, quantitative parameters, imino acid content, denaturation temperature, measurement method, and references. Quantitative parameters include extraction yield, collagen content, and protein content. These metrics were determined using different analytical definitions and calculation bases across studies (e.g., proportion of extracted collagen relative to initial wet or dry tissue mass, collagen fraction within extracted material, or total protein content), as reported in the original references. Imino acid content refers to the combined proline and hydroxyproline content and is reported either as residues per 1000 amino acid residues or as g kg^{-1} of collagen. Denaturation temperature values correspond to the measurement methods reported in the original studies. NA indicates data not available; FMOC-Cl, 9-fluorenylmethyloxycarbonyl chloride.

Abbreviations: AOAC, Association of Official Analytical Chemists; DSC, differential scanning calorimetry; HPLC, high-performance liquid chromatography.

[#]indicates extraction yield values estimated by the present authors using ImageJ analysis of published figures.

[$]indicates values calculated from reported proline and hydroxyproline percentages.

TABLE 4 | Collagen extraction from marine sources.

Marine source	Tissue origin	Collagen type(s)	Extraction techniques	Yield		Amino acid content			Denaturation temperature (°C)	Measurement method	Ref.
				Yield (%)	Yield (mg/g)	Pro + hyp (residues/1000)	Pro + hyp (g kg^{-1} collagen)	Pro (g kg^{-1} collagen)			
Abalone (*Haliotis discus hannai*)	Muscle	I	Enzyme	8.7	NA	221	NA	NA	22.9	- Yield: dry weight basis. - Amino acid analysis: HPLC. - Denaturation temperature: circular dichroism and viscometry	[100]
Freshwater Snail (*Pomacea paludosa*)	Flesh	Collagen (not specified)	Acid hydro/enzyme	9.79–14.49/19.59–30.72	NA	NA	NA	81.3–82.1/86.0–89.7[#]	NA	- Yield: dry weight basis. - Amino acid analysis: HPLC	[101]
Jellyfish (*Aurelia aurita*)	Umbrella	I	Acid	0.01	NA	NA	NA	NA	43.7	- Yield: wet weight basis. - Denaturation temperature: DSC	[102]
Jellyfish (*Aurelia aurita*)	Whole body	I	Acid/enzyme	NA	NA/0.0079	NA	NA	NA	NA	- Yield: wet weight basis	[103]
Jellyfish (*Cotylorhiza tuberculata*)	Umbrella and oral arms	I	Acid/enzyme	NA	NA/0.45–1.94	NA	NA	NA	NA	- Yield: wet weight basis	[103]
Jellyfish (*Pelagia noctiluca*)	Whole body	I	Acid/enzyme	NA	NA/0.074	NA	NA	NA	NA	- Yield: wet weight basis	[103]
Jellyfish (*Rhizostoma pulmo*)	Umbrella and oral arms	I	Acid/enzyme	NA	NA/0.83–10.3	NA	NA	NA	NA	- Yield: wet weight basis	[103]
Codfish (*Gadus morhua*)	Skin	I	Acid/CO_2-acidified water	NA/13.8	NA	139/152	NA	NA	32.3	- Yield: wet weight basis. - Amino acid analysis: automated amino acid analyzer. - Denaturation temperature: micro-DSC	[104]
Tilapia (*Oreochromis niloticus*)	Skin	I	Acid/enzyme	4.30/1.84	NA	172.10/164.18	NA	NA	26/25	- Yield: wet weight basis. - Amino acid analysis: HPLC. - Denaturation temperature: Viscosity-based thermal denaturation	[105]
Tilapia (*Oreochromis niloticus*)	Scale	I	Acid/enzyme	0.77/0.71	NA	205/199	NA	NA	NA	- Yield: hydroxyproline-based calculation. - Amino acid analysis: automated amino acid analyzer	[106]
Salmon (*Oncorhynchus nerka*)	Skin	I	Acid + isopropanol/acid + isopropanol + ultrasonication	25.95/23.18	NA	191/193	NA	NA	NA	- Yield: dry weight basis. - Amino acid analysis: automated amino acid analyzer	[107]
Salmon (*Salmo salar*)	Skin	I	Acid + enzyme	15.38	NA	NA	NA	113.4[#]	NA	- Yield: dry weight basis. - Amino acid analysis: UPLC	[108]
Shark (*Carcharhinus limbatus*)	Skin	I	Acid/enzyme	20.01/0.86	NA	197/203	NA	NA	NA	- Yield: wet weight basis. - Amino acid analysis: automated amino acid analyzer	[109]

(Continues)

TABLE 4 | (Continued)

Marine source	Tissue origin	Collagen type(s)	Extraction techniques	Yield		Amino acid content			Denaturation temperature (°C)	Measurement method	Ref.
				Yield (%)	Yield (mg/g)	Pro + hyp (residues/1000)	Pro + hyp (g kg^{-1} collagen)	Pro (g kg^{-1} collagen)			
Shark (*Prionace glauca*)	Cartilage	II	Acid + enzyme	7.69	70.80–83.00	219.08	NA	NA	42	- Yield: dry weight basis. - Amino acid analysis: automated amino acid analyzer. - Denaturation temperature: temperature sweep test	[110]
Flatfish (*Paralichthys olivaceus*)	Skin	I	Acid + ultrasound	31.3–46.2	NA	NA	315#	188#	NA	- Yield: biuret method. - Amino acid analysis: HPLC.	[111]
Silver catfish (*Pangasius*)	Skin	Collagen (not specified)	Acid/enzyme	4.27/2.27	NA	NA	NA	NA	NA	- Yield: wet weight basis	[112]
Yellowfin tuna (*Thunnus albacares*)	Skin	Collagen (not specified)	Acid + enzyme	NA	NA	NA	205#	125#	NA	- Amino acid analysis: automated amino acid analyzer	[113]
Sea cucumber (*Holothuria scabra*)	Body wall	I	Acid	6	NA	NA	NA	NA	NA	- Yield: dry weight basis	[114]
Sea cucumber (*Stichopus japonicus*)	Body wall	I	Acid + enzyme	NA	NA	NA	NA	154#	34	- Amino acid analysis: DNAMAN software. - Denaturation temperature: DSC	[115]
Sea cucumber (*Stichopus horrens*)	Body wall	I	Acid + enzyme	NA	NA	161	NA	NA	NA	- Amino acid analysis: HPLC	[116]
Sea cucumber (*Holothuria arenicola*)	Body wall	I	Acid + enzyme	NA	NA	151	NA	NA	NA	- Amino acid analysis: HPLC	[116]
Sea cucumber (*Stichopus hermanni*)	Body wall	Collagen (not specified)	Acid/enzyme	7.30/23.66	NA	NA	NA	NA	NA	- Yield: wet weight basis	[117]
Sea cucumber (*Bohadschia bivitatta*)	Body wall	Collagen (not specified)	Enzyme	65	NA	NA	NA	NA	NA	- Yield: dry weight basis	[118]
Sea cucumber (*Stichopus monotuberculatus*)	Body wall	I	Acid/enzyme	2.63/61.93	NA	NA/151	NA	NA/84	30.2	- Yield: Relative to crude collagen fibrils. - Amino acid analysis: automated amino acid analyzer. - Denaturation temperature: DSC	[119]

Note: This table summarizes collagen obtained from marine organisms, including marine source, tissue origin, collagen type(s), extraction techniques, yield, amino acid composition, denaturation temperature, measurement method, and references. Yield values are reported as presented in the original studies and may be expressed either as percentage (%) or as mass-based yield (mg g^{-1}), depending on the analytical approach, as specified in the cited references. Amino acid composition includes proline and hydroxyproline reported as residues per 1000 amino acid residues or as g kg^{-1} of collagen. Denaturation temperatures correspond to the measurement methods reported in the original studies. NA indicates data not available.

Abbreviations: DSC, differential scanning calorimetry; HPLC, high-performance liquid chromatography; UPLC, ultra-performance liquid chromatography.

#indicates values calculated from reported amino acid percentages.

tendon collagen obtained through acid extraction contains 231 residues of proline and hydroxyproline per 1000 amino acids, compared with 228 residues through enzyme digestion, highlighting how extraction conditions influence imino acid content (proline and hydroxyproline), which in turn affects retention and, consequently, collagen stability [90]. These biochemical characteristics, together with its abundance, mechanical strength, and biocompatibility, have established bovine collagen as the benchmark material widely utilized in biomedical, cosmetic, food, and industrial domains. However, despite these advantages, bovine collagen use poses certain risks, including rare allergic reactions and the potential for disease transmission, most notably bovine spongiform encephalopathy (BSE) [121, 122].

6.2 | Porcine Collagen

Porcine collagen is primarily obtained from skin, which serves as an abundant by-product of the meat industry. The major type isolated is Type I collagen, with Type III also commonly present depending on the tissue source [123, 124]. Extraction can be performed through simple acid solubilization, which yields very low recovery (0.97%), or through advanced methods such as high pressure combined with ultrasound and enzymatic digestion, which significantly enhance extraction efficiency and structural integrity [92, 93]. Reported biochemical and thermal properties of porcine collagen vary with extraction methodology. For example, acid-extracted porcine skin collagen has been reported with imino acid contents of 236.36 g kg^{-1} of collagen, while collagen obtained using high-pressure and ultrasound-assisted enzymatic protocols shows higher reported values (313.24 g kg^{-1} of collagen). Differential scanning calorimetry (DSC) analysis of porcine skin collagen obtained using this combined extraction approach revealed a denaturation temperature of 87.92°C [92, 93]. In addition to skin, porcine bone and tendon have also been investigated as collagen sources, typically producing Type I collagen with good fibril-forming ability, while porcine cartilage has been used to obtain Type II collagen for regenerative medicine applications [125]. Despite its favorable availability and physicochemical characteristics, porcine collagen faces ethical and religious limitations in certain populations and may retain residual antigenicity even after purification, which has been associated with immune responses in porcine-derived biomaterials [126, 127].

6.3 | Equine Collagen

Equine collagen, most obtained from horse tendon or hide, is an emerging land-animal collagen source composed predominantly of Type I collagen. Compared with bovine and porcine sources, equine collagen has been less extensively studied. Available quantitative data indicate that equine tendon-derived collagen exhibits a denaturation temperature of 42.6°C, as determined by DSC. In addition, a direct comparative study of equine- and bovine-derived Type I collagen matrices demonstrated species-dependent physicochemical differences, including higher shrinkage temperature, reduced swelling ratio after crosslinking, and greater resistance to collagenase degradation in equine collagen compared with bovine collagen, despite similar ultrastructural morphology and crosslinking density. These findings indicate that equine collagen may exhibit enhanced intrinsic stability and enzymatic resistance relative to bovine collagen, which could be advantageous for biomedical scaffold applications [94, 128]. Although equine-derived products show great promise, their acceptance is not universal. Like porcine sources, they may be restricted in certain cultures for religious reasons. Additionally, the availability of equine tissues is more limited than that of bovine or porcine sources. Nevertheless, equine collagen remains a valuable alternative due to its favorable safety profile and functional performance [129].

6.4 | Donkey Collagen

Historically, donkeys have served various purposes, functioning as companion animals in high-income countries and as essential working animals in low-income regions. Today, donkeys are increasingly recognized as a valuable source of collagen for biomedical and nutraceutical applications due to their demonstrated antioxidant and bioactive properties. Certain regions of donkey collagen contain bioactive peptides with functional benefits, including anti-inflammatory and wound-healing effects. Beyond these biomedical applications, donkey-derived products have been valued since ancient times for their medicinal properties, rejuvenating effects, and use in traditional beauty treatments [130]. Various parts of the donkey, including skin and bones, are utilized for different applications. One of the most well-known products derived from donkey skin is *Colla Corii Asini* (*Ejiao*; *pronounced eh-gee-yow*). Ejiao is a gelatin-like solid preparation obtained through a refining process following water extraction from donkey skin and is one of the highest-grade traditional Chinese medicines (TCM). In China, *Ejiao* has been widely recognized as both a health supplement and a TCM, traditionally used for over 2000 years in promoting overall well-being and as a therapeutic agent for anemia and blood-related disorders [131]. Biochemical analysis of donkey skin has identified three major proteins: collagen α1(I), collagen α2(I), and donkey serum albumin. Two forms of Type I collagen, citric-soluble and pepsin-soluble, have been successfully extracted, both containing two distinct α chains (α1 and α2). Gelatin, a key bioactive component of *Ejiao*, consists of peptides and proteins derived from partial hydrolysis of collagen, with hydroxyproline levels between 8.99% and 11.23% [131, 132]. Modern extraction studies have further characterized donkey tissues as promising collagen sources. Enzyme-based extraction from donkey bone resulted in a protein content of 56% in the extracted material, indicating a high proportion of protein within the recovered fraction. In a separate study, high-pressure, ultrasound-assisted enzymatic extraction from donkey skin reported an exceptionally high imino acid content of 323.34 g kg^{-1} of collagen and a denaturation temperature of 96.46°C [92, 98]. Despite these promising features, donkey-derived collagen also faces critical constraints, including limited global farming for collagen extraction and increasing demand for *Ejiao*, which has contributed to a shortage of authentic donkey hides and the emergence of imitation products using alternative animal skins. These issues raise concerns about product consistency and safety, highlighting the need for improved quality control and reliable sourcing in donkey collagen production [133, 134].

