

## A COMPREHENSIVE REVIEW ON MARINE COLLAGEN AND SKIN RENEWAL: A BIOACTIVE STRATEGY FOR ANTI-AGING

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### ABSTRACT

Collagen, the most abundant structural protein in animals, is fundamental for maintaining skin strength, elasticity, and hydration. However, age-related decline in collagen and elastin synthesis contributes to visible signs of aging, including wrinkles, dryness, and reduced firmness. Conventionally, collagen is sourced from terrestrial animals, but concerns related to disease transmission, cultural restrictions, and ethical considerations have limited its widespread application. Marine-derived collagen, primarily obtained from fish skin, scales, bones, and invertebrates, has emerged as a safer, more sustainable, and highly bioavailable alternative. Owing to its lower molecular weight and superior absorption, marine collagen peptides demonstrate potent anti-aging effects by stimulating fibroblast activity, enhancing extracellular matrix synthesis, and inhibiting collagen-degrading enzymes such as matrix metalloproteinases. In addition, marine-derived proteins and polysaccharides, including those from *Spirulina* and *Ulva rigida*, exhibit antioxidant and protective effects that complement collagen's role in skin regeneration. Clinical and preclinical studies indicate significant improvements in dermal thickness, hydration, elasticity, and wrinkle reduction following marine collagen supplementation or topical application. Despite these promising outcomes, large-scale utilization of marine collagen faces challenges in cost-effective extraction, product standardization, and clinical validation. With global fisheries generating substantial quantities of underutilized by-products, sustainable extraction and valorization strategies present a unique opportunity to address both environmental concerns and the growing demand for safe, effective cosmeceuticals. This review explores recent advances in marine collagen research, underlying mechanisms of skin health benefits, and future directions for its application in dermatology, nutraceuticals, and sustainable skincare.

**Keywords:** Marine collagen, Skin aging, Skin health, Extracellular matrix, Matrix metalloproteinases.

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### INTRODUCTION

As one of the most abundant proteins in animals, collagen accounts for approximately 30% of total body protein and is crucial for preserving the strength and structure of connective tissues such as skin, bone, and cartilage [1]. The term *collagen* is derived from the Greek words *kólla*, meaning "glue," and *-gen*, meaning "producing," reflecting its role in binding and supporting body tissues [2]. Collagen is the primary structural protein in connective tissues and the extracellular matrix (ECM), particularly abundant in fibrous tissues such as skin and tendons [3]. There are 28 types of collagen (designated I-XXVIII), each with distinct structures and tissue distributions. All collagens are composed of three amino acid chains forming a triple helix, with a repeating Gly-X-Y pattern, where proline or hydroxyproline often occupies the Y position. These helices form fibrils and are further organized into primary, secondary, and tertiary structures [4]. Collagen exhibits a complex hierarchical structure comprising four distinct levels: the primary structure (amino acid triplets), the secondary structure ( $\alpha$ -helix), the tertiary structure (triple-helical conformation), and the quaternary structure (fibrillar assembly) and is composed of three  $\alpha$ -chains twisted together into a compact and highly stable triple helix [5]. Among its various types, type I collagen is the most prevalent and contributes significantly to the tensile strength and flexibility of joints. Type I collagen, produced by fibroblasts in the dermis, makes up the majority of skin collagen and is essential for maintaining skin strength and elasticity, alongside collagen, fibroblasts also generate elastin, which supports the skin's stretchability and ability to return to its original shape, ensuring overall resilience [6]. Fibril-forming collagens (Types I, II, III, V, and XI) play crucial roles in connective tissues. Type I primarily provides structural integrity and high tensile strength, while Types II, III, V, and XI collectively enhance

mechanical stability and overall tissue resilience [7]. Table 1 provides an overview of the principal collagen types, detailing their roles, tissue distribution, molecular structures, and the specific genes responsible for encoding their protein chains [8,9]. Collagen is widely applied in tissue engineering and clinical therapies due to its safety and effectiveness as a biomaterial. It has found use in diverse medical fields such as orthopedics, urology, neurology, cardiovascular, plastic surgery, and ophthalmology. In addition, it serves as a key component in skin regeneration scaffolds, dental composites, and biodegradable systems [10]. Collagen's excellent biocompatibility and low immunogenic response make it an ideal candidate for use in pharmaceuticals, cosmetics, and tissue engineering [11]. Its functional benefits, such as protein enrichment, moisture retention, and emulsifying ability, also support its growing use in the food industry [2].

