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# Marine collagen: purification, properties and application

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Balu Alagar Venmathi Maran<sup>3</sup> and Saeid Tamadoni Jahromi<sup>4</sup>

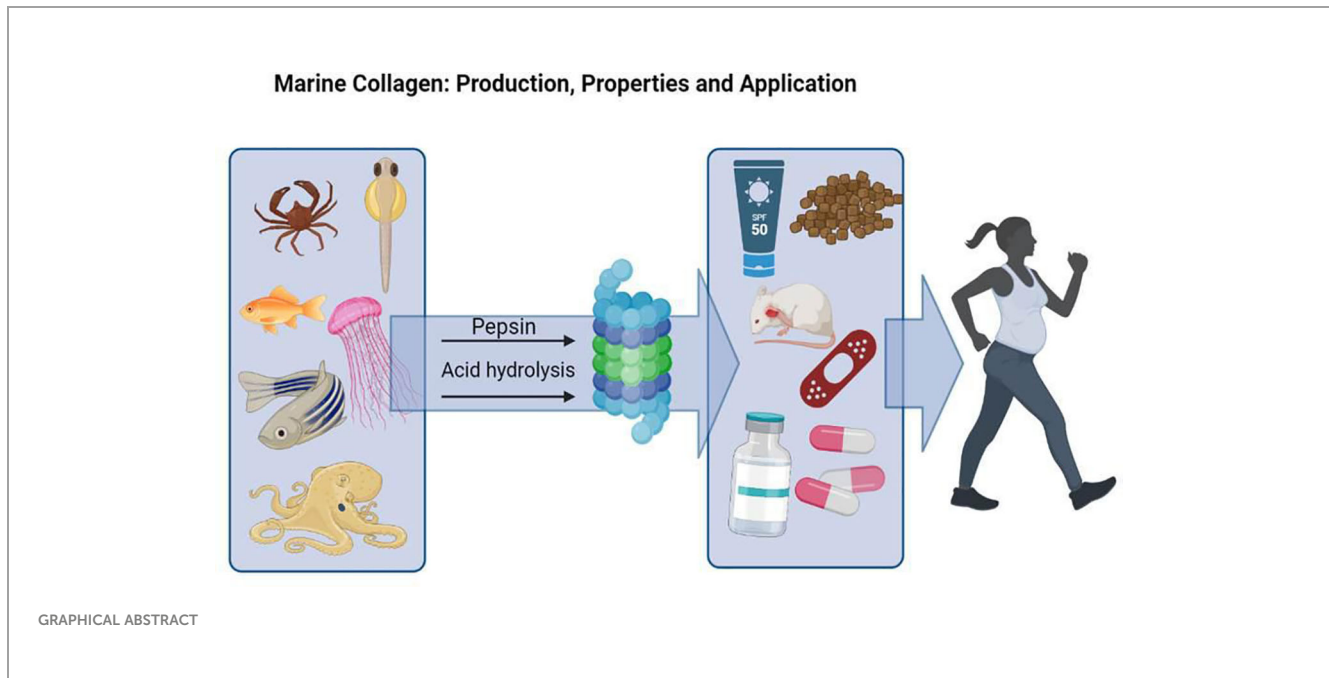
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Collagens are abundant structural proteins found in connective tissues such as bones, swim bladder, skin, blood vessels, intestines, and cartilage. They make up around 30% of the total protein. The purpose of this paper is to provide a summary of the current knowledge about collagen isolated from marine organisms and its possible applications. Collagen is widely used in pharmaceuticals, food, biomedical and cosmetic industries due to its cell adhesion, biocompatibility, and safety properties. This review discusses various methods for extracting collagen from marine vertebrates and its physicochemical properties. Enzymatic extractions might be a more effective at extracting collagen than acidic extractions. Peptides derived from collagen hydrolysates have biological activity that promotes health and relieves symptoms caused by chronic diseases. Aquaculture can help with collagen availability but an integrated technology for processing raw materials is necessary to address the negative effects of production waste. Marine collagen has many benefits over terrestrial sources including its versatility in healing skin damage and slowing down the aging process. The advantages of marine collagen over terrestrial sources are discussed along with its potential biotherapeutic applications in bone and skin injuries. The development of effective cosmetic products can become a strategic direction for technological development.

## KEYWORDS

collagen, marine organisms, collagen production, collagen application, application prospects



## Introduction

Collagens are proteins that provide structural support to connective tissues like bone, skin, and cartilage. There are 29 types of collagen present in the human body and they account for about 30% of the total protein in the body (Di Lullo et al., 2002; Rossert and de Crombrughe, 2002; Müller, 2003). Type I is the most common and can be found in various tissues such as bone, heart, and skin. It is used extensively in pharmaceuticals, food, biomedical products, and cosmetics due to its cell adhesion properties, biocompatibility, safety, low antigenicity, and biodegradability (Aruta et al., 2009; Yamada et al., 2014; Pal et al., 2015; Wang, 2021). Type III is the second most common type present in connective tissues like organs, skin, and lungs. Collagen types V and XI are less abundant but can be found along with types I and II in cartilage, bone, and other tissues (Daboor et al., 2010). Breakdown of interstitial collagens is important for biological processes like wound healing and tissue remodeling (Brett, 2008). Collagen hydrolysates are used to produce liquid matrices while controlled rate freezing methods are used for tissue engineering purposes like skin regeneration or bone reconstruction (Dai et al., 2013). Collagen plays a role in various pathologies such as tumor cell spreading or periodontal disease (Khan and Khan, 2013). As we age, collagen synthesis in our bodies decreases. This puts more strain on our bones, hair tissue, and skin. However, collagen is considered a promising anti-aging material with rejuvenating properties (Kapuler et al., 2015; Xu et al., 2021).

The commercial collagen available now is typically derived from the skins and bones of calves and pigs. Unfortunately, there have been outbreaks of animal diseases such as spongiform encephalopathy and foot-and-mouth disease that have affected these sources of collagen and their derived products (Pal et al., 2015). Additionally, some countries prohibit the use of bovine/

porcine collagen due to religious beliefs. Because purifying this type of protein is difficult and poses a risk for transmissible diseases, mammalian collagen has become less popular compared to marine collagen (Yemisen et al., 2023). Marine organisms like fish, jellyfish, sponges, and other invertebrates are a great source of bioavailable collagen that lack religious constraints and animal pathogens (Coppola et al., 2020b). Although marine collagen is both safe and easy to obtain, it does have a lower denaturation temperature than other sources which can limit its beneficial effects (Barzkar et al., 2018; Rajabimashhadi et al., 2023).