6.5 | Avian Collagen

Avian collagen is primarily obtained from chickens, which provide a wide range of collagen types depending on the anatomical source. The neck region yields a mixture of Types I, II,

III, and V collagen, with Type I being the most prevalent, while Type IX has been identified in the sternal cartilage of chicken embryos and Type IV in muscular tissues [120]. Chicken feet are especially rich in type I collagen, obtained through enzymatic extraction with a yield of 32.16% and an imino acid content of 228.5 g kg^{-1} of collagen [95]. Chicken skin, which contains both Type I and III collagens, has been extracted using different extraction methods. The yields vary between 25.1% and 38.9%, reflecting how the choice of extraction strategy strongly influences collagen recovery [96]. Duck collagen, though less extensively studied, is mainly obtained from feet, where acid extraction produces a yield of 28.37% and an imino acid content of 179.7 g kg^{-1} of collagen [97]. Avian-derived collagens offer several advantages. They carry no risk of prion-related diseases such as BSE and are often more acceptable in populations with religious or cultural restrictions compared with bovine or porcine sources. However, intensive exposure to poultry infected with avian influenza virus during rearing, slaughtering, or processing poses a significant health risk. Moreover, strict measures are required to prevent contaminated poultry products from entering the food chain, highlighting the importance of biosafety during the processing of avian-derived materials [135].

6.6 | Other Land Animal Collagen

Collagen has also been extracted from less commonly studied land animals such as sheep and alligators, although the available data remain limited compared with bovine or porcine sources. In sheepskin, high-pressure, ultrasound-assisted enzymatic extraction has produced collagen with a high imino acid content of 366.82 g kg^{-1} of collagen and a high denaturation temperature of 109.61°C, as determined by DSC. These compositional and thermal characteristics suggest that sheep collagen may be a robust option for specialized applications, although its broader use remains constrained by limited processing data [92]. Alligator bone has also been examined, with collagen obtained through acid and enzyme extraction. Biochemical analysis revealed an imino acid content of 194.1–196.1 residues and a denaturation temperature of approximately 38°C, which is more comparable to certain marine collagens [99]. Despite these findings, both sheep- and alligator-derived collagens remain less commonly investigated, and their potential applications are constrained by limited availability, low extraction yields, lack of large-scale processing infrastructure, and the scarcity of systematic studies validating their safety and reproducibility.

6.7 | Mollusk Collagen

Mollusks represent a less commonly explored marine source of collagen. Abalone has attracted interest as a collagen-rich resource. Collagen extracted from abalone muscle has been identified as Type I, with enzyme extraction achieving yields of 8.7%. Biochemical characterization revealed an imino acid content of 221 residues and a relatively low denaturation temperature of 22.9°C [100]. Freshwater snails are another reported mollusk collagen source. Acid and enzyme extraction methods have been applied, producing yields ranging from 9.79% to 14.49% with acid extraction and to as high as 19.59%–30.72% with enzymatic digestion. Amino acid analysis showed proline contents of approximately 81–82 g kg^{-1} of collagen for acid-extracted collagen and 86–89 g kg^{-1} of collagen for enzyme-extracted collagen [101]. Together, these studies indicate that mollusks, though underexplored, can provide collagen with distinctive biochemical features; however, limitations such as low denaturation temperature and variability in extraction yields remain important considerations.

6.8 | Jellyfish Collagen

Jellyfish represent an unconventional but increasingly investigated marine source of collagen. Several species have been studied, including *Aurelia aurita*, *Rhizostoma pulmo*, *Cotylorhiza tuberculata*, and *Pelagia noctiluca*. Collagen is typically isolated from the umbrella, oral arms, or whole body using acid extraction or enzyme methods. Reported collagen yields are predominantly expressed on a wet-weight basis and vary across species and tissues. For example, *A. aurita* umbrella collagen obtained by acid extraction showed a yield of 0.01%, while whole-body enzyme extraction yielded 0.0079 mg g^{-1}. In *R. pulmo*, collagen yields from the umbrella and oral arms ranged from 0.83 to 10.3 mg g^{-1}, whereas *C. tuberculata* yielded 0.45–1.94 mg g^{-1} from similar tissues. Whole-body extraction of *P. noctiluca* reported a yield of approximately 0.074 mg g^{-1}. Although these yields are lower than those reported for mammalian or fish collagens, jellyfish remain an attractive alternative source due to their abundance and underutilization during seasonal blooms. Type I collagen has been consistently identified across umbrella, oral arm, and whole-body extracts from multiple jellyfish species [102, 103]. Sequence alignment studies show significant similarity with human Types I and III collagens [136] while also displaying structural resemblance to mammalian Type II collagen, highlighting its potential for cartilage-related applications [137]. It exhibits excellent water solubility under neutral pH conditions despite its relatively low hydroxyproline content [138]. Thermal analysis by DSC reported a denaturation temperature of 43.7°C for *A. aurita* [102], which is comparable to the 42.6°C observed for equine tendon collagen [94] and represents the highest values among marine sources listed in Table 4. These structural and biochemical characteristics, even in the context of low recovery, support its relevance for biomedical and cosmetic applications.

6.9 | Fish Collagen

Fish are among the most widely studied marine sources of collagen, primarily obtained from processing by-products such as skin, scales, bones, and cartilage. These tissues are particularly rich in Type I collagen, while cartilage yields Type II, making fish a versatile source for both structural and cartilage-related applications. The relatively low risk of zoonotic disease transmission and broader cultural acceptance compared with land animal collagens further enhance their appeal [139, 140]. Extraction is commonly achieved using acid or enzyme-based methods, sometimes combined with ultrasound or other modifications, which strongly influence yield and structural characteristics. Codfish collagen, specifically Type I extracted from the skin, demonstrates high purity and presents a promising opportunity for utilizing marine by-products. Its molecular weight, amino acid profile, and structural characteristics are closely aligned with those of land animal collagen, supporting its potential as an alternative biomaterial in biomedical fields [141]. Codfish skin collagen was extracted using CO_2-acidified water, yielding 13.8% collagen with a denaturation temperature of 32.3°C as determined by DSC [104]. Tilapia skin is among the

most extensively studied fish collagen sources. Using comparable acid–enzyme extraction protocols, skin-derived collagen yields of 4.30% (acid extraction) and 1.84% (enzymatic extraction) have been reported when expressed on a wet-weight basis. In contrast, collagen yield from tilapia scales, obtained using the same extraction approach, has been quantified using a hydroxyproline-based calculation, resulting in apparent yields of 0.71%–0.77%. Amino acid analysis reported imino acid contents of 164–172 residues per 1000 amino acids for tilapia skin collagen and 199–205 residues per 1000 amino acids for scale-derived collagen, as determined using different analytical approaches [105, 106]. Salmon is another well-studied source of fish collagen, with skin serving as the primary extraction material and collagen predominantly classified as Type I. When reported on a dry-weight basis, acid–enzyme extraction of *Salmo salar* skin yielded 15.38% collagen, while collagen yields of 25.95% and 23.18% were obtained from *Oncorhynchus nerka* skin using acid–isopropanol extraction alone and in combination with ultrasonication, respectively. Amino acid analysis of *O. nerka* skin collagen reported an imino acid content of 191–193 residues per 1000 amino acids [107, 108]. Sharks are another important marine source of collagen, with both skin and cartilage serving as extraction materials. Shark skin collagen is classified as Type I, while shark cartilage collagen is Type II, reflecting their different tissue structures. For the skin, acid extraction provides relatively high yields, near 20%, whereas enzymatic extraction is much less efficient when reported on a wet-weight basis [109]. In contrast, cartilage requires a combined acid and enzymatic approach, producing yields of 7.69% on a dry-weight basis. Shark cartilage collagen is notable for its very high imino acid content of 219.08 residues and a denaturation temperature of 42°C [110]. Flatfish skin is a promising source of Type I collagen, with acid–ultrasound–assisted extraction achieving relatively high yields of 31.3%–46.2%. Amino acid analysis reported a high imino acid content of 315 g kg^{-1} of collagen, highlighting the effectiveness of physical-assisted extraction methods [111]. In comparison, silver catfish skin yields are much lower, at 4.27% with acid extraction and 2.27% with enzymatic extraction, when reported on a wet-weight basis [112]. Yellowfin tuna skin collagen obtained by acid–enzyme extraction exhibits an imino acid content of 205 g kg^{-1} of collagen [113].

6.10 | Sea Cucumber Collagen

Sea cucumbers possess a collagen-rich body wall, which represents the main edible portion and accounts for about 70% of the total protein content. This collagen is predominantly Type I and contributes not only to the structural integrity of the body wall but also to the characteristic texture and food quality of sea cucumbers, influencing how they respond to boiling, drying, soaking, and rehydration. Beyond structural importance, sea cucumber collagen displays favorable gelling properties and diverse bioactivities while also being notable for its unique biochemical profile [142]. In particular, it has a lower native molecular weight of 80–90 kDa, compared with fish and land animal collagens, a feature associated with enhanced bioavailability and absorption in the human body [143]. As summarized in Table 4, available studies report denaturation temperatures ranging from approximately 30°C to 34°C for sea cucumber collagen in species for which thermal data are available. For example, *Stichopus japonicus* body wall collagen extracted using an acid–enzyme approach showed a denaturation temperature of 34°C [115], while *Stichopus monotuberculatus* reported a denaturation temperature of 30.2°C, with both values determined by DSC [119]. Collagen yield data for sea cucumbers vary across species and extraction approaches. On a dry-weight basis, *Holothuria scabra* body wall collagen extracted using acid extraction showed a yield of 6% [114], whereas enzymatic extraction from *Bohadschia bivittata* body wall reported a substantially higher yield of 65% [118]. Together, these findings highlight sea cucumber as one of the most efficient marine collagen sources, with yields spanning a broader range than typically observed in fish or mollusks.

6.11 | Recombinant Collagen Source

Recombinant collagen represents a rapidly developing alternative to naturally sourced collagens, offering several advantages over both animal- and marine-derived origins. In addition, the collagen can be produced in controlled, pathogen-free systems, limiting risks of zoonotic disease transmission and immunogenicity. Recombinant approaches also allow for precise genetic modification and sequence design, enabling the production of collagen molecules with defined properties for specific biomedical or industrial applications. This overcomes batch-to-batch variability that often characterizes natural sources and addresses ethical concerns related to animal harvesting, supporting the development of more sustainable and animal-free biomaterials [144]. Collectively, these benefits make recombinant collagen an increasingly attractive source for clinical, industrial, and research applications. Among available hosts for recombinant collagen production, bacterial systems such as *Escherischia coli* (*E. coli*) are the most widely used due to their simplicity, rapid growth, and low production costs. However, they lack the enzymatic machinery necessary for hydroxylating proline and lysine residues, which is critical for stable triple-helix formation [145]. As a result, *E. coli* is generally limited to producing collagen fragments. Even so, recombinant human Type I collagen (rhLCOL-I) fragments expressed in *E. coli* have demonstrated bioactivity, enhancing keratinocyte adhesion and migration in vitro and promoting wound healing in mice [146]. Yeast systems, particularly *Pichia pastoris*, provide a more advanced platform, offering both cost-effectiveness and scalability. When co-expressed with prolyl 4-hydroxylase (P4H), Pichia can produce hydroxylated triple-helical collagens with improved stability [147]. A notable achievement is the production of recombinant human Type III collagen in Pichia, which demonstrated correct folding and structural stability, providing a safer and scalable alternative to animal-derived sources [147]. Mammalian cell lines, such as Chinese hamster ovary (CHO) and human embryonic kidney (HEK) cells, remain the most reliable hosts for generating full-length, fully hydroxylated collagens [148]. These systems inherently perform the complex post-translational modifications required for stable triple-helix collagen assembly. For example, recombinant human Type I collagen expressed in CHO cells produced the full-length α1(I) chain that assembled into a stable triple helix and significantly promoted fibroblast proliferation and migration, highlighting its potential in wound healing and tissue engineering [149]. Plant-based expression systems are an emerging alternative, combining sustainability, scalability, and biosafety. Plants are capable of performing some eukaryotic post-translational modifications

and can serve as a sustainable source of recombinant collagen [150]. Tobacco plant-derived recombinant human Type I collagen (RHCI), which was formulated into hydrogels and implanted in rats and minipigs, demonstrated biocompatibility and promoted regeneration of corneal epithelium, stroma, and nerves, highlighting its potential in ocular and broader regenerative applications [151]. Insect cell systems provide another eukaryotic environment for recombinant production, with efficient protein folding and secretion. However, their ability to perform hydroxylation is often incomplete, resulting in lower structural stability compared with mammalian and yeast systems [152]. While insect cells are not yet widely adopted for commercial collagen production, they represent a useful intermediate system and may become more competitive as bioengineering strategies advance. Overall, recombinant platforms differ considerably in yield, stability, and biochemical fidelity. Bacteria provide cost efficiency but only fragments, yeast balances scalability and stability, mammalian cells deliver the most native-like collagen, plants offer sustainability, and insect cells remain an emerging option. Their specific limitations and performance metrics are summarized in Table 5.