The ECM, apart from providing structural support, also plays a crucial role in regulating cellular processes including adhesion, migration, proliferation, and differentiation. Collagen obtained from terrestrial animals such as cattle and pigs has been associated with serious health concerns due to the potential transmission of diseases. Notable outbreaks, including transmissible spongiform encephalopathies, bovine spongiform encephalopathy, and foot-and-mouth disease, have raised global safety issues regarding the use of land animal-derived collagen [12]. In addition, religious and ethical objections further limit its applicability among major faiths such as Islam, Hinduism, and Judaism, covering over 38% of the global population, limiting the use of certain animal-based collagen products [13].

In contrast, collagen sourced from marine organisms presents a safer and more acceptable alternative. It is not only free from land animal

Table 1: Types of collagen and their biomedical applications

Collagen type	Primary role	Tissue/organ found in	Molecular structure*
Type I	Provides structural support in bones; used in guided tissue regeneration membranes	Skin, bones, teeth, tendons, ligaments, and blood vessels	$[\alpha 1(I)]_2\alpha 2(I)$
Type II	Predominant in cartilage; used in joint repair and arthritis therapies	Cartilage	$[\alpha 1(II)]_3$
Type III	Found in reticular fibers; used in wound healing products such as hemostats and sealants	Muscles and blood vessel walls	$[\alpha 1(III)]_3$
Type IV	Key structural element of the basement membrane aids in cell adhesion and serves as a marker for kidney disorders	Basal lamina, epithelial cell layer of the basement membranes	$[\alpha 1(IV)]_2\alpha 2(IV)$ , $[\alpha 3(IV)]_2\alpha 4(IV)$ , $[\alpha 5(IV)]_2\alpha 6(IV)$
Type V	Used in biomaterials for corneal applications	Hair, cell membranes, and placenta	$\alpha 1(V)$ , $\alpha 2(V)$ , $\alpha 3(V)$

\*The proteins  $\alpha 1(I)$ ,  $\alpha 2(I)$ ,  $\alpha 1(II)$ ,  $\alpha 1(III)$ ,  $\alpha 1(IV)$ ,  $\alpha 2(IV)$ ,  $\alpha 3(IV)$ ,  $\alpha 4(IV)$ ,  $\alpha 5(IV)$ ,  $\alpha 6(IV)$ ,  $\alpha 1(V)$ ,  $\alpha 2(V)$ , and  $\alpha 3(V)$  are encoded by the genes COL1A1, COL1A2, COL2A1, COL3A1, COL4A1, COL4A2, COL4A3, COL4A4, COL4A5, COL4A6, COL5A1, COL5A2, and COL5A3, respectively. Adapted from Boraschi-Diaz *et al.*, 2017, Silvipriya *et al.*, 2015 with little modification

pathogens but also offers improved physicochemical properties and greater availability [14]. Marine-derived collagen and collagen peptides are widely employed in nutraceuticals and functional food products owing to their close structural similarity to human collagen, proven safety record, chemical stability, biological compatibility, efficient absorption through the digestive tract, and significant biofunctional properties [15]. The figure 1 demonstrates the key marine sources of collagen and their significant roles across various biomedical fields. Collagen from marine sources like jellyfish, sponges, fish, and other invertebrates is highly valued [13]. These sources are favored because they avoid religious restrictions, are free from animal pathogens, and offer good metabolic compatibility. Marine-derived collagen stands out as a reliable, user-friendly, and potentially superior alternative due to these benefits. Marine collagen, particularly in the form of peptides, has gained popularity in anti-aging skincare due to its high bioavailability and beneficial properties such as antioxidant and antimicrobial activity [16]. Studies support its role in improving skin health, and demand for marine-based cosmetic products has significantly increased in recent years [17]. This review aims to highlight recent advancements in the understanding of marine collagen's functional properties and its growing significance as a natural bioactive ingredient for enhancing skin health and aging.

## SOURCES AND EXTRACTION OF MARINE COLLAGEN

Marine collagen is classified into two main categories based on its biological source: vertebrates and invertebrates. The collagen content and characteristics can vary considerably between these two groups of marine organisms [16]. Table 2 categorizes the primary sources of marine collagen into vertebrates, invertebrates, and processing byproducts.

Collagen is abundant not only in terrestrial organisms but also across a wide range of marine species. Notably, high collagen content is found in fish skin and bones, shark cartilage, jellyfish, starfish, sea urchin waste, and other bycatch marine organisms [13]. To understand the diverse potential of marine sources, Table 3 presents a comprehensive overview of collagen content across a range of marine species and their respective tissues. Fish is a widely consumed, protein-rich food, with over 33,600 species classified by habitat. Fish processing generates significant waste about 7.3 million tons annually, including bones, skin, and scales. These byproducts are rich in collagen, particularly fish bones, which contain ~30% organic collagen and ~70% inorganic minerals like hydroxyapatite [18]. Fish collagen differs from mammalian collagen in its amino acid composition, with lower levels of hydroxyproline, proline, and glycine, leading to a lower denaturation temperature [13]. However, due to its lower molecular weight and particle size, fish collagen is 1.5 times more bioavailable than porcine or bovine collagen, allowing for better absorption and faster circulation [19]. The thermal stability of fish collagen varies by species and habitat. Cold-water fish (e.g., chum salmon, Baltic cod) have lower imino acid content and thermal stability (10–19°C) compared to tropical species like Nile perch