Even though, studies have shown that marine-origin collagenous materials are biocompatible and have good potential for tissue engineering applications compared to terrestrial organisms-derived collagen (Lim et al., 2019; Martins et al., 2022; Rajabimashhadi et al., 2023). This makes it an ideal ingredient for not only wound healing devices but also cosmeceuticals, dietary supplements and nutraceuticals (Martins et al., 2023; Rigogliuso et al., 2023). Further studies demonstrated that type I collagen matrix from tilapia scales has similar light scatter and transmission to the human cornea, as well as good biocompatibility in various animal models. BioCornea, a fish-scale-derived collagen matrix, is currently undergoing phase I clinical trials (van Essen et al., 2013; Rajabimashhadi et al., 2023). Additionally, type II collagen from the cartilage of the *Peru jumbo* flying squid *Dosidicus gigas* has shown promise in reducing pro-inflammatory mediators and relieving symptoms of osteoarthritis (Dai et al., 2018).

This review provides brief information about properties of marine collagen and its potential applications due to its importance. The review's strengths are that it demonstrates that marine sources of collagen have numerous advantages over terrestrial and other sources. Marine collagen is widely available, does not have any religious restriction, and there have been only few reports on its toxicity (van Essen et al., 2013). In addition to what

we have discussed so far, the use of marine collagen is environmentally friendly and safe. Furthermore, collagen has many applications in many fields, such as drug delivery, wound healing, skin aging, and tissue regeneration. Marine collagen has been reported to be more susceptible to hydrolysis than mammalian collagen, making it suitable for further processing into peptide derivatives (Dai et al., 2018). Collagen has been shown to have structural and functional properties that make it a natural substrate for cell adhesion, cell growth, and differentiation (Li et al., 2020). However, it should be noted that marine collagen has less residual proline and hydrochloroproline than bovine collagen and has not been shown to have less thermal stability than bovine collagen (Diogo et al., 2021). Moreover, most studies involve examining the effects of marine collagen *in vitro* or in animal models. However, further studies investigating the efficacy and possible side effects of marine collagen in humans should be mentioned.

In Russia, due to sanctions by the European Union, the U.S., and other allies, imports of marine raw materials and products have been significantly reduced. Therefore, it is relevant to search for replacement of foreign raw materials with domestic ones. According to the authors (Chen et al., 2022), collagen can be derived from byproducts and wastes generated during the deep processing of marine organisms. The use of such sources contributes to environmental protection and meets the principles of resource conservation and innovation in technological solutions. The maximum and rational use of marine organisms is supported by the Government of the Russian Federation, which indicates the relevance and urgency of such research (Liu et al., 2010).

There are three main methods of collagen extraction: neutral salt solubilized collagen, acid solubilized collagen, and pepsin solubilized collagen (Barzideh et al., 2014; Li et al., 2020). Loosely cross-linked collagen molecules are extracted with neutral salt solutions (Attaran Fariman et al., 2016). The extracted material is purified by dialysis, sedimentation, and centrifugation. Dilute acidic solvents such as citrate buffer, 0.5 M acetic acid, or hydrochloric acid (pH 2-3) are more effective than neutral salt solutions. Collagen from bone, cartilage, or material from aged organisms contains a higher percentage of keto-imine bonds and has lower solubility in dilute acidic solvents (Blanco et al., 2017).

Significantly higher yields compared to acid extraction can be achieved by taking advantage of the fact that the triple helix of collagen is relatively resistant to the action of proteases, i.e., pepsin or chymotrypsin, below approximately 20°C (Mizuta et al., 1994). Figure 1 shows a flow chart of collagen extraction from marine sources.

## Marine sources of collagen

To date, collagen has been found in the varied range of marine organisms. Marine sources of collagen are presented in Table 1. Figure 2 presents technical function flowsheet for producing soluble collagen. A significant number of commercial and aquaculture fish species, as well as non-fish species, are used as a source of marine collagen. Among them the following can be noted (Lin et al., 2019; Ahmed et al., 2020a; Coppola et al., 2020a; Han et al., 2021):

- Ray-finned fishes: Priacanthidae Günther, Sciaenidae Cuvier, Latidae Jordan, Lutjanidae Gill, Nemipteridae Regan, Sparidae Rafinesque, Acropomatiformes, Aulopiformes, Gonorynchiformes, Tetraodontiformes, Syngnathiformes, Pleuronectiformes, Cypriniformes, Osmeriformes, Salmoniformes, Perciformes, Acipenseriformes, Clupeiformes, Scombriformes, Siluriformes, Carangiformes, Gadiformes, Anguilliformes, Cichliformes, Esociformes;
- Chondrichthyes: Orectolobiformes, Carcharhiniformes, Heterodontiformes, Rajiformes;
- Mammals: representatives of the Cetartiodactyla order;
- Reptiles: representatives of the alligator family (Alligatoridae Gray);
- Cephalopods: Oegopsida, Octopoda, Sepiida;
- Bivalvia: representatives of the Pectinida order;
- Starfishes: representatives of the Comatulida order.

## Physicochemical properties of marine collagen

Different methods for collagen extraction from marine organisms result in varying yields and physicochemical properties of the extracted collagens. Two common methods are acid soluble collagen (ASC) extraction and pepsin-solubilized (PSC) extraction (Mizuta et al., 1994; Liu et al., 2010; Barzideh et al., 2014; Attaran Fariman et al., 2016; Blanco et al., 2017; Li et al., 2020; Diogo et al., 2021; Chen et al., 2022). The acid-collagen reaction utilized in ASC extraction increases collagen extraction efficiency by breaking crosslinks in the collagen helix and increasing repulsion among tropocollagen molecules (Niu et al., 2016). PSC, also known as atelo-collagen, shows increased purity and reduced antigenicity compared to ASC due to pepsin treatment that removes telopeptide regions and related non-collagenous proteins (Kim et al., 2013). Enzymatic treatment using pepsin in combination with the acids has been shown by researchers to improve the yield of extracted collagen in multiple studies (Kim et al., 2013; Niu et al., 2016; Hadfi and Sarbon, 2019).