7 | Collagen Applications in Food, Medicine, and Cosmetics

Collagen is a versatile biomaterial with applications that continue to expand across multiple disciplines. Its unique structural, mechanical, and bioactive properties have supported its use in food and beverages, tissue engineering, wound healing, and cosmetics. Collagen can be obtained from diverse sources, including land animals, marine organisms, and recombinant systems, each offering distinct advantages in terms of availability, functionality, and sustainability. Together, these features highlight collagen's central role as a multifunctional ingredient and biomaterial with relevance to both biomedical and industrial sectors.

7.1 | Food and Beverage Applications

Collagen and its derivatives, particularly gelatin and hydrolyzed collagen (HC), play an important role in the food and beverage sector due to their ability to improve texture, stability, and nutritional quality, as well as provide bioactive functions such as antioxidant activity. These properties make collagen suitable for diverse applications, including fat replacement in meat products, protein enrichment in beverages, and functional improvements in dairy systems. However, the effectiveness of collagen depends on its physicochemical characteristics, which vary with the biological source [166]. Land animal and marine-derived collagens have both been investigated as functional fat replacers in meat products. In chicken burgers, partial substitution of chicken skin fat with hydrolyzed bovine collagen at 50% reduced fat content from 7.89 g/100 g to 5.41 g/100 g and increased protein from 20.72 g/100 g to 26.98 g/100 g, while maintaining consumer acceptance and purchase intention comparable to the control [167]. Similarly, hydrolyzed fish collagen hydrolysate (FCH) has been incorporated into buffalo meat patties, where the addition of 7.5% FCH lowered the fat content to 2.46% and increased protein concentration to 22.14%, without negatively affecting sensory quality [168]. Together, these studies demonstrate that both bovine and fish collagens can enhance the nutritional profile of meat products by reducing fat and increasing protein, with consumer acceptance maintained when moderate replacement levels are used. Beyond meat systems, both land animal and marine HCs have been investigated in beverages and dairy applications. In probiotic-fermented sheep's milk, the addition of bovine collagen increased pH and lactic acid production; however, unlike collagen hydrolysates, it also promoted syneresis, reduced cohesiveness, and introduced off-flavors [169]. In contrast, hydrolyzed fish collagen in fruit juice blends enhanced protein content and antioxidant activity while maintaining high consumer acceptability [170].

7.2 | Tissue Engineering Applications

Collagen and its derivatives play a central role in tissue engineering because of their biocompatibility, biodegradability, and ability to mimic the native ECM. These properties make collagen particularly suitable for diverse biomedical applications, including use as scaffolds for skin regeneration, cartilage repair, bone reconstruction, and vascular repair. However, the performance of collagen scaffolds depends heavily on their physicochemical characteristics, which vary with the biological source and processing method [7]. Land animal–derived collagens, such as bovine, porcine, and donkey, have been widely investigated and shown to support cell adhesion, proliferation, and matrix deposition in engineered constructs. For example, bovine tendon-derived Type I collagen was mineralized to form collagen–hydroxyapatite scaffolds, which supported high human mesenchymal stem cell (hMSC) viability, uniform cell infiltration, and extensive ECM remodeling throughout the collagen scaffold during in vitro culture [171]. In addition to scaffold-based applications, bovine collagen peptides have been shown to enhance osteogenic differentiation. Treatment of MC3T3-E1 cells with 3 mg/mL collagen peptides increased the proportion of cells in the G2/S phase and significantly upregulated key markers such as runt-related transcription factor 2 (Runx2), alkaline phosphatase (ALP), and osteocalcin (OC), which are commonly used indicators of osteogenic differentiation and bone formation [172]. Similarly, porcine bone collagen composites promoted MG-63 cell viability and increased ALP activity, demonstrating osteoblast-like cell differentiation in vitro and indicating their potential as a bone substitute [173]. Unlike bovine and porcine collagens, which primarily promote osteoblast proliferation and osteogenic differentiation, donkey bone collagen also exhibits antioxidant and osteoprotective effects, improving osteoblast survival under oxidative stress by 27.31%, increasing ALP activity by 62.65%, and restoring bone mineral density [98]. Marine-derived collagens have attracted increasing attention in tissue engineering due to their biocompatibility, low immunogenicity, and sustainable availability as alternatives to land animal sources. In cartilage repair, jellyfish collagen scaffolds have been shown to support hMSC viability, upregulate chondrogenic markers such as SOX9, collagen II, and aggrecan, and enhance ECM deposition, highlighting their potential for regenerative applications [137]. Similar to bovine, porcine, and donkey collagens that promote osteoblast proliferation and osteogenic differentiation, salmon collagen has also been applied in bone tissue engineering. Importantly, mineralized salmon collagen scaffolds supported hMSC adhesion and osteogenic differentiation with elevated ALP activity [174]. While specific studies on land animal and marine collagens have focused on

TABLE 5 | Overview of recombinant human collagen expression across different systems.

Expression host	Collagen type	Key findings	Limitations	Refs.
Prokaryote (*Escherichia coli*)	Human collagen Type I	- Successfully produced recombinant collagen with Gly–X–Y repeats.	- Lack of post-translational modifications (hydroxylation).	[145, 153–155]
Prokaryote (*Escherichia coli*)	Human collagen Type I	- Combination of recombinant collagen and silk fibroin produced scaffolds characterized by ~90% porosity. - Scaffold had ~30× higher compressive strength than fibroin alone. - Supported adhesion, proliferation, and protein synthesis of vascular smooth muscle cells. - Successfully produced recombinant collagen in *E. coli*. - Fabricated composite scaffold (nano-hydroxyapatite/recombinant human-like collagen/poly(lactic acid)). - Interconnected porous structure (10–300-μm pore size) mimicking cancellous bone. - Bone regeneration in rabbit defect model	- Challenge of regulating hydroxylation with co-expressed hydroxylase. - Instability of hydroxylation rate with hydroxylase. - Limited folding and modification machinery in *E. coli*	
Yeast (*Pichia pastoris*)	Human collagen Type I	- The yeast system (*Pichia pastoris*) can successfully produce human Type I collagen in high amounts. - The collagen formed proper triple helices, was fully hydroxylated, and could assemble into native-type fibrils. - Yields in a fermenter reached up to 0.5 g/L, showing good potential for large-scale production. - Recombinant Type I, Type II, and Type III collagens produced. - The expression levels varied with collagen type, reaching 0.2–0.6 g/L in 2-L bioreactors. - Recombinant collagens identical in hydroxyproline content to native proteins and formed native-type fibrils. - Engineered recombinant human collagen with added cysteines was successfully produced. - The collagen variants maintained a stable triple-helical structure. - They supported normal cell adhesion comparable to native collagen	- Lack of efficient hydroxylases - Oxygen supply needed for proper hydroxylation. - Codon usage and copy number optimization are needed to further increase yields. - Low yields (low titers). - Lack of telopeptides. - Reduced thermal stability compared to native collagen. - Limited use at body temperature	[156–159]
Yeast (*Pichia pastoris*)	Human collagen Type I			
Yeast (*Saccharomyces cerevisiae*)	Human collagen Types I, II, and III			
	Human collagen Type III			

(Continues)

TABLE 5 | (Continued)

Expression host	Collagen type	Key findings	Limitations	Refs.
Mammalian cell line (Human embryonic kidney cells) Mammalian cell line (Chinese Hamster Ovary cells (CHO))	Human collagen Type V Human Type VII Collagen	- High-yield production of human Type V collagen (α1(V) homotrimer) in human cells. - Correct triple-helix formation and stability. - First evidence of C-propeptide cleavage in recombinant fibrillar collagen. - Functional recombinant Type VII collagen was successfully produced in CHO cells. - The CHO-produced Type VII collagen formed a properly folded, stable trimer that was resistant to protease degradation. - It incorporated into the dermal–epidermal junction after intravenous injection in recessive dystrophic epidermolysis bullosa (RDEB) mice. - It restored anchoring fibrils and skin adhesion, leading to improved survival	- Poor lysine hydroxylation. - Slightly reduced thermal stability. - Low production yield and high cost - Difficult-to-express large proteins (e.g., collagens). - Improper folding may occur	[160–163]
Plant (*Transgenic tobacco*)	Human collagen Type I	- Recombinant human Type I collagen was successfully produced in transgenic tobacco plants. - The plant-produced collagen formed stable triple helices with a thermal stability comparable to human collagen. - It was resistant to pepsin digestion and showed structural similarity to native human collagen. - It supported attachment and proliferation of human endothelial progenitor-like cells	- Exhibit different glycosylation patterns compared to human collagen, leading to plant-specific modifications. - Limit proper hydroxylysine modification, since endogenous plant lysyl hydroxylase activity is insufficient. - Inefficient enzymatic support	[164, 165]
Insect (*Spodoptera frugiperda*) Insect (*Trichoplusia ni*)	Human collagen Type III Human collagen Type III	- *Spodoptera frugiperda* (Sf9 cells) produced lower amounts of Type III collagen overall but secreted a higher proportion of the collagen they synthesized. - *Trichoplusia ni* (High Five cells) produced much higher amounts of Type III collagen and showed stronger hydroxylation but secreted a smaller percentage of the total collagen.	- Low secretion efficiency. - Lower hydroxylation without P4H. - Poor hydroxylysine content	[152]

Note: This table summarizes recombinant collagen expression systems, organized by expression host, collagen type, key experimental findings, reported limitations, and references. Expression hosts include bacterial, yeast, insect, plant, and mammalian systems. Key findings and limitations are reported as described in the original studies and reflect system-specific outcomes such as expression feasibility, post-translational modification capability, structural fidelity, and scalability.

osteogenic or chondrogenic regeneration, the function of recombinant human-like collagen produced in *E. coli* has been explored in vascular tissue engineering, where it promotes smooth muscle cell adhesion, proliferation, and scaffold integration [153].

7.3 | Wound Healing Applications

Collagen is a major structural component of the dermis, accounting for 70%–80% of skin and providing an ECM that supports fibroblast proliferation and tissue repair. Its pivotal role in wound healing spans all four overlapping phases, hemostasis, inflammation, proliferation, and remodeling, by creating a provisional matrix, modulating immune responses, and guiding fibroblast and keratinocyte activity. During the early phases, collagen facilitates platelet adhesion and immune cell recruitment, while in later phases, it supports granulation tissue formation, angiogenesis, and re-epithelialization. In the final remodeling phase, Type III collagen is gradually replaced by Type I collagen, and fibers become cross-linked and organized, restoring tensile strength to the repaired tissue [175, 176]. Collagen from both land animal and marine sources has been widely used in wound healing due to its biocompatibility, hemostatic properties, and ability to support re-epithelialization. These materials act as bioactive dressings that provide a temporary ECM, stimulating cell migration and accelerating tissue repair [177]. To illustrate, porcine dermal collagen has been shown to accelerate wound repair, with burn wounds in rats achieving 69% re-epithelialization by Day 10 compared with only 24% in controls [178]. Building on this, equine collagen has been particularly studied for its hemostatic properties. In vitro, it significantly reduced the clotting time to 32.0 ± 5.30 s (mean $\pm$ SE), as compared with 50.34 ± 2.52 s (mean $\pm$ SE) for porcine collagen, and when combined with carboxymethyl cellulose (CMC), the clotting time improved further to 20.67 ± 3.06 s (mean $\pm$ SE). In vivo, equine collagen composites achieved rapid hemostasis, stopping bleeding in as little as 2.50 ± 0.97 s (mean $\pm$ SE), highlighting their strong potential for surgical and wound management applications [179]. In addition to these land animal sources, marine-derived collagens have recently gained attention in wound healing applications as safe and sustainable alternatives. They not only provide biocompatibility and low immunogenicity but also exert biological activities such as anti-inflammatory and angiogenic effects that accelerate tissue repair. For example, jellyfish-derived collagen has shown promising wound-healing potential. Jellyfish *Rhopilema hispidum* collagen showed a higher water absorption capacity (13.25 ± 1.1 mmol/mL) (mean $\pm$ SE) compared with jellyfish *A. aurita* (7.03 ± 0.57 mmol/mL) (mean $\pm$ SE), and both sources significantly enhanced endothelial cell migration in vitro, confirming their biocompatibility and ability to support early wound repair [180].