Table 2: Classification of marine collagen sources

Category	Examples	Description
Vertebrates	Fish	Marine collagen derived mainly from various fish species
Invertebrates	Poriferans (sponges), Mollusks (octopus, squid), Crustaceans (shrimp), Echinoderms (starfish), Coelenterates (jellyfish), Annelids (worms)	Diverse marine animals without backbones, sources of collagen
Processing byproducts	Fish heads, skin, and other discarded fish parts	Waste materials from fish processing used as collagen sources

Table 3: Collagen content in various marine species and tissues

Species	Tissue Type	Collagen Content (%)	Reference
<i>Lagocephalus gloveri</i>	Skin	54.3	[34]
<i>Illex argentinus</i>	Skin	53	[35]
<i>Stomolophus meleagris</i>	Mesoglea	46.4	[36]
<i>Takifugu rubripes</i>	Skin	44.7	[37]
<i>Rhopilema asamushi</i>	Whole body	35.2	[38]
<i>Syngnathus schlegeli</i>	Skin	33.2	[39]
<i>Rhizostoma pulmo</i>	Oral arms	26 – 90	[28]
<i>Hemibagrus macropterus</i>	Skin	28.0	[40]
<i>Sepiella inermis</i>	Skin	16.2	[41]
<i>Cotylorhiza tuberculata</i>	Oral arms	19.4	[28]
<i>Chrysaora sp.</i>	Bell	9 – 19	[42]
<i>Carcharhinus limbatus</i>	Cartilage	10.3	[43]
<i>Chiloscyllium punctatum</i>	Cartilage	9.6	[43]
<i>Anthocidaris crassispina</i>	Whole body	35	[44]
<i>Patiria pectinifera</i>	Body wall	6.1	[45]
<i>Catostylus tagi</i>	Bell	2.7 – 4.5	[28,46]
<i>Nemopilema nomurai</i>	Mesoglea	2.2	[47]
<i>Trachurus japonicus</i>	Scales	1.5	[48]
<i>Priacanthus tayenus</i>	Bone	1.6	[49]
	Skin	10.9	
<i>Rhopilema esculentum</i>	Mesoglea	0.28	[50]
<i>Pelagia noctiluca</i>	Whole body	0.07	[28]
<i>Aurelia aurita</i>	Whole body	0.01	[28]
<i>Saurida spp.</i>	Scales	0.79	[48]
<i>Dentex tumifrons</i>	Scales	0.9	[48]
<i>Cheilopogon melanurus</i>	Scales	0.7	[48]
<i>Mugil cephalus</i>	Scales	0.4	[48]

or eel (26–36°C). Despite some fish like sturgeon having imino acid levels similar to mammals, their collagen still shows lower heat resistance [20]. This low thermal stability poses a challenge for wider

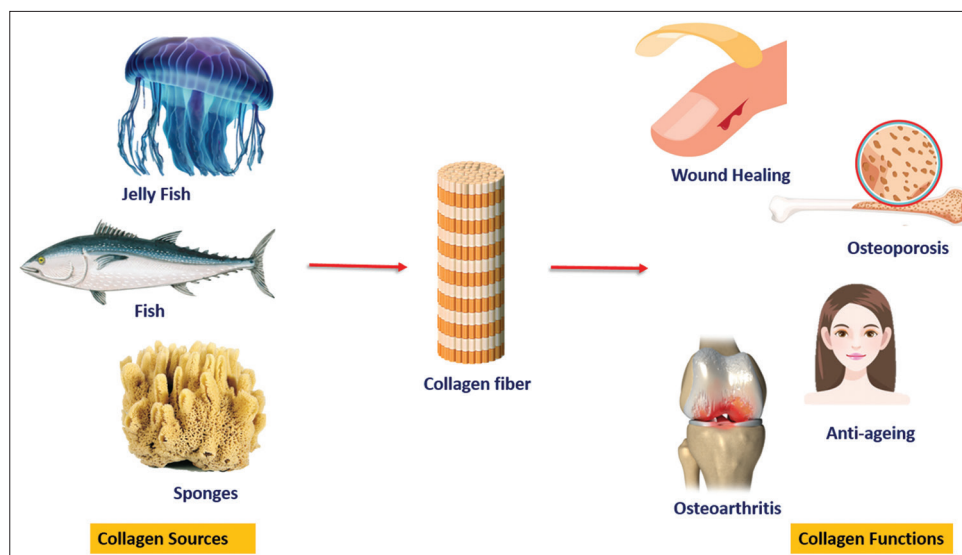


Fig. 1: Marine-derived collagen: Key sources and biomedical utility (Created using Microsoft PowerPoint)