## Marine collagen hydrolyzed with industrial potency

Peptides derived from collagen hydrolysates possess not only nutritional properties, but also have biological activities and regulatory roles that can alleviate symptoms related to chronic diseases and promote good health. Clinical studies and drug development have shown various peptides with hyperlipidemic, immuno-modulatory, chelating/absorbing metals, and anti-osteoporotic activity (Hadfi and Sarbon, 2019). Moreover, short peptides (<5 kDa) from hydrolyzed collagen of the squid *Dosidicus gigas* exhibit antioxidant and anti-inflammatory properties (Ogawa et al., 2003). Collagen also increases fibroblast proliferation and hyaluronic acid synthesis while detectable in human blood at molar

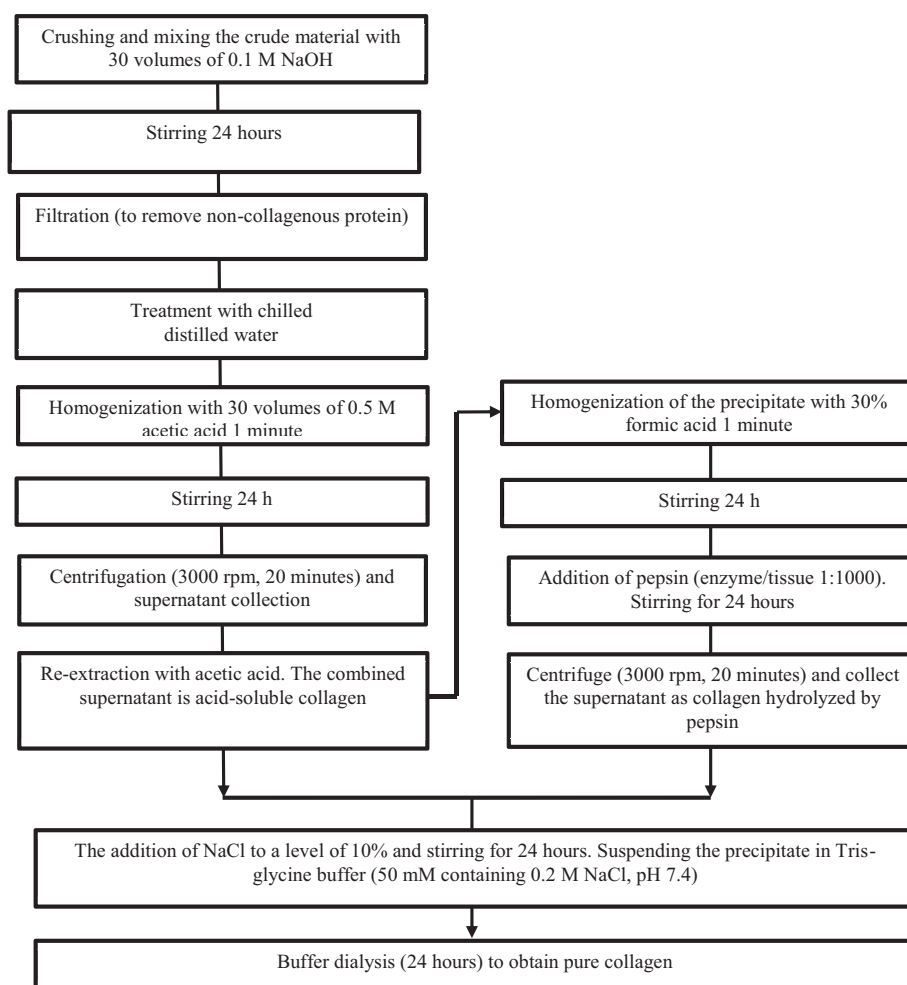


FIGURE 1

Flowchart of collagen extraction from marine sources [Venkatesan, J. & Anil, Sukumaran & Kim, Se-Kwon & Shim, Min. (2017). Marine Fish Proteins and Peptides for Cosmeceuticals: A Review. Marine Drugs. 15. 143. 10.3390/md15050143].

concentrations after consuming collagen hydrolysate. These are some of the positive effects of collagen on human health (Wahyu and Widjanarko, 2018). Table 2 lists the applications for animal and marine collagen in Europe.

Hydrolyzed collagen has various biological activities that are useful in nutrition, food, industry, and medicine (Mizuta et al., 1994; Morishige et al., 2011; Ahmed et al., 2020a). Additionally, it is believed that hydrolysate can have a positive impact on treating osteoporosis, diabetes mellitus, gastric ulceration, skin hydration, hypertension and preservatives (Lima et al., 2011a; Santos et al., 2013; Barzkar and Sohail, 2020). Collagen is becoming an increasingly popular ingredient in drugs, food, drinks, cosmetics, tissue engineering and health care products due to its wide range of industrial applications (Liu et al., 2010; Bilek and Bayram, 2015; Hadfi and Sarbon, 2019; Carvalho et al., 2020a). The reason for the extensive use of collagen in medical and pharmacological industries is due to its exceptional biological properties like hemostatic activity, biodegradability and low antigenicity (Ogawa et al., 2003).

The purpose of the 196th study was to examine the significance of collagen-derived peptide secondary and tertiary structure after

removal of fatty acids. The hydrolyzate efficiency of fish collagen reached 70%, with peptides (8.2–9.7 kDa) produced in the form of polyloine 2 (PP-II) at a concentration of at least 1 mg/mL and pH levels between 7–8. Moreover, the antioxidant activity of CF-CH increased as the ionic stability of aggregates increased, and protein isolation led to a decrease in antioxidant activity from 84.5% to 98.9%. After six months, soybean oil shelf life was extended by five times. Collagen's unique charge distribution, protonation of amino acid residues, and affinity through the fiber optic network contribute to its high potency. Fish are high in fat energy-wise (Porfirio and Fanaro, 2016).