7.4 | Cosmetic Applications

Collagen from both land animal and marine sources has been widely applied in cosmetics due to its role in maintaining skin structure, hydration, and elasticity. As the major protein of the dermis, collagen supports skin firmness and smoothness, while degradation of native collagen with age contributes to wrinkle formation and loss of elasticity. Supplementation with collagen or its hydrolysates has been shown to enhance skin hydration, improve elasticity, and reduce wrinkle depth, making it a key ingredient in anti-aging and skincare formulations [181]. Among land animal sources, bovine and porcine collagens have been particularly well studied as injectable dermal fillers for wrinkle correction. For example, in a randomized, double-blind, split-face clinical study involving 61 patients, the performance of a porcine collagen filler (TheraFill®) was compared with a bovine collagen filler (KOKEN®) for correction of nasolabial folds. After 12 months, both products produced significant wrinkle improvement, but the TheraFill® group demonstrated slightly greater reductions in wrinkle severity scores than KOKEN®, although the difference did not reach statistical significance. Importantly, no severe adverse events were reported, supporting the safety and tolerability of both fillers while suggesting that porcine collagen may offer an advantage over bovine collagen [182]. Beyond injectable fillers, collagen hydrolysates from donkey hides have also shown cosmetic potential, as low molecular weight peptides protected fibroblasts from UVB-induced photoaging by restoring procollagen Type I synthesis (11.12% vs. 1.05% in untreated cells, $p < 0.05$) and inhibiting the mitogen-activated pathway kinase (MAPK) pathway, highlighting their utility as antiphotoaging agents [183]. Similarly, chicken-derived collagen hydrolysate has been demonstrated to have significant cosmetic benefits. In a clinical study, the application of a cosmetic gel containing 1% chicken collagen hydrolysate twice daily for 8 weeks increased skin hydration by 11.8% on the right and 9.5% on the left temple, reduced transepidermal water loss by up to 25.7%, and improved elasticity in 85% of measured parameters. Wrinkle depth was also reduced by 35.4% on the right and 41.2% on the left temple, confirming its strong anti-aging potential [184]. Similar to chicken collagen hydrolysate, sea cucumber collagen hydrolysate has also shown antiphotoaging benefits. In hairless mice, oral supplementation with sea cucumber collagen significantly reduced transepidermal water loss, restored stratum corneum hydration, and decreased wrinkle area and maximum wrinkle width, as compared with UVA-exposed controls [185].

8 | Research Gaps and Future Directions

Although substantial progress has been made in collagen research, several key limitations continue to restrict its broader application. A major concern is the variability in collagen quality, which is strongly influenced by source material, extraction methods, and purification processes [7]. This variability underscores an urgent need for standardized protocols to improve reproducibility and cross-study comparability. Ethical and sustainability concerns associated with mammalian collagen also remain unresolved, emphasizing the need to further develop marine and recombinant collagen sources [186, 187]. Accordingly, innovative strategies such as cross-linking approaches or composite biomaterial designs are required to enhance its structural integrity. Although marine collagens are frequently reported to elicit lower immunogenic responses than mammalian counterparts, their immunogenicity and allergenic potential have not been systematically or clinically characterized across all species, processing routes, and applications, particularly in the context of long-term implantation and repeated exposure. This limitation highlights the need for detailed, application-specific preclinical and clinical investigations to establish robust safety profiles. Meanwhile, recombinant collagen technologies remain constrained by low production yields and incomplete post-translational modifications, necessitating further advances in

host system engineering and process optimization [160]. Finally, there is a lack of comparative clinical studies directly evaluating the efficacy and biocompatibility of different collagen sources and formulations. Addressing these gaps through well-designed, comparative clinical studies is essential for informing clinical decision-making and accelerating regulatory approval of collagen-based products.

9 | Conclusions

Collagen is a highly versatile biomaterial with biological properties that support its wide use in biomedical, cosmetic, and food and beverage applications. Its biocompatibility, biodegradability, and ability to interact with cellular receptors make it well-suited for tissue regeneration and wound healing. In cosmetic and nutraceutical fields, HC peptides have shown benefits in improving skin health, elasticity, and hydration, while in food systems, collagen contributes to enhanced nutritional and functional qualities. The ability of collagen to be processed into different forms such as hydrogels, films, sponges, and scaffolds adds to its usefulness across diverse applications. Importantly, collagen can be obtained from multiple sources, including land animals, marine organisms, and recombinant systems, each offering distinct advantages in terms of availability, functionality, and sustainability. It is expected that as research continues to expand our knowledge of collagen's structure and functions, its role in future biomaterial development will grow. With ongoing innovation and collaboration across scientific fields, collagen can contribute to safer, more sustainable, and more effective solutions in medicine, food, and skincare.

Author Contributions

Noushin Rezaeivandchali: conceptualization, data curation, formal analysis, investigation, validation, visualization, and writing–original draft. Lionel Hebbard: conceptualization, methodology, project administration, resources, funding acquisition, supervision, and writing–review and editing. Craig McFarlane: conceptualization, methodology, project administration, resources, funding acquisition, supervision, and writing–review and editing.

Acknowledgments

ChatGPT was used only for minor improvements in the English language; it was not used for data generation, interpretation, or scientific content development.

Funding

This work was supported by a Department of Education Australia's Economic Accelerator (AEA) Ignite grant (IG240100362, Australian Government; awarded to Lionel Hebbard and Craig McFarlane). Open access publishing facilitated by James Cook University, as part of the Wiley - James Cook University agreement via the Council of Australasian University Librarians.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

No new data were generated in this study. All data presented in this review were extracted, compiled, and analyzed from previously published literature.

References

1. R. Naomi, H. Bahari, P. M. Ridzuan, and F. Othman, "Natural-Based Biomaterial for Skin Wound Healing (Gelatin Vs. Collagen): Expert Review," *Polymers* 13, no. 14 (2021): 2319, https://doi.org/10.3390/polym13142319.

2. R. Sowbhagya, H. Muktha, T. N. Ramakrishnaiah, et al., "Collagen as the Extracellular Matrix Biomaterials in the Arena of Medical Sciences," *Tissue and Cell* 90 (2024): 102497, https://doi.org/10.1016/j.tice.2024.102497.

3. H. Xing, H. Lee, L. Luo, and T. R. Kyriakides, "Extracellular Matrix-Derived Biomaterials in Engineering Cell Function," *Biotechnology Advances* 42 (2020): 107421, https://doi.org/10.1016/j.biotechadv.2019.107421.

4. A. T. Rowley, R. R. Nagalla, S. W. Wang, and W. F. Liu, "Extracellular Matrix-Based Strategies for Immunomodulatory Biomaterials Engineering," *Advanced Healthcare Materials* 8 (2019): 1801578, https://doi.org/10.1002/adhm.201801578.

5. R. Chen, J. Wang, and C. Liu, "Biomaterials Act as Enhancers of Growth Factors in Bone Regeneration," *Advanced Functional Materials* 26, no. 48 (2016): 8810–8823, https://doi.org/10.1002/adfm.201603197.

6. S. Goller and N. J. Turner, "The Antimicrobial Effectiveness and Cytotoxicity of the Antibiotic-Loaded Chitosan: ECM Scaffolds," *Applied Sciences* 10 (2020): 3446, https://doi.org/10.3390/app10103446.

7. H. Wosicka-Frąckowiak, K. Poniedziałek, S. Woźny, et al., "Collagen and Its Derivatives Serving Biomedical Purposes: A Review," *Polymers* 16, no. 18 (2024): 2668, https://doi.org/10.3390/polym16182668.

8. I. N. Amirrah, Y. Lokanathan, I. Zulkiflee, M. M. R. Wee, A. Motta, and M. B. Fauzi, "A Comprehensive Review on Collagen Type I Development of Biomaterials for Tissue Engineering: From Biosynthesis to Bioscaffold," *Biomedicines* 10, no. 9 (2022): 2307, https://doi.org/10.3390/biomedicines10092307.

9. F. Carafoli and E. Hohenester, "Collagen Recognition and Transmembrane Signalling by Discoidin Domain Receptors," *Biochimica et Biophysica Acta (BBA)-Proteins & Proteomics* 1834, no. 10 (2013): 2187–2194, https://doi.org/10.1016/j.bbapap.2012.10.014.

10. C. Zeltz and D. Gullberg, "The Integrin–Collagen Connection–A Glue for Tissue Repair?" *Journal of Cell Science* 129 (2016): 653–664, https://doi.org/10.1242/jcs.180992.

11. L. D. Campos, V. A. S. Junior, J. D. Pimentel, G. L. F. Carregã, and C. B. B. Cazarin, "Collagen Supplementation in Skin and Orthopedic Diseases: A Review of the Literature," *Heliyon* 9, no. 4 (2023): e14961, https://doi.org/10.1016/j.heliyon.2023.e14961.

12. M. Wu, A. Sapin-Minet, L. Stefan, J. Perrin, I. Raeth-Fries, and C. Gaucher, "Heparinized Collagen-Based Hydrogels for Tissue Engineering: Physical, Mechanical and Biological Properties," *International Journal of Pharmaceutics* 670 (2025): 125126, https://doi.org/10.1016/j.ijpharm.2024.125126.

13. M. Maher, V. Glattauer, C. Onofrillo, et al., "Suitability of Marine-and Porcine-Derived Collagen Type I Hydrogels for Bioprinting and Tissue Engineering Scaffolds," *Marine Drugs* 20, no. 6 (2022): 366, https://doi.org/10.3390/md20060366.

14. J. Li, Y.-N. Zhai, J.-P. Xu, et al., "An Injectable Collagen Peptide-Based Hydrogel With Desirable Antibacterial, Self-Healing and Wound-Healing Properties Based on Multiple-Dynamic Crosslinking," *International Journal of Biological Macromolecules* 259 (2024): 129006, https://doi.org/10.1016/j.ijbiomac.2023.129006.

15. T. Williams, D. S. Leon, Y. Kaizawa, et al., "A Human-Derived, Collagen-Rich Hydrogel Augments Wound Healing in a Diabetic Animal Model," *Annals of Plastic Surgery* 85, no. 3 (2020): 290–294, https://doi.org/10.1097/SAP.0000000000002380.

16. M. Xeroudaki, M. Thangavelu, A. Lennikov, et al., "A Porous Collagen-Based Hydrogel and Implantation Method for Corneal Stromal Regeneration and Sustained Local Drug Delivery," *Scientific Reports* 10, no. 1 (2020): 16936, https://doi.org/10.1038/s41598-020-73730-9.

17. E. Jarman, J. Burgess, A. Sharma, K. Hayashigatani, A. Singh, and P. Fox, "Human-Derived Collagen Hydrogel as an Antibiotic Vehicle for Topical Treatment of Bacterial Biofilms," *PLoS One* 19, no. 5 (2024): e0303039, https://doi.org/10.1371/journal.pone.0303039.

18. L. Song, H. Qiu, Z. Chen, et al., "Injectable Hyaluronate/Collagen Hydrogel With Enhanced Safety and Efficacy for Facial Rejuvenation," *Collagen and Leather* 6, no. 1 (2024): 21, https://doi.org/10.1186/s42825-024-00165-7.

19. N. Jabeen, M. Sohail, A. Mahmood, S. A. Shah, A. H. M. Qalawlus, and T. Khaliq, "Nanocrystals Loaded Collagen/Alginate-Based Injectable Hydrogels: A Promising Biomaterial for Bioavailability Improvement of Hydrophobic Drugs," *Journal of Drug Delivery Science and Technology* 91 (2024): 105291, https://doi.org/10.1016/j.jddst.2023.105291.

20. X. Shi, X. Li, Y. Tian, et al., "Physical, Mechanical, and Biological Properties of Collagen Membranes for Guided Bone Regeneration: A Comparative In Vitro Study," *BMC Oral Health* 23, no. 1 (2023): 510, https://doi.org/10.1186/s12903-023-03223-4.

21. A. Kilinc and M. Ataol, "How Effective is Collagen Resorbable Membrane Placement After Partially Impacted Mandibular Third Molar Surgery on Postoperative Morbidity? A Prospective Randomized Comparative Study," *BMC Oral Health* 17 (2017): 1–8, https://doi.org/10.1186/s12903-017-0416-z.

22. V. S. Shubina, M. I. Kobyakova, N. V. Penkov, G. V. Mitenko, S. N. Udaltsov, and Y. V. Shatalin, "Two Novel Membranes Based on Collagen and Polyphenols for Enhanced Wound Healing," *International Journal of Molecular Sciences* 25, no. 22 (2024): 12353, https://doi.org/10.3390/ijms252212353.

23. K. Sivaraman, P. Sujitha, A. Arunkumar, and C. Shanthi, "Biocompatible Films of Collagen-Procyanidin for Wound Healing Applications," *Applied Biochemistry and Biotechnology* 194, no. 9 (2022): 4002–4017, https://doi.org/10.1007/s12010-022-03956-y.