application, though species differences, habitats, and extraction methods play significant roles [21]. Crustaceans such as shrimp, crabs, prawns, lobsters, and krill are widely consumed marine invertebrates and form a significant segment of the global aquaculture industry, valued at over \$57 billion annually. While they are prized for their nutritional richness in protein, unsaturated fatty acids, and essential minerals (such as  $Mg^{2+}$ ,  $Ca^{2+}$ , and  $Zn^{2+}$ ), their processing generates substantial waste [22]. Notably, 60–85% of their body mass sea including shells, heads, and appendages is discarded during processing, though these by-products are rich in chitin, protein, and calcium carbonate [16]. Although collagen constitutes only a minor portion of total protein in crustaceans, it is still extractable and holds structural similarity to vertebrate collagen [21]. Studies have identified type I collagen in species such as mantis shrimp and spiny lobsters. Collagen content in crustacean muscle varies by species such as Squilla (*Oratosquilla oratoria*, 5.9–6.2%), Crayfish (*Procambarus clarkia*, 3.4–3.6%), Prawn (*Penaeus japonicus*, 2.6–2.9%), Lobster (*Panulirus longipes*, 2.5–2.7%), Shrimp (*Pandalus borealis*, 1.1–2.2%), and Crabs (various species, 0.2–0.8%) [23]. Although collagen content is relatively low, especially in crab and shrimp muscles, the extracted collagen demonstrates physicochemical properties comparable to vertebrate sources, making it a promising material for biomedical and nutraceutical applications [22]. Sea cucumbers, which fall under the class Holothuroidea, serve as an ancestral treat in Southeast Asia, China, Japan, and Korea. Their main edible component, the body wall, is particularly important since it contains up to 70% collagen, which makes up the whole protein content [24]. There are more than 1,250 species in the world, and many of them are prized for their abundant nutritive and bioactive components in addition to being eaten as food [21]. The versatile collagenous tissue that makes up this collagen-rich body wall is composed of glycoproteins, proteoglycans, and collagen fibers that are organized into fibrils and microfibrils. These structural proteins, which work similarly to vertebrate connective tissues, offer mechanical strength and flexibility [25]. According to research, sea cucumber collagen is high in glutamic acid and has a distinctive triple helix structure, mainly composed of three identical  $\alpha 1$  chains [26]. Its sequence and characteristics show clear evolutionary characteristics, even if it shares structural similarities with mammalian collagen [16]. The structural diversity and complexity of sea cucumber collagen, as shown by proteomic and bioinformatic studies, call for additional research for potential use in clinical and nutritional applications [21]. Jellyfish, traditionally consumed in several Asian countries such as China and Japan for over 1700 years, have gained recognition as a rich and sustainable source of marine collagen. With global annual production now exceeding 800,000 tons, surpassing that

of lobsters and mussels, only 23 of the over 1400 known jellyfish species have been extensively studied for their collagen potential [27]. Jellyfish are valued for their low-fat, low-calorie profile and high collagen content, which can account for up to 75% of their total protein. Their collagen is typically composed of types I and II, though types III, IV, and V have also been identified in certain species [13]. Unlike collagen from vertebrates, jellyfish collagen displays minimal inflammatory and immunogenic responses, high biocompatibility, and a reduced risk of zoonotic disease transmission, making it highly attractive for biomedical applications [28]. Physicochemically, jellyfish collagen differs across species. For example, collagen extracted from *Stomolophus meleagris* resembles vertebrate type II collagen in terms of its solubility, hydroxylysine content, hygroscopicity, and molecular properties, despite low sequence similarity [29]. Its invertebrate origin, absence of disulfide bonds, and lack of calcified tissues contribute to unique functional characteristics not found in mammalian sources [21]. Overall, jellyfish collagen holds promise for innovative applications in wound healing, drug delivery, and tissue engineering, particularly due to its bioactivity, safety, and functional diversity [28]. Marine sponges are simple, filter-feeding invertebrates mainly found in saltwater. Their bodies contain a collagen-rich internal matrix called spongin, which forms a fibrous network providing structural support [30]. Spongin is considered a collagen-like protein, although its full composition varies by species and remains not fully defined. Studies have shown differences in sponge collagen structure and composition [21]. For example, *Axinella cannabina* contains about 12.6% insoluble collagen and 42.8% spongin-like collagen, while *Suberites carnosus* has lower amounts [31]. These variations are reflected in thermal stability, solubility, and amino acid profiles. Despite the existence of around 15,000 sponge species, only a few have been explored for collagen extraction. Two major challenges limit industrial use that is low thermal stability due to sponges' cold-water habitat and lack of scalable cultivation methods making large-scale production difficult [30]. Nevertheless, sponge-derived collagen holds potential for biomedical and biotechnological applications due to its unique properties. The phylum Mollusca includes over 120,000 species such as squids, mussels, scallops, oysters, and clams, found across a range of aquatic environments. Mollusks are nutritionally valuable, with ~80% of their soft tissue being edible and rich in protein and minerals but low in fat [32]. Certain mollusks, especially bivalves and cephalopods, are notable for their collagen-rich tissues. For example, *Anadara broughtonii* and *Macrura chinensis* contain 6.8–7.9% collagen in their muscle and mantle tissues [27]. Collagen from *Doryteuthis singhalensis* (squid) has shown good thermal stability (denaturation temp ~34.8–35.7°C) and high glycine content (~33%), indicating its potential for commercial applications [33]. Research on