It was observed that copper had a higher chelating activity in intact collagen hydrolysis (Sinthusamran et al., 2013). The collagen hydrolyzate extracted from the gastric phase showed moderate ACE inhibitory activity with an IC<sub>50</sub> value of 2.92 ± 0.22 mg/mL, which significantly increased to 0.49 ± 0.02 mg/mg after intestinal digestion (Lima et al., 2011b; Lima et al., 2015). Upon SGID, the inhibitory activity of collagen hydrolyzate against DPP IV was higher than that of collagen hydrolyzate trypsin (IC<sub>50</sub> 2.59 ± 0.04 mg/mL). The antioxidant activity of collagen and CTH after SGID

TABLE 1 Marine collagen sources.

No.	Organism	Parts from which collagen is derived	Source
<b>Vertebrates</b>			
1	<i>Thunnus albacares</i>	Swim bladder	(Andersen and Wold, 2003; Kittiphattanabawon et al., 2005)
2	<i>Cynoscion othonopterus</i>	Swim bladder	(Kaewdang et al., 2014)
3	<i>Nibeia coibor</i>	Skin, waste	(Idrus et al., 2018; Cruz-López et al., 2021)
4	<i>Protonibea diacanthus</i>	Swim bladder	(Chen et al., 2019)
5	<i>Priacanthus tayenus</i>	Skin, muscle tissue	(Lin et al., 2020)
6	<i>Saurida tumbil</i>	Scales	(He et al., 2021)
7	<i>Theragra chalcogramma</i>	Muscle tissue and internal organs	(Oslan et al., 2022)
8	<i>Pangasius</i> sp.	Skin	(Jaziri et al., 2022)
9	<i>Odonus niger</i>	Skin, bones, muscles	(Yan et al., 2008)
10	<i>Magalaspis cordyla</i>	Skin, scales	(Hukmi and Sarbon, 2018)
11	<i>Otolithes ruber</i>	Bone tissue	(Hukmi and Sarbon, 2018)
12	<i>Thunnus obesus</i>	Bones, skin, waste	(Muralidharan et al., 2013; Sampath Kumar and Nazeer, 2013; Ahmed et al., 2018; Ahmed et al., 2019; Lin et al., 2019)
13	<i>Oreochromis niloticus</i>	Skin, by-products	(Devita et al., 2021; Fu et al., 2022)
14	<i>Chanos chanos</i>	Scales	(Zeng et al., 2009; Chen et al., 2016)
15	<i>Cynoscion othonopterus</i>	Skin, bones	(Kaewdang et al., 2014)
16	<i>Lutjanus</i> sp.	Bones, waste	(Chen et al., 2016; Kusumaningtyas et al., 2019)
17	<i>Pangasius</i> sp.	Skin	(Wibawa et al., 2015; Zaelani et al., 2019; Han et al., 2021)
18	<i>Ictalurus punctatus</i>	Skin	(Hukmi and Sarbon, 2018)
19	<i>Oncorhynchus keta</i>	Skin	(Pei et al., 2010; Burkel et al., 2016; Almuqoddas et al., 2019; Zhao et al., 2020; Xue et al., 2022)
20	<i>Epinephelus malabaricus</i>	Skin	(Tan and Chang, 2018)
21	<i>Lateolabrax japonicus</i>	Skin	(Pei et al., 2010; Hema et al., 2017)
22	<i>Carassius auratus</i>	Skin, scales	(Kim et al., 2012; Kim et al., 2013)
23	<i>Prionace glauca</i>	Fins, bones, skin	(Diogo et al., 2021)
24	<i>Thunnus albacares</i>	Bones, skin	(Lee et al., 1997; Woo et al., 2008; Nurilmala et al., 2019a; Jia et al., 2020; Nurilmala et al., 2020; Nguyen et al., 2021)
25	<i>Priacanthus macracanthus</i>	Skin, muscle tissue	(Yoo et al., 2008; Nurilmala et al., 2019b)
26	<i>Priacanthus tayenus</i>	Tissues, skin	(Jongjareonrak et al., 2005; Jongjareonrak, 2006; La Noce et al., 2014; Nurilmala et al., 2019b)
27	<i>Pogonias cromis</i>	Skin, scales	(Benjakul et al., 2010; Lin et al., 2019)
28	<i>Archosargus probatocephalus</i>	Skin	(Chen et al., 2019; Allouche et al., 2020)
29	<i>Istiophorus platypterus</i>	Skin, scales	(Nalinanon et al., 2007)
30	<i>Aseraggodes umbratilis</i>	Skin, scales	(Ogawa et al., 2004; Tamilmozhi et al., 2013)
31	<i>Oreochromis niloticus</i>	Skin	(Arumugam et al., 2018)
32	<i>Saurida</i> spp.	Skin, scales, bone tissue	(He et al., 2021)
33	<i>Saurida tumbil</i>	Skin, scales, bone tissue	(He et al., 2021)
34	<i>Trachurus japonicus</i>	Skin	(Viji et al., 2019)

(Continued)