24. S. Ber, G. T. Köse, and V. Hasırcı, "Bone Tissue Engineering on Patterned Collagen Films: An In Vitro Study," *Biomaterials* 26, no. 14 (2005): 1977–1986, https://doi.org/10.1016/j.biomaterials.2004.07.007.

25. T. Zheng, P. Tang, and G. Li, "Development of Composite Film Based on Collagen and Phenolic Acid-Grafted Chitosan for Food Packaging," *International Journal of Biological Macromolecules* 241 (2023): 124494, https://doi.org/10.1016/j.ijbiomac.2023.124494.

26. X. Qiao, S. J. Russell, X. Yang, G. Tronci, and D. J. Wood, "Compositional and In Vitro Evaluation of Nonwoven Type I Collagen/Poly-dl-Lactic Acid Scaffolds for Bone Regeneration," *Journal of Functional Biomaterials* 6, no. 3 (2015): 667–686, https://doi.org/10.3390/jfb6030667.

27. E. C. Chan, S.-M. Kuo, A. M. Kong, et al., "Three Dimensional Collagen Scaffold Promotes Intrinsic Vascularisation for Tissue Engineering Applications," *PLoS One* 11, no. 2 (2016): e0149799, https://doi.org/10.1371/journal.pone.0149799.

28. B. León-Mancilla, M. Araiza-Téllez, J. Flores-Flores, and M. Piña-Barba, "Physico-Chemical Characterization of Collagen Scaffolds for Tissue Engineering," *Journal of Applied Research and Technology* 14, no. 1 (2016): 77–85, https://doi.org/10.1016/j.jart.2016.01.001.

29. M. B. Keogh, F. J. O'Brien, and J. S. Daly, "A Novel Collagen Scaffold Supports Human Osteogenesis—Applications for Bone Tissue Engineering," *Cell and Tissue Research* 340, no. 1 (2010): 169–177, https://doi.org/10.1007/s00441-010-0939-y.

30. L. Wang, Y. Qu, W. Li, K. Wang, and S. Qin, "Effects and Metabolism of Fish Collagen Sponge in Repairing Acute Wounds of Rat Skin," *Frontiers in Bioengineering and Biotechnology* 11 (2023): 1087139, https://doi.org/10.3389/fbioe.2023.1087139.

31. E. D'Amico, T. V. Pierfelice, S. Lepore, et al., "Hemostatic Collagen Sponge With High Porosity Promotes the Proliferation and Adhesion of Fibroblasts and Osteoblasts," *International Journal of Molecular Sciences* 24, no. 9 (2023): 7749, https://doi.org/10.3390/ijms24097749.

32. K. Bardakova, E. Grebenik, E. Istranova, et al., "Reinforced Hybrid Collagen Sponges for Tissue Engineering," *Bulletin of Experimental Biology and Medicine* 165, no. 1 (2018): 142–147, https://doi.org/10.1007/s10517-018-4116-8.

33. L. Wang, W. Li, Y. Qu, et al., "Preparation of Super Absorbent and Highly Active Fish Collagen Sponge and Its Hemostatic Effect In Vivo and In Vitro," *Frontiers in Bioengineering and Biotechnology* 10 (2022): 862532, https://doi.org/10.3389/fbioe.2022.862532.

34. Y. Luo, F. Tao, J. Wang, et al., "Development and Evaluation of Tilapia Skin-Derived Gelatin, Collagen, and Acellular Dermal Matrix for Potential Use as Hemostatic Sponges," *International Journal of Biological Macromolecules* 253 (2023): 127014, https://doi.org/10.1016/j.ijbiomac.2023.127014.

35. O. Chan, K.-F. So, and B. Chan, "Fabrication of Nano-Fibrous Collagen Microspheres for Protein Delivery and Effects of Photochemical Crosslinking on Release Kinetics," *Journal of Controlled Release* 129, no. 2 (2008): 135–143, https://doi.org/10.1016/j.jconrel.2008.04.011.

36. B. P. Chan, T. Y. Hui, M. Y. Wong, K. H. K. Yip, and G. C. F. Chan, "Mesenchymal Stem Cell–Encapsulated Collagen Microspheres for Bone Tissue Engineering," *Tissue Engineering Part C Methods* 16, no. 2 (2010): 225–235, https://doi.org/10.1089/ten.tec.2008.0709.

37. E. Rezvani Ghomi, N. Nourbakhsh, M. Akbari Kenari, M. Zare, and S. Ramakrishna, "Collagen-Based Biomaterials for Biomedical Applications," *Journal of Biomedical Materials Research Part B: Applied Biomaterials* 109, no. 12 (2021): 1986–1999, https://doi.org/10.1002/jbm.b.34881.

38. W. Al Hajj, M. Salla, M. Krayem, et al., "Exploring Its Applications in the Food and Beverage Industries and Assessing Its Impact on Human Health–A Comprehensive Review," *Heliyon* 10, no. 16 (2024): e36433, https://doi.org/10.1016/j.heliyon.2024.e36433.

39. S. Ricard-Blum, "The Collagen Family," *Cold Spring Harbor Perspectives in Biology* 3, no. 1 (2011): a004978, https://doi.org/10.1101/cshperspect.a004978.

40. C. Tang, K. Zhou, Y. Zhu, et al., "Collagen and Its Derivatives: From Structure and Properties to Their Applications in Food Industry," *Food Hydrocolloids* 131 (2022): 107748, https://doi.org/10.1016/j.foodhyd.2022.107748.

41. S. Jayaprakash, Z. M. A. Razeen, R. N. Kumar, et al., "Enriched Characteristics of Poultry Collagen Over Other Sources of Collagen and Its Extraction Methods: A Review," *International Journal of Biological Macromolecules* 273 (2024): 133004, https://doi.org/10.1016/j.ijbiomac.2024.133004.

42. M. I. Ahmad, Y. Li, J. Pan, et al., "Collagen and Gelatin: Structure, Properties, and Applications in Food Industry," *International Journal of Biological Macromolecules* 254 (2024): 128037, https://doi.org/10.1016/j.ijbiomac.2023.128037.

43. J. Bella, J. Liu, R. Kramer, B. Brodsky, and H. M. Berman, "Conformational Effects of Gly–X–Gly Interruptions in the Collagen Triple Helix," *Journal of Molecular Biology* 362, no. 2 (2006): 298–311, https://doi.org/10.1016/j.jmb.2006.07.014.

44. E. Eryilmaz, W. Teizer, and W. Hwang, "In Vitro Analysis of the Co-Assembly of Type-I and Type-III Collagen," *Cellular and Molecular Bioengineering* 10, no. 1 (2017): 41–53, https://doi.org/10.1007/s12195-016-0466-3.

45. R. Lubart, I. Yariv, D. Fixler, and A. Lipovsky, "A Novel Facial Cream Based on Skin-Penetrable Fibrillar Collagen Microparticles," *The Journal of Clinical and Aesthetic Dermatology* 15, no. 5 (2022): 59–64.

46. T. Baltazar, N. S. Kajave, M. Rodriguez, et al., "Native Human Collagen Type I Provides a Viable Physiologically Relevant Alternative to Xenogeneic Sources for Tissue Engineering Applications: A Comparative In Vitro and In Vivo Study," *Journal of Biomedical Materials Research Part B: Applied Biomaterials* 110, no. 10 (2022): 2323–2337, https://doi.org/10.1002/jbm.b.35080.

47. E. S. Gorell, T. H. Leung, P. Khuu, and A. T. Lane, "Purified Type I Collagen Wound Matrix Improves Chronic Wound Healing in Patients With Recessive Dystrophic Epidermolysis Bullosa," *Pediatric Dermatology* 32, no. 2 (2015): 220–225, https://doi.org/10.1111/pde.12492.

48. S. J. Hwang, G.-H. Ha, W.-Y. Seo, C. K. Kim, K. Kim, and S. B. Lee, "Human Collagen Alpha-2 Type I Stimulates Collagen Synthesis, Wound Healing, and Elastin Production in Normal Human Dermal Fibroblasts (HDFs)," *BMB Reports* 53, no. 10 (2020): 539–544, https://doi.org/10.5483/BMBRep.2020.53.10.120.

49. N. Rajan, J. Habermehl, M.-F. Coté, C. J. Doillon, and D. Mantovani, "Preparation of Ready-to-Use, Storable and Reconstituted Type I Collagen From Rat Tail Tendon for Tissue Engineering Applications," *Nature Protocols* 1, no. 6 (2006): 2753–2758, https://doi.org/10.1038/nprot.2006.430.

50. A. Ampitiya, S. Gonapinuwala, C. Fernando, and M. De Croos, "Extraction and Characterisation of Type I Collagen From the Skin Offcuts Generated at the Commercial Fish Processing Centres," *Journal of Food Science and Technology* 60, no. 2 (2023): 484–493, https://doi.org/10.1007/s13197-022-05630-x.

51. C. Bagi, E. Berryman, S. Teo, and N. Lane, "Oral Administration of Undenatured Native Chicken Type II Collagen (UC-II) Diminished Deterioration of Articular Cartilage in a Rat Model of Osteoarthritis (OA)," *Osteoarthritis and Cartilage* 25, no. 12 (2017): 2080–2090, https://doi.org/10.1016/j.joca.2017.08.013.

52. F. Rui, K. Jiawei, H. Yuntao, et al., "Undenatured Type II Collagen Prevents and Treats Osteoarthritis and Motor Function Degradation in T2DM Patients and db/db Mice," *Food & Function* 12, no. 10 (2021): 4373–4391, https://doi.org/10.1039/d0fo03011b.

53. Z. Zhang, X. Hu, M. Jin, et al., "Collagen Type II-Based Injectable Materials for In Situ Repair and Regeneration of Articular Cartilage Defect," *Biomaterials Research* 28 (2024): 0072, https://doi.org/10.34133/bmr.0072.

54. Y. Shiojima, M. Takahashi, R. Takahashi, et al., "Efficacy and Safety of Dietary Undenatured Type II Collagen on Joint and Motor Function in Healthy Volunteers: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study," *Journal of the American Nutrition Association* 42, no. 3 (2023): 224–241, https://doi.org/10.1080/07315724.2021.2024466.

55. R. Gibney, J. Patterson, and E. Ferraris, "High-Resolution Bioprinting of Recombinant Human Collagen Type III," *Polymers* 13, no. 17 (2021): 2973, https://doi.org/10.3390/polym13172973.

56. S. D'hondt, B. Guillemyn, D. Syx, et al., "Type III Collagen Affects Dermal and Vascular Collagen Fibrillogenesis and Tissue Integrity in a Mutant Col3a1 Transgenic Mouse Model," *Matrix Biology* 70 (2018): 72–83, https://doi.org/10.1016/j.matbio.2018.03.008.

57. R. J. Wenstrup, J. B. Florer, E. W. Brunskill, S. M. Bell, I. Chervoneva, and D. E. Birk, "Type V Collagen Controls the Initiation of Collagen Fibril Assembly," *Journal of Biological Chemistry* 279, no. 51 (2004): 53331–-53337, https://doi.org/10.1074/jbc.M409622200.

58. T. Yokota, J. McCourt, F. Ma, et al., "Type V Collagen in Scar Tissue Regulates the Size of Scar After Heart Injury," *Cell* 182, no. 3 (2020): 545–562, https://doi.org/10.1016/j.cell.2020.06.030.

59. J. Xu, X. Luo, Y. Zhang, et al., "Extraction and Characterization of Bovine Collagen Type V and Its Effects on Cell Behaviors," *Regenerative Biomaterials* 9 (2022): rbac028, https://doi.org/10.1093/rb/rbac028.

60. M. Sun, E. Y. Luo, S. M. Adams, et al., "Collagen XI Regulates the Acquisition of Collagen Fibril Structure, Organization and Functional Properties in Tendon," *Matrix Biology* 94 (2020): 77–94, https://doi.org/10.1016/j.matbio.2020.09.001.

61. A. Li, Y. Wei, C. Hung, and G. Vunjak-Novakovic, "Chondrogenic Properties of Collagen Type XI, A Component of Cartilage Extracellular Matrix," *Biomaterials* 173 (2018): 47–57, https://doi.org/10.1016/j.biomaterials.2018.05.004.

62. J. Freire, L. García-Berbel, P. García-Berbel, et al., "Collagen Type XI Alpha 1 Expression in Intraductal Papillomas Predicts Malignant Recurrence," *BioMed Research International* 2015 (2015): 812027, https://doi.org/10.1155/2015/812027.

63. R. Rodriguez, R. Seegmiller, M. Stark, and L. Bridgewater, "A Type XI Collagen Mutation Leads to Increased Degradation of Type II Collagen in Articular Cartilage," *Osteoarthritis and Cartilage* 12, no. 4 (2004): 314–320, https://doi.org/10.1016/j.joca.2003.12.002.

64. N. Matsuo, S. Tanaka, H. Yoshioka, M. Koch, M. K. Gordon, and F. Ramirez, "Collagen XXIV (Col24A1) Gene Expression is a Specific Marker of Osteoblast Differentiation and Bone Formation," *Connective Tissue Research* 49, no. 2 (2008): 68–75, https://doi.org/10.1080/03008200801913502.