**Table 4: Characterization of marine collagen: Sources, types, characterization methods, and amino acid content**

Source	Collagen type	Methods used	Composition and features
Skin of Nile tilapia	Marine collagen peptides	Amino acid analysis	Contains 7 essential (16.18%) and 10 non-essential amino acids (79.56%); over 58% are hydrophilic residues.
Jellyfish <i>Rhizostoma pulmo</i>	Collagen	Biochrome	-
Sponges ( <i>Axinella cannabina</i> , <i>Suberites carnosus</i> )	ICC	UV or fluorometry	-
Mussel byssus	Collagen	HPLC	Amino acid makeup consistent regardless of hydrolysis.
Tra catfish, clown knifefish, tilapia	ASC	Amino acid analysis	Glycine 33.2–33.7%; proline and hydroxyproline (imino acids) around 19.2–20%.
Takifugu flavidus	Collagen	Amino acid analysis	Glycine is the most abundant, making up about 25% of total amino acids.
Various fish species	ASC	CD	Substitution of hydroxyproline to serine increases flexibility while maintaining triple helix stability.
Codfish skin	Collagen	Biochrome	Type I collagen with 20 amino acids forming a stable triple-helix structure.
Sturgeon hybrid	Type II collagen	Automated amino acid analyzer	High glycine content.
Skipjack tuna	Scale gelatin and antioxidant peptides	SDS-PAGE, FTIR, ESI-MS, radical scavenging assays	Gelatin yields about 3.46%; rich in glycine; less stable than type I collagen.
Surf clam shell	Collagen	Automated amino acid analyzer	Glycine is the major amino acid in soluble collagens.

Adapted with little modification [3]. ICC: Intercellular collagen, ASC: Acid-soluble collagens, CD: Circular Dichroism, UV: Ultraviolet, HPLC: High-performance liquid chromatography, SDS-PAGE: Sodium dodecyl sulfate–polyacrylamide gel electrophoresis, FTIR: Fourier-transform infrared spectroscopy, ESI-MS: Electrospray ionization mass spectrometry

*Mytilus chilensis* (Chilean mussel) revealed high levels of proline, hydroxyproline, and glycine, with strong cross-linking in the collagen structure [32]. While the full molecular understanding of mollusk collagen remains incomplete due to species diversity, multiple studies confirm the presence of type I collagen in squid, clams, mussels, and byssus threads, positioning mollusks as promising sources of marine collagen for food and industrial uses [21].

The efficiency of collagen extraction is a key factor in the overall process. Various methods have been developed to obtain collagen, based on the marine sources. However, using three steps – preparation, extraction, and recovery – a basic system for separating collagen from fish byproducts as well as other marine sources can be established [42]. The initial step involves pretreating the raw materials to enhance the purity of the final product by eliminating contaminants. In this pre-treatment phase, marine byproducts like skin, bone, swim bladder, and scales are first sorted [51]. This initial sorting streamlines the subsequent processes of cleaning, reducing material size, and eliminating contaminants. Notably, the extracted raw materials are often rich in lipids, pigments, non-collagenous proteins, and fats. When compared to traditional methods like acid-assisted and pepsin-assisted extraction, collagen obtained through an enhanced physical-assisted technique preserves a greater molecular weight and shows a peptide profile closely resembling that of collagen extracted solely by acid [29]. Table 4 summarizes various marine collagen sources, their types, and the key amino acid characteristics based on different characterization methods [3]. Ethylenediaminetetraacetic acid is commonly used for demineralization to enhance collagen extraction from bone, cartilage, and scales. Alternatively, hydrochloric acid can serve as a demineralizing agent. Collagen types I, II, III, and V due to their fibrous structure are poorly soluble in water but can be extracted in acidic media [52]. Acid treatment enhances the repulsion between tropocollagen molecules, thereby solubilizing less cross-linked collagens. This leads to acid-soluble collagen (ASC) through the breakdown of non-covalent bonds [21]. Fibrous collagen is poorly soluble in water but readily extracted in acidic media (e.g., 0.5 M acetic acid) as ASC. Acid induces repulsion among tropocollagen molecules, enhancing solubilization [54]. Extraction yield depends on species, acid type/concentration, time, temperature, and acid-to-material ratio [53]. Among acids, 0.5 M acetic acid is preferred, yielding up to 90%, while others such as citric, lactic, and hydrochloric acids typically result in lower yields. However, the method is time-intensive, often