TABLE 1 Continued

No.	Organism	Parts from which collagen is derived	Source
35	<i>Mugil cephalis</i>	Bones, skin	(Viji et al., 2019)
36	<i>Cypselurus melanurus</i>	Mesogloea	(Viji et al., 2019)
37	<i>Dentex tumifrons</i>	Bones, muscle tissue	(Viji et al., 2019)
38	<i>Pogonia cromis</i>	Scales	(Benjakul et al., 2010)
39	<i>Archosargus probatocephalus</i>	Skin, scales	(Benjakul et al., 2010)
40	<i>Thunnus obesus</i>	Skin	(Muralidharan et al., 2013)
41	<i>Aseraggodes umbratilis</i>	Skin, scales	(Tamilmozhi et al., 2013)
42	<i>Thunnus albacares</i>	Skin, scales	(Menezes et al., 2020)
43	<i>Sciaenops ocellatus</i>	Skin, scales, waste	(Minh Thuy et al., 2014; Chen et al., 2022)
44	<i>Chanos chanos</i>	Waste, scales	(Han et al., 2010; Chen et al., 2016; Chen et al., 2018a; Chen et al., 2018b)
45	<i>Parupeneus heptacanthus</i>	Scales	(Susanti et al., 2019)
46	<i>Esox lucius</i>	Scales	(Wahyu and Widjanarko, 2018)
47	<i>Pagrus major</i>	Skin, scales	(Matmaroh et al., 2011; Kozłowska et al., 2015)
48	<i>Oreochromis niloticus</i>	Skin, scales, waste	(Matmaroh et al., 2011)
49	<i>Oreochromis niloticus</i>	Skin, scales, waste	(Ikoma et al., 2003; Sugiura et al., 2009; Youn and Shin, 2009; Lin et al., 2020; Rajabimashhadi et al., 2023)
50	<i>Saurida tumbil</i>	Scales	(He et al., 2021)
51	<i>Pogonia cromis</i>	Bones, scales	(Benjakul et al., 2010)
52	<i>Archosargus probatocephalus</i>	Bones, skin	(Benjakul et al., 2010)
53	<i>Odonus niger</i>	Skin, bones, muscles	(Youn and Shin, 2009)
54	<i>Priacanthus tayenus</i>	Skin, bones	(Sugiura et al., 2009)
55	<i>Thunnus albacares</i>	Skin	(El-Rashidy et al., 2015)
56	<i>Thunnus obesus</i>	Skin	(Muralidharan et al., 2013; Ahmed et al., 2018; Chen et al., 2018)
57	<i>Katsuwonus pelamis</i>	Skin, bones, scales, fins	(Natsir et al., 2019)
58	<i>Odonus niger</i>	Skin, bones, muscles	(Andersen and Wold, 2003)
59	<i>Lateolabrax japonicus</i>	Skin, bones, scales, fins	(Jeong et al., 2013)
60	<i>Prionace glauca</i>	Skin, fins	(Ding et al., 2019)
61	<i>Lateolabrax japonicus</i>	Skin	(Yang et al., 2022)
<b>Invertebrates</b>			
62	<i>Anadara broughtonii</i>	Pallium, arm	(Lu et al., 2022)
63	<i>Mactra chinensis</i>		(Lu et al., 2022)
64	<i>Mytilus Chilensis</i>	Pallium, arm	(Nagai, 2004a; Vallejos et al., 2014; Rodríguez et al., 2017; Tabakaeva et al., 2018)
65	<i>Mytilus galloprovincialis</i>	Pallium, arm	(CunhaNeves et al., 2022)
66	<i>Septifer virgatus</i>	Stroma, adjustor muscle	(CunhaNeves et al., 2022)
67	<i>Patinopecten yessoensis</i>	Muscle tissue, adjustor muscle	(CunhaNeves et al., 2022)
68	<i>Crassostrea gigas</i>	Muscle tissue, adjustor muscle	(CunhaNeves et al., 2022)
69	<i>Meretrix lusoria</i>	Muscle tissue, adjustor muscle	(CunhaNeves et al., 2022)

(Continued)



TABLE 1 Continued

No.	Organism	Parts from which collagen is derived	Source
70	<i>Coelomactra antiquata</i>	Muscles, tentacles	(Rodríguez et al., 2015)
71	<i>Illex coindetii</i>	Muscles, tentacles	(Mizuta et al., 2004)
72	<i>Toradopsis eblanae</i>	Muscles, tentacles	(Mizuta et al., 2004)
73	<i>Eledone cirrhosa</i>	Muscles, tentacles	(Mizuta et al., 2004)
74	<i>Dosidicus gigas</i>	Fins, tentacles	(Wu et al., 2019)
75	<i>Dosidicus gigas</i>	Fins, tentacles	(Morales et al., 2000)
76	<i>Todarodes pacificus</i>	Pallium, skin	(Ezquerria-Brauer et al., 2018)
77	<i>Photololigo edulis</i>	Fins, pallium	(Ezquerria-Brauer et al., 2018)
78	<i>Sepioteuthis lessoniana</i>	Pallium, skin	(Ezquerria-Brauer et al., 2018)
79	<i>Sepia esculenta</i>	Larvae	(Ezquerria-Brauer et al., 2018)
80	<i>Sepia longipes</i>	Larvae	(Ezquerria-Brauer et al., 2018)
81	<i>Todaropsis eblanae</i>	Pallium, skin	(Sarabia-Sainz et al., 2018)
82	<i>Eledone cirrhosa</i>	Muscles, tentacles	(Sarabia-Sainz et al., 2018)
83	<i>Sepia officinalis</i>	Larvae	(Mizuta et al., 2009)
84	<i>Thysanoteuthis rhombus</i>	Waste	(Moral et al., 2002)
85	<i>Sepia officinalis</i>	Larvae	(Bairati et al., 1987)
86	<i>Sepia pharaonis</i>	Larvae	(Nagai, 2004b)
87	<i>Exumbrella plus subumbrella</i>	Mesogloea, muscles	(Sivakumar et al., 2003)
88	<i>Pelagia noctiluca</i>	Mesogloea, muscles	(Sivakumar et al., 2003)
89	<i>Aurelia aurita</i>	Mesogloea, muscles	(Sivakumar et al., 2003)
90	<i>Stomolophus nomurai</i>	Mesogloea, muscles	(Krishnamoorthi et al., 2017)
91	<i>Nemopilema nomurai</i>	Mesogloea, muscles	(Addad et al., 2011)
92	<i>Rhopilema esculentum</i> <i>Kishinouye</i>	Mesogloea, muscles	(Sugahara et al., 2006)
93	<i>Rhopilema asamushi</i>	Mesogloea, muscles	(Morishige et al., 2011)
94	<i>Acromitus hardenbergi</i>	Mesogloea, stoma	(Cheng et al., 2017)
95	<i>Rhopilema hispidum</i>	Mesogloea, muscles	(Cheng et al., 2017)
96	<i>Rhopilema esculentum</i>	Mesogloea, muscles	(Cheng et al., 2017)
97	<i>Catostylus mosaicus</i>	Mesogloea, muscles	(Nagai et al., 2000)
98	<i>Rhopilema esculentum</i>	Mesogloea, muscles	(Khong et al., 2016)
99	<i>Rhopilema esculentum</i>	Mesogloea, muscles	(Zhuang et al., 2012; Hoyer et al., 2014; Pozzolini et al., 2018b; Rastian et al., 2018; Felician et al., 2019)
100	<i>Acromitus hardenbergi</i>	Mesogloea, stoma	(Ding et al., 2011; Sewing et al., 2017)
101	<i>Aurelia Aurita</i>	Mesogloea, muscles	(Khong et al., 2018)
102	<i>Rhizostoma pulmo</i>	Mesogloea, muscles	(Hoe, 2014; Ahmed et al., 2021; Rachmawati et al., 2021)
103	<i>Nemopilema nomurai</i>	Mesogloea, muscles	(Derkus et al., 2016)
104	<i>Stichopus japonicus</i>	Body walls	(Cui et al., 2007; Dong et al., 2011; Zhu et al., 2012; Putra et al., 2014; Zhong et al., 2015; Arslan et al., 2017; Liu et al., 2018)