65. W. Wang, D. Olson, G. Liang, et al., "Collagen XXIV (Col24A1) Promotes Osteoblastic Differentiation and Mineralization Through TGF-β/Smads Signaling Pathway," *International Journal of Biological Sciences* 8, no. 10 (2012): 1310–1322, https://doi.org/10.7150/ijbs.5136.

66. M. Koch, F. Laub, P. Zhou, et al., "A Vertebrate Fibrillar Collagen With Structural Features of Invertebrate Collagens: Selective Expression in Developing Cornea and Bone," *Journal of Biological Chemistry* 278 (2003): 43236–43244, https://doi.org/10.1074/jbc.M302112200.

67. R. Hjorten, U. Hansen, R. A. Underwood, et al., "Type XXVII Collagen at the Transition of Cartilage to Bone During Skeletogenesis," *Bone* 41, no. 4 (2007): 535–542, https://doi.org/10.1016/j.bone.2007.06.024.

68. D. A. Plumb, L. Ferrara, T. Torbica, et al., "Collagen XXVII Organises the Pericellular Matrix in the Growth Plate," *PLoS One* 6, no. 12 (2011): e29422, https://doi.org/10.1371/journal.pone.0029422.

69. J. Myllyharju and K. I. Kivirikko, "Collagens, Modifying Enzymes and Their Mutations in Humans, Flies and Worms," *Trends in Genetics* 20, no. 1 (2004): 33–43, https://doi.org/10.1016/j.tig.2003.11.004.

70. M. D. Shoulders and R. T. Raines, "Collagen Structure and Stability," *Annual Review of Biochemistry* 78, no. 1 (2009): 929–958, https://doi.org/10.1146/annurev.biochem.77.032207.120833.

71. J. Xie, M. Bao, S. M. Bruekers, and W. T. Huck, "Collagen Gels With Different Fibrillar Microarchitectures Elicit Different Cellular Responses," *ACS Applied Materials and Interfaces* 9, no. 23 (2017): 19630–19637, https://doi.org/10.1021/acsami.7b03883.

72. S. W. Hamaia, D. Luff, E. J. Hunter, et al., "Unique Charge-Dependent Constraint on Collagen Recognition by Integrin *A10B1*," *Matrix Biology* 59 (2017): 80–94, https://doi.org/10.1016/j.matbio.2016.08.010.

73. F. N. Kenny and J. T. Connelly, "Integrin-Mediated Adhesion and Mechano-Sensing in Cutaneous Wound Healing," *Cell and Tissue Research* 360, no. 3 (2015): 571–582, https://doi.org/10.1007/s00441-014-2064-9.

74. J. Elango, C. Hou, B. Bao, S. Wang, J. E. Maté Sánchez de Val, and W. Wenhui, "The Molecular Interaction of Collagen With Cell Receptors for Biological Function," *Polymers* 14, no. 5 (2022): 876, https://doi.org/10.3390/polym14050876.

75. E. Fuentes, "Modulation of Glycoprotein VI and Its Downstream Signaling Pathways as an Antiplatelet Target," *International Journal of Molecular Sciences* 23, no. 17 (2022): 9882, https://doi.org/10.3390/ijms23179882.

76. A. D. Barrow, N. Raynal, T. L. Andersen, et al., "OSCAR is a Collagen Receptor That Costimulates Osteoclastogenesis in DAP12-Deficient Humans and Mice," *The Journal of Clinical Investigation* 121, no. 9 (2011): 3505–3516, https://doi.org/10.1172/JCI45913.

77. F. Van Laethem, L. Donaty, E. Tchernonog, et al., "LAIR1, An ITIM-Containing Receptor Involved in Immune Disorders and in Hematological Neoplasms," *International Journal of Molecular Sciences* 23, no. 24 (2022): 16136, https://doi.org/10.3390/ijms232416136.

78. F. Gucciardo, S. Pirson, L. Baudin, A. Lebeau, and A. Noël, "uPARAP/Endo180: A Multifaceted Protein of Mesenchymal Cells," *Cellular and Molecular Life Sciences* 79, no. 5 (2022): 255, https://doi.org/10.1007/s00018-022-04249-7.

79. W. Sun, M. H. Shahrajabian, K. Ma, and S. Wang, "Advances in Molecular Function and Recombinant Expression of Human Collagen," *Pharmaceuticals* 18, no. 3 (2025): 430, https://doi.org/10.3390/ph18030430.

80. Y.-X. Liu, Z.-Q. Liu, L. Song, et al., "Effects of Collagenase Type I on the Structural Features of Collagen Fibres From Sea Cucumber (Stichopus Japonicus) Body Wall," *Food Chemistry* 301 (2019): 125302, https://doi.org/10.1016/j.foodchem.2019.125302.

81. L. Merly and S. L. Smith, "Collagen Type II, Alpha 1 Protein: A Bioactive Component of Shark Cartilage," *International Immunopharmacology* 15, no. 2 (2013): 309–315, https://doi.org/10.1016/j.intimp.2012.12.001.

82. Z. Rastian, S. Pütz, Y. Wang, et al., "Type I Collagen From Jellyfish Catostylus Mosaicus for Biomaterial Applications," *ACS Biomaterials Science & Engineering* 4, no. 6 (2018): 2115–2125, https://doi.org/10.1021/acsbiomaterials.7b00979.

83. N. Boute, J. Y. Exposito, N. Boury-Esnault, et al., "Type IV Collagen in Sponges, the Missing Link in Basement Membrane Ubiquity," *Biology of the Cell* 88, no. 1-2 (1996): 37–44, https://doi.org/10.1016/s0248-4900(97)86829-3.

84. N. V. Salim, B. Madhan, V. Glattauer, and J. A. Ramshaw, "Comprehensive Review on Collagen Extraction From Food by-Products and Waste as a Value-Added Material," *International Journal of Biological Macromolecules* 278 (2024): 134374, https://doi.org/10.1016/j.ijbiomac.2024.134374.

85. M. K. Maher, J. F. White, V. Glattauer, et al., "Variation in Hydrogel Formation and Network Structure for Telo-Atelo-and Methacrylated Collagens," *Polymers* 14, no. 9 (2022): 1775, https://doi.org/10.3390/polym14091775.

86. T. R. Senadheera, D. Dave, and F. Shahidi, "Sea Cucumber Derived Type I Collagen: A Comprehensive Review," *Marine Drugs* 18, no. 9 (2020): 471, https://doi.org/10.3390/md18090471.

87. A. M. E. Matinong, Y. Chisti, K. L. Pickering, and R. G. Haverkamp, "Collagen Extraction From Animal Skin," *Biology* 11, no. 6 (2022): 905, https://doi.org/10.3390/biology11060905.

88. S. Farooq, M. I. Ahmad, S. Zheng, et al., "A Review on Marine Collagen: Sources, Extraction Methods, Colloids Properties, and Food Applications," *Collagen and Leather* 6, no. 1 (2024): 11, https://doi.org/10.1186/s42825-024-00152-y.

89. D. Li, C. Mu, S. Cai, and W. Lin, "Ultrasonic Irradiation in the Enzymatic Extraction of Collagen," *Ultrasonics Sonochemistry* 16, no. 5 (2009): 605–609, https://doi.org/10.1016/j.ultsonch.2009.02.004.

90. H. Ju, X. Liu, G. Zhang, D. Liu, and Y. Yang, "Comparison of the Structural Characteristics of Native Collagen Fibrils Derived From Bovine Tendons Using Two Different Methods: Modified Acid-Solubilized and Pepsin-Aided Extraction," *Materials* 13, no. 2 (2020): 358, https://doi.org/10.3390/ma13020358.

91. S. Noorzai, C. J. R. Verbeek, M. C. Lay, and J. Swan, "Collagen Extraction From Various Waste Bovine Hide Sources," *Waste and Biomass Valorization* 11 (2020): 5687–5698, https://doi.org/10.1007/s12649-019-00843-2.

92. M. Zhu, S. Li, L. Chen, et al., "Insights Into Microstructure, Physicochemical Characteristics and Functional Properties of Collagen Extracted From Various Livestock Skins," *Journal of the Science of Food and Agriculture* 105, no. 14 (2025): 7779–7787, https://doi.org/10.1002/jsfa.70023.

93. A. A. Andayani, H. Harmita, and B. P. Maggadani, "Isolation, Purification, and Characterization of Porcine Skin Collagen: Analysis of the Glycine, Proline, and Hydroxyproline Components Using High-Performance Liquid Chromatography," *International Journal of Applied Pharmaceutics* 10, no. 1 (2018): 294–298, https://doi.org/10.22159/ijap.2018.v10s1.65.

94. L. Salvatore, N. Gallo, D. Aiello, et al., "An Insight on Type I Collagen From Horse Tendon for the Manufacture of Implantable Devices," *International Journal of Biological Macromolecules* 154 (2020): 291–306, https://doi.org/10.1016/j.ijbiomac.2020.03.082.

95. D. Dhakal, P. Koomsap, A. Lamichhane, M. B. Sadiq, and A. K. Anal, "Optimization of Collagen Extraction From Chicken Feet by Papain Hydrolysis and Synthesis of Chicken Feet Collagen Based Biopolymeric Fibres," *Food Bioscience* 23 (2018): 23–30, https://doi.org/10.1016/j.fbio.2018.03.003.

96. S. Cliche, J. Amiot, C. Avezard, and C. Gariepy, "Extraction and Characterization of Collagen With or Without Telopeptides From Chicken Skin," *Poultry Science* 82, no. 3 (2003): 503–509, https://doi.org/10.1093/ps/82.3.503.

97. N. Huda, E. Seow, M. Normawati, and N. N. Aisyah, "Preliminary Study on Physicochemical Properties of Duck Feet Collagen," *International Journal of Poultry Science* 12, no. 10 (2013): 615–621, https://doi.org/10.3923/ijps.2013.615.621.

98. J. Wang, H. Hou, Y. Li, et al., "Isolation, Purification, and Anti-osteoporosis Activity of Donkey Bone Collagen From Discarded Bone and Its Antioxidant Peptides," *Heliyon* 10, no. 1 (2024): e23531, https://doi.org/10.1016/j.heliyon.2023.e23531.

99. A. Wood, M. Ogawa, R. J. Portier, M. Schexnayder, M. Shirley, and J. N. Losso, "Biochemical Properties of Alligator (*Alligator mississippiensis*) Bone Collagen," *Comparative Biochemistry and Physiology Part B: Biochemistry and Molecular Biology* 151, no. 3 (2008): 246–249, https://doi.org/10.1016/j.cbpb.2008.05.015.

100. X. Dong, Y. Q. Xin, H. Qi, et al., "Isolation and Characterization of Pepsin-Soluble Collagen From Abalone (Haliotis Discus Hannai) Gastropod Muscle Part II," *Food Science and Technology Research* 18, no. 2 (2012): 271–278, https://doi.org/10.3136/fstr.18.271.

101. S. Dharmawati, A. Gunawan, A. Pardede, and O. Sjofjan, "Characteristics of Natural Collagen of Freshwater Snail Flesh (*Pomacea paludosa*) Extracted With Bromelain Enzyme and Acid-Hydro-Extraction Method," *Tropical Journal of Natural Product Research* 9 (2025): https://doi.org/10.26538/tjnpr/v9i3.7.

102. E. Balikci, E. T. Baran, A. Tahmasebifar, and B. Yilmaz, "Characterization of Collagen From Jellyfish Aurelia Aurita and Investigation of Biomaterials Potentials," *Applied Biochemistry and Biotechnology* 196, no. 9 (2024): 6200–6221, https://doi.org/10.1007/s12010-023-04848-5.

103. S. Addad, J.-Y. Exposito, C. Faye, S. Ricard-Blum, and C. Lethias, "Isolation, Characterization and Biological Evaluation of Jellyfish Collagen for Use in Biomedical Applications," *Marine Drugs* 9, no. 6 (2011): 967–983, https://doi.org/10.3390/md9060967.

104. R. O. Sousa, E. Martins, D. N. Carvalho, et al., "Collagen From Atlantic Cod (*Gadus morhua*) Skins Extracted Using CO2 Acidified Water With Potential Application in Healthcare," *Journal of Polymer Research* 27, no. 3 (2020): 73, https://doi.org/10.1007/s10965-020-02048-x.

105. H. A.-G. AbdEl-aal, H. M. A. Mohamed, S. A. Saleh, and R. Koriem, "Characteristics and Functional Properties of Collagen Extracted From Nile Tilapia (*Oreochromis niloticus*) Skin," *Journal of Modern Research* 3 (2021): 36–43, https://doi.org/10.21608/JMR.2020.37541.1034.