taking 2–4 days [55]. For baltic fish skin, acetic and lactic acids yield ~90%, citric ~60%, and hydrochloric acid ~18%. When acid extraction proves inadequate, enzymatic methods using pepsin, trypsin, papain, or collagenases are preferred. Pepsin is especially common for marine sources, often used alongside acetic acid. Enzymatic (pepsin) treatment combined with acid increases collagen recovery [21]. This approach maintains the collagen's triple-helical structure, reduces antigenicity, and increases yield. For instance, increasing pepsin levels raised the extraction from giant croaker skin from 66.35% to 79.93%. More recently, proteases from *Bacillus cereus* strains yielded even higher recoveries from bigeye tuna skin compared to acid-only extraction (Ahmed et al., 2018). Collagen extraction from various marine sources employs diverse methods, each with specific advantages and limitations. Sponges like *A. cannabina* and *S. carnosus* are processed through alkaline and trypsin treatments; the alkaline method efficiently isolates insoluble collagen, while trypsin disrupts the matrix to release collagen fibrils [31]. Mussel byssus utilizes pepsin digestion, which selectively cleaves cross-linked regions without damaging the triple helix structure, thus preserving collagen integrity [56]. Codfish skin collagen is obtained through acid-base procedures, although this method is less effective for byssal thread collagen. However, these methods may leave chemical residues and contribute to environmental pollution. Electrodialysis extraction of collagen from *Takifugu flavidus* uses ion-exchange membranes under an electric field, offering high efficiency, yield, and better environmental sustainability [57]. In the case of surf clam shells (*Coelomactra antiquata*), collagen extraction via guanidine hydrochloride and pepsin offers a safer, cost-effective, and milder alternative to harsh acid hydrolysis [58]. Sharks and rays are processed using similar acidic and enzymatic protocols [59]. Enzymatic methods [60] are commonly applied for species like Indian major carp (*Labeo rohita*), while bigeye tuna collagen is extracted using a combined acetic acid and pepsin process [61]. Extrusion–Hydro extraction helps separate collagen from tightly bound minerals like hydroxyapatite in fish scales. Extrusion breaks these bonds, allowing easier water-based extraction [62]. Using this method on tilapia fish scales, collagen yield increased by 2–3 times compared to non-extruded samples, with quality comparable to traditional methods [21]. Salmon byproducts benefit from bacterial protease fermentation, which enhances the release of bioactive peptides and reduces extraction time [63]. Nile tilapia skin undergoes fermentation pretreatment before collagen extraction, yielding high-purity Type I collagen with a preserved triple helix [64]. For jellyfish (*Acromitus hardenbergi*), a physical-aided



acid-assisted extraction preserves both amino acid composition and molecular weight distribution [29]. Supercritical fluid extraction uses fluids like CO<sub>2</sub> above their critical temperature and pressure to dissolve and extract bioactive compounds [21]. It is efficient, selective, and has a lower environmental impact. For example, collagen recovery from *Chondrosia reniformis* sponges increased by 30% using CO<sub>2</sub>-acidified water at 10 bar. Similar success was reported from Atlantic cod skin, where the method significantly outperformed conventional extraction in both yield and time [65]. Electrospinning presents a simple and effective method for extracting collagen from tilapia [66]. Finally, combining physical treatments such as homogenization, sonication, pH adjustment with acid or enzymatic methods enhances collagen solubility and yield. For example, sonication increased collagen extraction from jellyfish by up to 7 times compared to acid methods. Similarly, CO<sub>2</sub> ultrafine bubbles in acetic acid boosted the yield from tilapia scales significantly. Ultrasonication, particularly, can yield up to 94.88% ASC but must be carefully controlled to avoid protein degradation [21].