(Continued)

TABLE 1 Continued

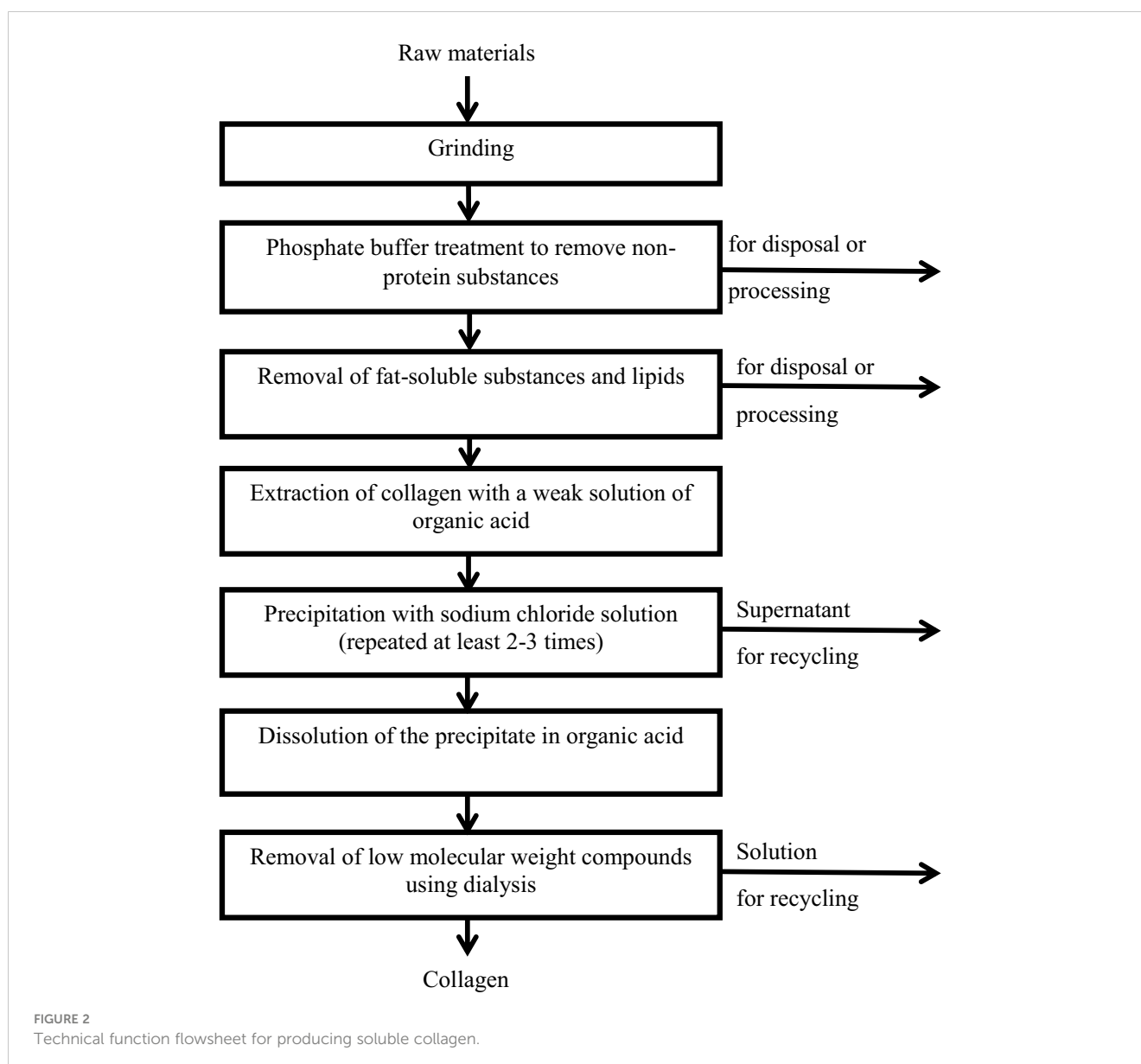
No.	Organism	Parts from which collagen is derived	Source
105	<i>Stichopus monotuberculatus</i>	Body walls	(Putra et al., 2014)
106	<i>Apostichopus japonicus</i>	Body walls	(Dong et al., 2011; Park et al., 2012; Song et al., 2022)
107	<i>Holothuria cinerascens</i>	Body walls	(Li et al., 2020)
108	<i>Parastichopus californicus</i>	Skin, connective tissue	(Tian et al., 2020)
109	<i>Acaudina leucoprocta</i>	Body walls	(Wang et al., 2018)
110	<i>Holothuria scabra</i>	Body walls	(Liu et al., 2010)
111	<i>Acaudina Molpadioides</i>	Body walls	(Lin et al., 2017)
112	<i>Stichopus vastus</i>	Skin	(Saallah et al., 2021)
113	<i>Holothuria parva</i>	Body walls	(Jin et al., 2019)
114	<i>Stichopus horrens</i>	Skin	(Abedin et al., 2014)
115	<i>Scylla serrata</i>	Intramuscular connective tissue	(Adibzadeh et al., 2014)
116	<i>Anthocidaris crassispina</i>	Tissues	(Attaran Fariman et al., 2016)
117	<i>Asthenosoma ijimai</i>	External hard coating	(Sivakumar et al., 2000)
118	<i>Paracentrotus lividus</i>	Waste	(Nagai and Suzuki, 2000)
119	<i>Asthenosoma ijimai</i>	External hard coating	(Shimizu et al., 1990)
120	<i>Actinia equina L.</i>	Muscle tissue	(Benedetto et al., 2014)
121	<i>Metridium dianthus</i>	Muscles, tentacles	(Shimizu et al., 1990)
122	<i>Prionace glauca</i>	Cartilage	(Nordwig et al., 1973)