106. P. Kittiphattanabawon, C. Sriket, H. Kishimura, and S. Benjakul, "Characteristics of Acid and Pepsin Solubilized Collagens From Nile Tilapia (*Oreochromis niloticus*) Scale," *Emirates Journal of Food and Agriculture* 31 (2019): 95–101, https://doi.org/10.9755/ejfa.2019.v31.i2.1911.

107. K. Nilsuwan, K. Fusang, P. Pripatnanont, and S. Benjakul, "Properties and Characteristics of Acid-Soluble Collagen From Salmon Skin

Defatted With the Aid of Ultrasonication," *Fishes* 7, no. 1 (2022): 51, https://doi.org/10.3390/fishes7010051.

108. A. Afifah, O. Suparno, L. Haditjaroko, K. Tarman, A. Setiyono, and A. W. Nugraha, "Isolation and Characterization of Collagen From Salmon (*Salmo salar*) Skin Using Papain Enzyme," *Jurnal Pengolahan Hasil Perikanan Indonesia* 27, no. 6 (2024): 536–552, https://doi.org/10.17844/jphpi.v27i6.53285.

109. P. Kittiphattanabawon, S. Benjakul, W. Visessanguan, and F. Shahidi, "Isolation and Properties of Acid-and Pepsin-Soluble Collagen From the Skin of Blacktip Shark (*Carcharhinus limbatus*)," *European Food Research and Technology* 230, no. 3 (2010): 475–483, https://doi.org/10.1007/s00217-009-1191-0.

110. Z. Pan, B. Ge, M. Wei, J. Elango, and W. Wu, "Isolation and Biochemical Properties of Type II Collagen From Blue Shark (*Prionace glauca*) Cartilage," *Marine Drugs* 21, no. 5 (2023): 260, https://doi.org/10.3390/md21050260.

111. K.-M. Song, S. K. Jung, Y. H. Kim, Y. E. Kim, and N. H. Lee, "Development of Industrial Ultrasound System for Mass Production of Collagen and Biochemical Characteristics of Extracted Collagen," *Food and Bioproducts Processing* 110 (2018): 96–103, https://doi.org/10.1016/j.fbp.2018.04.001.

112. N. M. M. Hukmi and N. M. Sarbon, "Isolation and Characterization of Acid Soluble Collagen (ASC) and Pepsin Soluble Collagen (PSC) Extracted From Silver Catfish (Pangasius Sp.) Skin," *International Food Research Journal* 25 (2018).

113. J.-W. Woo, S.-J. Yu, S.-M. Cho, Y.-B. Lee, and S.-B. Kim, "Extraction Optimization and Properties of Collagen From Yellowfin Tuna (*Thunnus albacares*) Dorsal Skin," *Food Hydrocolloids* 22, no. 5 (2008): 879–887, https://doi.org/10.1016/j.foodhyd.2007.04.015.

114. G. Syahputra, H. Hariyatun, M. Firdaus, and P. Santoso, "Extraction and Characterization of Collagen From Sand Sea Cucumber (Holothuria Scabra)," *Jurnal Ilmu Pertanian Indonesia* 26, no. 3 (2021): 319–327, https://doi.org/10.18343/jipi.26.3.319.

115. L.-J. Yan, L.-C. Sun, K.-Y. Cao, et al., "Type I Collagen From Sea Cucumber (Stichopus Japonicus) and the Role of Matrix Metalloproteinase-2 in Autolysis," *Food Bioscience* 41 (2021): 100959, https://doi.org/10.1016/j.fbio.2021.100959.

116. N. Barzkar, G. Attaran-Fariman, A. Taheri, and B. A. V. Maran, "Extraction and Characterization of Collagen and Gelatin From Body Wall of Sea Cucumbers Stichopus Horrens and Holothuria Arenicola," *PeerJ* 12 (2024): e18149, https://doi.org/10.7717/peerj.18149.

117. M. I. Shaik, A. N. A. Kadir, and N. M. Sarbon, "Physicochemical and Thermal Properties of Pepsin-and Acid-Soluble Collagen Isolated From the Body Wall of Sea Cucumbers (Stichopus Hermanni)," *Journal of Food Science* 89, no. 1 (2024): 320–329, https://doi.org/10.1111/1750-3841.16858.

118. Y. D. Siddiqui, E. Mochamad Arief, A. Yusoff, et al., "Extraction, Purification and Physical Characterization of Collagen From Body Wall of Sea Cucumber (Bohadschia Bivitatta)," *Journal of Environmental Health* 4 (2013): 53–65.

119. M. Zhong, T. Chen, C. Hu, and C. Ren, "Isolation and Characterization of Collagen From the Body Wall of Sea Cucumber Stichopus Monotuberculatus," *Journal of Food Science* 80, no. 4 (2015): C671–C679, https://doi.org/10.1111/1750-3841.12826.

120. K. Silvipriya, K. K. Kumar, A. Bhat, B. D. Kumar, A. John, and P. Lakshmanan, "Collagen: Animal Sources and Biomedical Application," *Journal of Applied Pharmaceutical Science* 5 (2015): 123–127, https://doi.org/10.7324/JAPS.2015.50322.

121. G. Charriere, M. Bejot, L. Schnitzler, G. Ville, and D. J. Hartmann, "Reactions to a Bovine Collagen Implant: Clinical and Immunologic Study in 705 Patients," *Journal of the American Academy of Dermatology* 21, no. 6 (1989): 1203–1208, https://doi.org/10.1016/s0190-9622(89)70330-3.

122. H. Wang, "A Review of the Effects of Collagen Treatment in Clinical Studies," *Polymers* 13, no. 22 (2021): 3868, https://doi.org/10.3390/polym13223868.

123. L. Ge, S. Zheng, and H. Wei, "Comparison of Histological Structure and Biocompatibility Between Human Acellular Dermal Matrix (ADM) and Porcine ADM," *Burns* 35, no. 1 (2009): 46–50, https://doi.org/10.1016/j.burns.2008.05.007.

124. Y. Zhang, Y. Chen, B. Zhao, et al., "Detection of Type I and III Collagen in Porcine Acellular Matrix Using HPLC–MS," *Regenerative Biomaterials* 7, no. 6 (2020): 577–582, https://doi.org/10.1093/rb/rbaa032.

125. S. Periasamy, Y.-J. Chen, D.-Z. Hsu, and D.-J. Hsieh, "Collagen Type II Solution Extracted From Supercritical Carbon Dioxide Decellularized Porcine Cartilage: Regenerative Efficacy on Post-Traumatic Osteoarthritis Model," *Bioresources and Bioprocessing* 11, no. 1 (2024): 21, https://doi.org/10.1186/s40643-024-00731-1.

126. C. Easterbrook and G. Maddern, "Porcine and Bovine Surgical Products: Jewish, Muslim, and Hindu Perspectives," *Archives of Surgery* 143, no. 4 (2008): 366–370, https://doi.org/10.1001/archsurg.143.4.366.

127. K. Casós, R. Llatjós, A. Blasco-Lucas, et al., "Differential Immune Response to Bioprosthetic Heart Valve Tissues in the *A*1, 3Galactosyltransferase-Knockout Mouse Model," *Bioengineering* 10, no. 7 (2023): 833, https://doi.org/10.3390/bioengineering10070833.

128. P. Angele, J. Abke, R. Kujat, et al., "Influence of Different Collagen Species on Physico-Chemical Properties of Crosslinked Collagen Matrices," *Biomaterials* 25, no. 14 (2004): 2831–2841, https://doi.org/10.1016/j.biomaterials.2003.09.066.

129. N. Gallo, M. L. Natali, A. Sannino, and L. Salvatore, "An Overview of the Use of Equine Collagen as Emerging Material for Biomedical Applications," *Journal of Functional Biomaterials* 11, no. 4 (2020): 79, https://doi.org/10.3390/jfb11040079.

130. R. Bennett and S. Pfuderer, *Demand for Donkey Hides and Implications for Global Donkey Populations* (2019), https://doi.org/10.22004/ag.econ.289683.

131. D. Wang, W. Ru, Y. Xu, et al., "Chemical Constituents and Bioactivities of Colla Corii Asini," *Drug Discoveries & Therapeutics* 8, no. 5 (2014): 201–207, https://doi.org/10.5582/ddt.2014.01038.

132. M. Râpă, C. Gaidau, L. M. Stefan, et al., "Donkey Gelatin and Keratin Nanofibers Loaded With Antioxidant Agents for Wound Healing Dressings," *Gels* 10, no. 6 (2024): 391, https://doi.org/10.3390/gels10060391.

133. R. Bennett and S. Pfuderer, "The Potential for New Donkey Farming Systems to Supply the Growing Demand for Hides," *Animals* 10, no. 4 (2020): 718, https://doi.org/10.3390/ani10040718.

134. J. Zhang, M. Wu, Z. Ma, Y. Zhang, and H. Cao, "Species-Specific Identification of Donkey-Hide Gelatin and Its Adulterants Using Marker Peptides," *PLoS One* 17, no. 8 (2022): e0273021, https://doi.org/10.1371/journal.pone.0273021.

135. T. C. Harder, S. Buda, H. Hengel, M. Beer, and T. C. Mettenleiter, "Poultry Food Products—A Source of Avian Influenza Virus Transmission to Humans?" *Clinical Microbiology and Infection* 22, no. 2 (2016): 141–146, https://doi.org/10.1016/j.cmi.2015.11.015.

136. Z. Ahmed, L. C. Powell, N. Matin, et al., "Jellyfish Collagen: A Biocompatible Collagen Source for 3D Scaffold Fabrication and Enhanced Chondrogenicity," *Marine Drugs* 19, no. 8 (2021): 405, https://doi.org/10.3390/md19080405.

137. B. Hoyer, A. Bernhardt, A. Lode, et al., "Jellyfish Collagen Scaffolds for Cartilage Tissue Engineering," *Acta Biomaterialia* 10, no. 2 (2014): 883–892, https://doi.org/10.1016/j.actbio.2013.10.022.

138. A. Miki, S. Inaba, T. Baba, K. Kihira, H. Fukada, and M. Oda, "Structural and Physical Properties of Collagen Extracted From Moon Jellyfish Under Neutral pH Conditions," *Bioscience, Biotechnology, and*

Biochemistry 79, no. 10 (2015): 1603–1607, https://doi.org/10.1080/09168451.2015.1046367.

139. L. Salvatore, N. Gallo, M. L. Natali, et al., "Marine Collagen and Its Derivatives: Versatile and Sustainable Bio-Resources for Healthcare," *Materials Science and Engineering: C* 113 (2020): 110963, https://doi.org/10.1016/j.msec.2020.110963.

140. A. L. Alves, A. L. Marques, E. Martins, T. H. Silva, and R. L. Reis, "Cosmetic Potential of Marine Fish Skin Collagen," *Cosmetics* 4 (2017): 39, https://doi.org/10.3390/cosmetics4040039.

141. A. M. Carvalho, A. P. Marques, T. H. Silva, and R. L. Reis, "Evaluation of the Potential of Collagen From Codfish Skin as a Biomaterial for Biomedical Applications," *Marine Drugs* 16, no. 12 (2018): 495, https://doi.org/10.3390/md16120495.

142. M. Tian, C. Xue, Y. Chang, et al., "Collagen Fibrils of Sea Cucumber (Apostichopus Japonicus) are Heterotypic," *Food Chemistry* 316 (2020): 126272, https://doi.org/10.1016/j.foodchem.2020.126272.

143. N. Nabilla, I. Shofiyah, D. Alvitasari, et al., "Organization, Density, and Content of Collagen in the Body Wall of Sea Cucumbers Acaudina Rosettis and Phyllophorus Sp," *Aquaculture and Fisheries* (2024): https://doi.org/10.1016/j.aaf.2024.09.003.

144. L. Cao, Z. Zhang, D. Yuan, M. Yu, and J. Min, "Tissue Engineering Applications of Recombinant Human Collagen: A Review of Recent Progress," *Frontiers in Bioengineering and Biotechnology* 12 (2024): 1358246, https://doi.org/10.3389/fbioe.2024.1358246.

145. Z. Cheng, B. Hong, Y. Li, and J. Wang, "Preparation and Characterization of Hydroxylated Recombinant Collagen by Incorporating Proline and Hydroxyproline in Proline-Deficient *Escherichia coli*," *Bioengineering* 11, no. 10 (2024): 975, https://doi.org/10.3390/bioengineering11100975.

146. W. Xie, Q. Wu, Z. Kuang, et al., "Temperature-Controlled Expression of a Recombinant Human-Like Collagen I Peptide in *Escherichia coli*," *Bioengineering* 10, no. 8 (2023): 926, https://doi.org/10.3390/bioengineering10080926.

147. J. Fang, Z. Ma, D. Liu, et al., "Co-Expression of Recombinant Human Collagen *A*1 (III) Chain With Viral Prolyl 4-Hydroxylase in Pichia Pastoris GS115," *Protein Expression and Purification* 201 (2023): 106184, https://doi.org/10.1016/j.pep.2022.106184.