### MECHANISMS OF ACTION IN SKIN HEALTH

Human skin comprises two main layers: The epidermis and the dermis. The dermis, which forms the skin's structural foundation, is rich in collagen and elastin. With age, the dermis receives fewer nutrients, leading to reduced skin elasticity and increased fragility of collagen bundles [67]. Combatting the aesthetic decline of skin that accompanies aging critically relies on the biomedical use of collagen in regeneration. Wrinkles and expression lines are frequently the result of this natural aging process, especially around the mouth, eyes, and forehead [68]. The age-related reduction in collagen and elastin fibers, which are essential for skin's elasticity, strength, and structure, is a primary cause of wrinkles and decreased firmness [69]. Skin aging is known to be accelerated by a number of factors, including telomere shortening, hormonal changes, mitochondrial DNA mutations, and ultraviolet (UV)-induced oxidative stress [68]. Although plant-derived dietary components such as vitamins and amino acids can promote skin health, their limited bioavailability due to issues with gut absorption and quick metabolism often reduces their impact [70]. Conversely, marine collagen and its peptide forms offer superior absorption, strong effectiveness, and a commendable safety record.

Marine collagen has emerged as a promising biomaterial for skin regeneration due to its excellent biocompatibility, biodegradability, and safety profile. Sourced primarily from fish skin, bones, and scales, it offers an ethical and disease-free alternative to mammalian collagen [1]. Collagen, particularly Type I (80–90% of skin collagen), is essential for maintaining skin firmness and elasticity resilience [6]. It is synthesized by fibroblasts, mesenchymal cells located in the dermis, which also produce elastin (for skin flexibility) and glycosaminoglycans (GAGs) such as hyaluronic acid and dermatan sulfate, crucial for skin hydration due to their high water-binding capacity [71]. Fibroblast activity is influenced by mechanical cues from the ECM and Biochemical signals such as growth factors and ligands. These stimuli trigger signaling pathways that boost the production of collagen, elastin, and GAGs [6]. Its natural structure closely mimics human dermal collagen, making it suitable for use in wound dressings, skin grafts, and anti-aging formulations resilience [6]. In addition, marine collagen exhibits antioxidant, anti-inflammatory, and antibacterial properties, further enhancing its effectiveness in repairing damaged or aging skin [21]. Marine collagen-based cosmetic products can improve skin hydration, reduce wrinkles and pore size, and visibly brighten the complexion within 2 weeks of regular use. Its antioxidant, anti-aging, moisturizing, and skin-repairing properties contribute to overall skin health [16].

Research shows that oral intake of collagen peptides enhances skin properties. Once ingested, peptides reach fibroblasts and stimulate increased collagen, elastin, and hyaluronic acid synthesis. A study found that hydrolyzed collagen peptides increase collagen and elastin production and decrease activity of matrix metalloproteinase

(MMP)-1 and MMP-3, enzymes that degrade ECM. This suggests that collagen-based supplements can help rejuvenate skin by strengthening fibroblast-derived ECM and reducing degradation from oxidative stress and UV damage [72]. Clinical evidence supports these claims, with one study reporting that daily oral intake of 10 g of *Pangasius hypophthalmus* hydrolyzed collagen powder for 12 weeks led to notable improvements in cheek skin hydration, elasticity, and a reduction in facial wrinkles [67]. Studies consistently demonstrate the benefits of marine collagen for skin rejuvenation. For instance, fish-derived collagen peptides, particularly when combined with ornithine, have been observed to improve skin elasticity, hydration (by reducing trans-epidermal water loss), and even pore size, while also boosting age-declining insulin-like growth factor-1 (IGF-1) levels [73]. Further human trials revealed that 570 mg of fish-sourced collagen peptides safely enhanced skin's dermal thickness, density, sebum production, and elasticity [15]. Oral collagen supplementation has recently gained attention for its potential skin benefits. A randomized, double-blind, placebo-controlled study involving 72 healthy women over the age of 35 evaluated the effects of a drinkable collagen supplement. Half of the participants received a daily dose of 2.5 grams of collagen peptides along with biotin, vitamin C, acerola extract, zinc, and a natural vitamin E complex for a period of 12 weeks, while the other half received a placebo. The results showed that those who consumed the collagen supplement experienced significant improvements in skin hydration, elasticity, smoothness, and dermal density compared to the placebo group. These findings indicate that oral collagen supplementation may effectively enhance skin quality and structure [74]. Research in aged mice showed that both topical and oral collagen hydrolysates improved skin structure by increasing critical antioxidant enzymes (superoxide dismutase and glutathione peroxidase) and boosting collagen fiber density (types I and III). In addition, marine collagen peptide treatment has been linked to increased fibroblast activity, epidermal thickness, and antioxidant enzyme levels [75]. Studies in rodents revealed that a specific Spirulina-derived peptide, acetyl amidated peptide I, exerted mild anti-aging effects by decreasing MMP-1 and MMP-3 expression, thereby increasing collagen content and activating antioxidant enzymes [2]. A compelling human study reported that women aged 45–60 experienced a significant 35% reduction in wrinkles and notable improvements in skin hydration, radiance, firmness, and elasticity after just 12 weeks of freshwater fish collagen supplementation [67]. Recent advances highlight the superior anti-aging potential of starfish (*Asterias pectinifera*) collagen peptides over traditional fish collagen, particularly in their effectiveness in suppressing UV-induced MMPs, enzymes responsible for collagen degradation [76]. Beyond collagen, other marine-derived carbohydrates also contribute to skin health through their antioxidant and immune-boosting properties. Ultimately, marine collagen presents compelling opportunities in both dermatological repair and aesthetic enhancement. Its dual action – providing crucial structural components alongside powerful antioxidant defense – positions it as an effective agent for accelerating skin regeneration and actively fighting against the signs of aging.