was measured to be  $0.87 \pm 0.10$  and  $1.27 \pm 0.03$   $\mu\text{mol TE g}^{-1}$ , respectively (Lin et al., 2011; Pozzolini et al., 2018a; Zheng and Zheng, 2019). Out of the four skin conditions linked to inflammation or oxidative stress, dermatitis is the most common. Research has demonstrated that fish collagen peptide (FSCP) safeguards human keratinocyte-derived HaCaT cells against  $\text{CoCl}_2$ -induced cytotoxicity and  $\text{TNF-}\alpha$ -induced inflammatory responses. In HaCaT cells, key inflammatory cytokines, such as  $\text{TNF-}\alpha$ ,  $\text{IL-1}\beta$ ,  $\text{IL-8}$ , and  $\text{iNOS}$ , lessen cellular oxidative damage. As a result of FSCP gene expression, caspase activity and cytochrome C release inhibit and reduce apoptosis. When exposed to  $\text{CoCl}_2$  or  $\text{TNF-}\alpha$ , HaCaT cells increase Bcl-2 protein levels and ROS, MAPK (p38/MAPK, ERK and JNK). This study has revealed how marine collagen peptides (MCP) protect carotenoid endothelial cells (CAVEC) in type 2 diabetes mellitus (DM2), as well as the mechanisms behind this process. For an *in vivo* experiment involving diabetic patients, four groups were created randomly: a diabetic control group and three diabetic groups treated with MCP (2.25 g/kg bw/day, 4.5 g/kg bw/day or 9.0 g/kg bw/day). To serve as controls, 10 healthy mice were used. Human umbilical vein endothelial cells (HUVEC) were subjected to normal and high glucose levels as well as MCP (3.0, 15.0 and 3.0 mg/mL, respectively) for 24, 48, or 72 hours *in vitro* experiments. With the use of CAVEC, vascular/endocrine patterns, inflammation and related molecular biomarkers were detected and analyzed. The

results of the study showed that MCP treatment was able to reduce blood glucose levels in rat coronary artery cells for four weeks and decreased endothelial fibrosis and inflammation (Langasco et al., 2017; Parisi et al., 2020). *In vitro* experiments showed that high glucose exposure caused a significant increase in cellular apoptosis in HUVEC while medium to high doses of MCP (4.5 and 9.0 g/kg bw/day respectively) inhibited this high glucose-mediated apoptosis (Ehrlich, 2010). Finally, moderate oral doses of MCP (0.5-4.5 g/kg bw/day) inhibited apoptosis, decreased binding factor and microbial expression, and reduced the early stages of type 2 diabetes which is a new treatment option to prevent cardiovascular complications (Ehrlich et al., 2006; Ehrlich et al., 2011).

A study was conducted to explore the therapeutic benefits of marine collagen peptides (MCP) from fish hydrolysates on Chinese patients diagnosed with type 2 diabetes mellitus (DM2). The study involved 100 diabetic patients and 50 healthy individuals. The diabetic patients were randomly assigned to either a treatment group or a control group. For three months, the treatment group received 13g of MCP every day. Blood samples were collected from all participants before treatment, at 1.5 months, and at 3 months after treatment to assess glucose and lipid metabolism (Heinemann et al., 2007). The researchers also measured serum levels of highly sensitive C-reactive protein (hs-CRP), nitric oxide (NO), bradykinin, prostacyclin (PGI<sub>2</sub>), and lipids. Results showed that





fasting blood glucose, human glycated hemoglobin A1c (GHbA1c), fasting insulin, triglycerides, total cholesterol, low-density lipoprotein, and free fatty acids were all significantly lower in type 2 diabetes patients who received MCP treatment compared to those in the control group. Additionally, insulin sensitivity index and HDL levels improved. Interestingly, hs-CRP and NO levels decreased significantly while bradykinin, PGI<sub>2</sub>, and adiponectin levels were increased in MCP-treated T2DM patients compared with baseline or control levels ( $p < 0.1$ ). MCP treatment improves glucose and lipid metabolism in diabetic patients (Lahoud, 2010).

In order to monitor the neurodegenerative effects of marine collagen peptides (MCPs) obtained from chum salmon skin through enzymatic hydrolysis, 20-month-old C57BL/6J mice were given 0.22%, 0.44%, or 1.32% (1.2% w/w) MCP for a period of three months (Pei et al., 2010). The researchers then used a step test and the Morris water maze to evaluate negative avoidance, spatial memory, and learning abilities in comparison to an older adult

control group. Interestingly, there were no discernible differences between the MCP-treated group and the same-age control group in terms of learning and memory scores, even at doses as high as 0.44% and 1.32%. However, the MCP-treated group did exhibit alleviation of oxidative stress, reduced autophagy, and increased levels of brain-derived neurotrophic factor (BDNF) and post-operative density protein 95 (PSD95) when compared to the elderly control group (Xue et al., 2022). Despite these positive outcomes, there was still no significant difference between the MCP group and the same-age control group overall. Nonetheless, these findings suggest that MCP could be a potential functional food candidate for improving aging-related memory loss (Zhao et al., 2020).

In order to investigate how marine collagen peptides (MCP) derived from salmon skin (*Oncorhynchus keta*) impact lifespan and spontaneous carcinogenesis, a group of Sprague-Dawley rats were given varying concentrations of MCP mixed with their feed. There were 40 mice in each group, maintaining an equal male to female

TABLE 2 Application of animal and marine collagen in Europe.