148. T. Wang, J. Lew, J. Premkumar, C. L. Poh, and M. Win Naing, "Production of Recombinant Collagen: State of the Art and Challenges," *Engineering Biology* 1 (2017): 18–23, https://doi.org/10.1049/enb.2017.0003.

149. C. Wang, X. Guo, M. Fan, et al., "Production of Recombinant Human Type I Collagen Homotrimers in CHO Cells and Their Physicochemical and Functional Properties," *Journal of Biotechnology* 395 (2024): 149–160, https://doi.org/10.1016/j.jbiotec.2024.09.011.

150. K. Rattanapisit, S. Abdulheem, D. Chaikeawkaew, et al., "Recombinant Human Osteopontin Expressed in Nicotiana Benthamiana Stimulates Osteogenesis Related Genes in Human Periodontal Ligament Cells," *Scientific Reports* 7, no. 1 (2017): 17358, https://doi.org/10.1038/s41598-017-17666-7.

151. M. Haagdorens, E. Edin, P. Fagerholm, et al., "Plant Recombinant Human Collagen Type I Hydrogels for Corneal Regeneration," *Regenerative Engineering and Translational Medicine* 8, no. 2 (2022): 269–283, https://doi.org/10.1007/s40883-021-00220-3.

152. A. Lamberg, T. Helaakoski, J. Myllyharju, et al., "Characterization of Human Type III Collagen Expressed in a Baculovirus System: Production of a Protein With a Stable Triple Helix Requires Coexpression With the Two Types of Recombinant Prolyl 4-Hydroxylase Subunit (∗)," *Journal of Biological Chemistry* 271, no. 20 (1996): 11988–11995, https://doi.org/10.1074/jbc.271.20.11988.

153. J. Yan, K. Hu, Y. Xiao, et al., "Preparation of Recombinant Human-Like Collagen/Fibroin Scaffold and Its Promoting Effect on Vascular Cells Biocompatibility," *Journal of Bioactive and Compatible Polymers* 33, no. 4 (2018): 416–425, https://doi.org/10.1177/0883911518769680.

154. A. Bhatwa, W. Wang, Y. I. Hassan, N. Abraham, X.-Z. Li, and T. Zhou, "Challenges Associated With the Formation of Recombinant Protein Inclusion Bodies in *Escherichia coli* and Strategies to Address Them for Industrial Applications," *Frontiers in Bioengineering and Biotechnology* 9 (2021): 630551, https://doi.org/10.3389/fbioe.2021.630551.

155. Y. Wang, F. Cui, K. Hu, X. Zhu, and D. Fan, "Bone Regeneration by Using Scaffold Based on Mineralized Recombinant Collagen," *Journal of Biomedical Materials Research Part B: Applied Biomaterials: An Official Journal of The Society for Biomaterials, The Japanese Society for Biomaterials, and The Australian Society for Biomaterials and the Korean Society for Biomaterials* 86, no. 1 (2008): 29–35, https://doi.org/10.1002/jbm.b.30984.

156. M. Nokelainen, H. Tu, A. Vuorela, H. Notbohm, K. I. Kivirikko, and J. Myllyharju, "High-Level Production of Human Type I Collagen in the Yeast Pichia Pastoris," *Yeast* 18, no. 9 (2001): 797–806, https://doi.org/10.1002/yea.730.

157. S. de Moura Campos, G. dos Santos Costa, S. G. Karp, V. Thomaz-Soccol, and C. R. Soccol, "Innovations and Challenges in Collagen and Gelatin Production Through Precision Fermentation," *World Journal of Microbiology and Biotechnology* 41, no. 2 (2025): 63, https://doi.org/10.1007/s11274-025-04276-z.

158. J. Myllyharju, M. Nokelainen, A. Vuorela, and K. Kivirikko, "Expression of Recombinant Human Type I-III Collagens in the Yeast Pichia Pastoris," *Biochemical Society Transactions* 28, no. 4 (2000): 353–357, https://doi.org/10.1042/bst0280353.

159. R. Que, A. Mohraz, N. A. Da Silva, and S.-W. Wang, "Expanding Functionality of Recombinant Human Collagen Through Engineered Non-Native Cysteines," *Biomacromolecules* 15, no. 10 (2014): 3540–3549, https://doi.org/10.1021/bm500735d.

160. A. Fertala, "Three Decades of Research on Recombinant Collagens: Reinventing the Wheel or Developing New Biomedical Products?" *Bioengineering* 7, no. 4 (2020): 155, https://doi.org/10.3390/bioengineering7040155.

161. A. Fichard, E. Tillet, F. Delacoux, R. Garrone, and F. Ruggiero, "Human Recombinant *A*1 (V) Collagen Chain: Homotrimeric Assembly and Subsequent Processing," *Journal of Biological Chemistry* 272, no. 48 (1997): 30083–30087, https://doi.org/10.1074/jbc.272.48.30083.

162. Y. Hou, L. T. Guey, T. Wu, et al., "Intravenously Administered Recombinant Human Type VII Collagen Derived From Chinese Hamster Ovary Cells Reverses the Disease Phenotype in Recessive Dystrophic Epidermolysis Bullosa Mice," *Journal of Investigative Dermatology* 135, no. 12 (2015): 3060–3067, https://doi.org/10.1038/jid.2015.291.

163. J. Zhang, C. Du, Y. Pan, et al., "Optimization of a Novel Expression System for Recombinant Protein Production in CHO Cells," *Scientific Reports* 14, no. 1 (2024): 24913, https://doi.org/10.1038/s41598-024-76995-6.

164. H. Stein, M. Wilensky, Y. Tsafrir, et al., "Production of Bioactive, Post-Translationally Modified, Heterotrimeric, Human Recombinant Type-I Collagen in Transgenic Tobacco," *Biomacromolecules* 10, no. 9 (2009): 2640–2645, https://doi.org/10.1021/bm900571b.

165. O. Shoseyov, Y. Posen, and F. Grynspan, "Human Recombinant Type I Collagen Produced in Plants," *Tissue Engineering Part A* 19, no. 13-14 (2013): 1527–1533, https://doi.org/10.1089/ten.TEA.2012.0347.

166. M. D. Berechet, C. Gaidau, A. Nešić, et al., "Antioxidant and Antimicrobial Properties of Hydrolysed Collagen Nanofibers Loaded With Ginger Essential Oil," *Materials* 16, no. 4 (2023): 1438, https://doi.org/10.3390/ma16041438.

167. A. C. L. Pavanello, R. P. Catarino, C. S. Portela, et al., "Hydrolyzed Collagen as a Partial Fat Substitute in Chicken Burgers Produced With

White Striping Meat," *Poultry Science* 104, no. 1 (2025): 104622, https://doi.org/10.1016/j.psj.2024.104622.

168. F. N. Ibrahim, M. R. Ismail-Fitry, M. M. Yusoff, and R. Shukri, "Effects of Fish Collagen Hydrolysate (FCH) as Fat Replacer in the Production of Buffalo Patties," *Journal of Advanced Research in Applied Sciences and Engineering Technology* 11 (2018): 108–117.

169. K. Szopa, A. Znamirowska-Piotrowska, K. Szajnar, and M. Pawlos, "Effect of Collagen Types, Bacterial Strains and Storage Duration on the Quality of Probiotic Fermented Sheep's Milk," *Molecules* 27, no. 9 (2022): 3028, https://doi.org/10.3390/molecules27093028.

170. S. E. Bilek and S. K. Bayram, "Fruit Juice Drink Production Containing Hydrolyzed Collagen," *Journal of Functional Foods* 14 (2015): 562–569, https://doi.org/10.1016/j.jff.2015.02.024.

171. B. Antebi, X. Cheng, J. N. Harris, L. B. Gower, X.-D. Chen, and J. Ling, "Biomimetic Collagen–Hydroxyapatite Composite Fabricated Via a Novel Perfusion-Flow Mineralization Technique," *Tissue Engineering Part C Methods* 19, no. 7 (2013): 487–496, https://doi.org/10.1089/ten.TEC.2012.0452.

172. J. Liu, B. Zhang, S. Song, et al., "Bovine Collagen Peptides Compounds Promote the Proliferation and Differentiation of MC3T3-E1 Pre-Osteoblasts," *PLoS One* 9, no. 6 (2014): e99920, https://doi.org/10.1371/journal.pone.0099920.

173. E. Salamanca, C.-C. Hsu, H.-M. Huang, et al., "Bone Regeneration Using a Porcine Bone Substitute Collagen Composite In Vitro and In Vivo," *Scientific Reports* 8, no. 1 (2018): 984, https://doi.org/10.1038/s41598-018-19629-y.

174. B. Hoyer, A. Bernhardt, S. Heinemann, I. Stachel, M. Meyer, and M. Gelinsky, "Biomimetically Mineralized Salmon Collagen Scaffolds for Application in Bone Tissue Engineering," *Biomacromolecules* 13, no. 4 (2012): 1059–1066, https://doi.org/10.1021/bm201776r.

175. R. B. Diller and A. J. Tabor, "The Role of the Extracellular Matrix (ECM) in Wound Healing: A Review," *Biomimetics* 7, no. 3 (2022): 87, https://doi.org/10.3390/biomimetics7030087.

176. L. F. S. Gushiken, F. P. Beserra, J. K. Bastos, C. J. Jackson, and C. H. Pellizzon, "Cutaneous Wound Healing: An Update From Physiopathology to Current Therapies," *Life* 11, no. 7 (2021): 665, https://doi.org/10.3390/life11070665.

177. S. S. Mathew-Steiner, S. Roy, and C. K. Sen, "Collagen in Wound Healing," *Bioengineering* 8, no. 5 (2021): 63, https://doi.org/10.3390/bioengineering8050063.

178. Z. Gao, Z. Hao, Y. Li, M. Im, and R. Spence, "Porcine Dermal Collagen as a Wound Dressing for Skin Donor Sites and Deep Partial Skin Thickness Burns," *Burns* 18 (1992): 492–496, https://doi.org/10.1016/0305-4179(92)90183-u.

179. M. Sedlář, K. Kacvinská, Z. Fohlerová, et al., "A Synergistic Effect of Fibrous Carboxymethyl Cellulose With Equine Collagen Improved the Hemostatic Properties of Freeze-Dried Wound Dressings," *Cellulose* 30, no. 17 (2023): 11113–11131, https://doi.org/10.1007/s10570-023-05499-9.

180. Y. Kulikova, S. Sukhikh, A. Zhikhreva, S. Noskova, and O. Babich, "Comparative Analysis of Collagen From Different Sources for Wound and Burn Management," *Biomaterials Translational* (2025): 00013, https://doi.org/10.12336/bmt.25.00013.

181. A. Sionkowska, K. Adamiak, K. Musiał, and M. Gadomska, "Collagen Based Materials in Cosmetic Applications: A Review," *Materials* 13, no. 19 (2020): 4217, https://doi.org/10.3390/ma13194217.

182. J. H. Lee, Y. S. Choi, S. M. Kim, Y. J. Kim, J. W. Rhie, and Y. J. Jun, "Efficacy and Safety of Porcine Collagen Filler for Nasolabial Fold Correction in Asians: A Prospective Multicenter, 12 Months Follow-Up Study," *Journal of Korean Medical Science* 29, no. 3 (2014): S217–S221, https://doi.org/10.3346/jkms.2014.29.S3.S217.

183. J.-S. Kim, D. Kim, H.-J. Kim, and A. Jang, "Protection Effect of Donkey Hide Gelatin Hydrolysates on UVB-Induced Photoaging of Human Skin Fibroblasts," *Process biochemistry* 67 (2018): 118–126, https://doi.org/10.1016/j.procbio.2018.02.004.

184. A. Prokopová, J. Pavlačková, P. Mokrejš, and R. Gál, "Collagen Hydrolysate Prepared From Chicken By-Product as a Functional Polymer in Cosmetic Formulation," *Molecules* 26, no. 7 (2021): 2021, https://doi.org/10.3390/molecules26072021.

185. S. Liu, Y. Lu, M. Kurono, Y. Matahira, Y. Manabe, and T. Sugawara, "Oral Supplementation of Sea Cucumber and Its Hydrolysate Mitigates Ultraviolet A-Induced Photoaging in Hairless Mice," *Journal of the Science of Food and Agriculture* 102, no. 5 (2022): 1987–1994, https://doi.org/10.1002/jsfa.11537.

186. D. Coppola, M. Oliviero, G. A. Vitale, et al., "Marine Collagen From Alternative and Sustainable Sources: Extraction, Processing and Applications," *Marine Drugs* 18, no. 4 (2020): 214, https://doi.org/10.3390/md18040214.

187. X. Zhai, X. Geng, W. Li, H. Cui, Y. Wang, and S. Qin, "Comprehensive Review on Application Progress of Marine Collagen Cross-Linking Modification in Bone Repairs," *Marine Drugs* 23, no. 4 (2025): 151, https://doi.org/10.3390/md23040151.