### CHALLENGES AND FUTURE PROSPECTS

Significant research has focused on extracting beneficial chemicals from these marine by-products for human health and, more recently, for cosmetic applications [77]. To effectively utilize these raw materials in industrial processing, careful management including separation, classification, stabilization, and preservation is essential to ensure their quality and condition. The global increase in fisheries and aquaculture production, significantly boosted by technological advancements, means a substantial amount of marine by-products are generated annually over 25% of total marine production [78]. These by-products, including fish heads, bones, skins, and shellfish shells, are often discarded as waste. However, they represent a significant untapped resource of valuable organic compounds with considerable potential for developing value-added products, such as cosmeceuticals, and for addressing environmental contamination concerns [75]. Despite extensive research and development, only a limited number of

cosmetic ingredients derived from marine by-products have reached commercial markets [16]. This slow adoption is primarily due to the availability of cheaper, more reliable production methods like chemical synthesis or genetically modified microbes, and the high cost and small quantities typically associated with isolating specific compounds from natural sources. The market for products using marine by-products remains relatively small compared to the vast quantities produced. This disparity highlights a considerable opportunity to create more value-added products. To truly maximize the potential of extracting bioactive chemicals from these by-products, it is crucial to adopt environmentally sustainable extraction and processing methods [19]. This approach not only enhances the value of these resources but also aligns with broader environmental conservation goals. Furthermore, while marine collagen sources offer immense potential, their utilization can pose risks to marine ecosystems. It's imperative to implement measures that maintain ecological balance. A key solution to mitigate this impact is promoting the use of marine organism by-products. By responsibly utilizing materials such as fish skin, scales, and bones, which are typically discarded as waste, we can significantly reduce the need for additional fishing or harvesting solely for collagen production. As consumers become more sensitive to the ethical and environmental implications of cosmetic products, ensuring that marine by-product-derived cosmetics meet high standards of hygiene, ecology, safety, and ethics will be critical for their widespread acceptance.

## CONCLUSION

Marine-derived collagen represents a major advancement in the pursuit of safe, effective, and sustainable solutions for skin health and anti-aging. Compared to terrestrial sources, it offers distinct advantages including higher bioavailability, lower molecular weight, and reduced immunogenicity, which together enhance absorption and biological activity. Numerous studies have demonstrated its ability to stimulate fibroblast function, promote collagen and elastin synthesis, inhibit MMPs, and improve clinical outcomes such as hydration, elasticity, dermal density, and wrinkle reduction. In addition, the antioxidant and anti-inflammatory effects of marine collagen, along with synergistic bioactive compounds from marine plants and algae, broaden its potential applications in cosmeceuticals and functional foods. Despite these benefits, large-scale commercialization remains limited by high production costs, lack of standardization, and the need for long-term clinical validation. However, the abundant marine by-products generated globally present a valuable and underutilized resource that can be harnessed through sustainable extraction and processing technologies. As awareness grows regarding the ethical and environmental implications of cosmetic ingredients, the valorization of marine resources provides a dual opportunity addressing ecological challenges while meeting consumer demand for natural, safe, and scientifically proven skincare solutions. With continued research, technological innovation, and commitment to sustainability, marine collagen is well-positioned to become a cornerstone bioactive in cosmeceuticals, nutraceuticals, and regenerative medicine.

## AUTHOR'S CONTRIBUTIONS

Aastha Sharma: Conceptualization, literature collection, writing – original draft preparation. Dr. Govind P Tagalpallewar: Supervision, critical review, editing, and validation of the manuscript. Susmita Ranjan: Data curation, literature survey, and writing – review and editing. Aswathy VP: Visualization, preparation of figures/tables, and technical inputs. Pranabha Sontakke: Methodology support, resource management, and manuscript proofreading.

## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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