Key players in the market	Application		Geography	Collagen type	Source
	Collagen of terrestrial animal origin	Marine-based Collagen			
Kiehls India, The Face Shop	Multifunctional feed additives, food ingredients, personal care products, and cosmetics		India and Pakistan	Intact tropocollagen	(Katzman et al., 1972)
Weishardt, Gelita AG, Darling Ingredients Inc, Tessenderlo Group, Koninklijke DSM N.V.	Production of peptides as meat substitutes, bone and skin health, nutritional supplements, food and beverages, cosmetics and personal care, medical care, cosmetic surgery, biomaterials, and packaging		Europe (Germany, France, UK, Russia, Italy, Spain)	Intact tropocollagen, hydrolyzed collagen	(Seixas et al., 2020)
Weishardt Group, Seagarden AS, Vital Proteins LLC, Ashland, Darling Ingredients Inc.	Bone, muscle and joint health, utilization of excess and waste from marine organisms, collagen scaffolds, antibacterial films, biopolymers	Pastries, drinks, breakfast cereal, snacks, senior nutrition and therapeutic foods, sports nutrition	North America, Europe, Asia Pacific, South America, Middle East, Africa	Hydrolyzed collagen	(Feng et al., 2023)
Gelita AG, Lapi Gelatine SpA Unipersonal Company, Weishardt Gelatines, Ajinomoto Co. Inc., Tessenderlo Group	Food and beverages, nutritional supplements, cosmetics, and personal care	Just beginning to be used	Africa	Hydrolyzed collagen	(Crini et al., 2020)

ratio. The study found that MCP had no significant effect on the body weight or food intake of male and female rats over the course of their lives (Burkel et al., 2016; Rajabimashhadi et al., 2023). However, it did inhibit the age-related decrease in antioxidant enzyme activity and lipid peroxidation in both sexes, resulting in an increase in maximum survival time. Interestingly, the incidence of spontaneous tumors decreased by 4.5% in males and 9% in females who were treated with MCP. Additionally, tumor mortality was significantly reduced compared to the control group for both males and females who received MCP treatment. As a result, it was concluded that MCP has a dose-dependent effect on increasing lifespan and reducing spontaneous tumorigenesis in Sprague-Dawley rats. The antioxidant properties of MCP may also play a role in prolonging life and preventing tumorigenesis (Burkel et al., 2016; Zhao et al., 2020; Xue et al., 2022).

## A new approach to the use of marine collagen: collagen hydrogels

Collagen hydrogels are prepared from collagen solutions by polymerization at room temperature for 10-15 minutes. Gels should become opaque after polymerization. After they become opaque, the cup is moved to 37°C for another 45-60 minutes to complete polymerization. After 45-60 min, 2-3 mL of medium is added and gels are released from the walls of the cup by running the tip of a p200 pipette around the perimeter of the cup. The mixture is gently shaken to release the gel. The collagen gel should float in the medium (Govindharaj et al., 2019). Collagen hydrogels are a type of three-dimensional network that can absorb and hold large amounts of water (Di Lullo et al., 2002). This structure has many advantages, including biocompatibility, fluidity, and the ability to accommodate various biotherapeutic agents. These hydrogels are suitable for cell

cultures, tissue engineering, drug delivery, and softgels. Marine polymers have emerged as an excellent natural alternative for creating new biomedical materials over the past decade (Jahromi and Barzkar 2018 a,b; Barzkar et al., 2019; Barzkar, 2020; Barzkar et al., 2021 a,b; Barzkar et al., 2022 a,b; Sankarapandian et al., 2022; Barzkar et al., 2023; Sankarapandian et al., 2023). Many collagen biopolymers can be obtained from marine by-products like fish skin or untapped resources like jellyfish, which can add value to biomaterials as part of circular economics strategies. Additionally, using marine resources like collagen can help reduce the risk of infection and boost immunity (Govindharaj et al., 2019; Venmathi Maran et al., 2023).

The physical characteristics of collagen hydrogels are directly influenced by certain factors such as porosity, molecular weight, density, and cross-linking between side chains. It is important to consider these factors when using collagen for therapeutic purposes (Im et al., 2017; Diogo et al., 2020). To gain a better understanding of the relationship between biopolymer structure and mechanical properties, research is needed on natural ionic ring polymer hydrogel formulations (Im et al., 2017).

When predicting the impact of collagen biopolymers on scaffold mechanical properties, it's important to consider factors such as molecular weight and solution viscosity (Sousa et al., 2020). The collagen biopolymer, which has a high molecular weight of approximately 260 kDa, differs from other polymers like chitosan and fucoidan due to the extraction process. During this process, smaller molecules are removed while higher molecular weight ones are retained (Gao et al., 2023). Factors such as source, extraction method, life cycle, environment, and collection location can all affect the chemical composition and molecular weight of collagen. Additionally, there is growing interest in the potential health benefits of collagen due to its antioxidant, anti-inflammatory, antiviral, wound-healing properties and more (Liang et al., 2010).

In a study conducted in (Liang et al., 2011), the relationship between the texture/composition and rheological characteristics of hydrogels made from collagen, chitosan, and fucoidan was investigated. Hydrogels containing various mixtures of these three biopolymers generally exhibited better mechanical properties than others. When comparing hydrogels made from two marine polymers, those with a higher polymer concentration had better mechanical properties (Liang et al., 2011). The presence of chitosan did not significantly affect the mechanical properties of these hydrogels, which is consistent with previous studies on two-component hydrogels. The study confirmed that these hydrogels have a well-structured microenvironment that can support cell growth and stimulate cell migration because the structural pores are larger than the size of cells (Wang et al., 2015). These marine-based hydrogel systems have potential applications in tissue engineering and regenerative medicine, particularly in treating articular cartilage (Liang et al., 2014). Additionally, using marine collagen in these hydrogel structures is considered a “green” technology that can be scaled up without negative environmental impacts (Hema et al., 2017). The rheological properties and relative density of terrestrial and marine collagen-glycosaminoglycan scaffolds were determined in a study (Hema et al., 2017). Data from Harley et al. is presented in Table 3. Collagen’s original purpose was to provide stability and strength to body tissues by forming a support network for cellular structures. This function has led to many applications, including cosmetics, due to its unique properties such as biocompatibility, biodegradation, biomimicry, and hemostasis (Das et al., 2021). Collagen can also form cross-linked matrices when dissolved, similar to gelatin (Tran et al., 2020). The use of fibrillar collagen in cosmetics is based on its functional purpose, while types I-III and V are used for their largest functional component and market dominance (Tran et al., 2020). The main collagen functions are summarized in Table 4.

The extracellular matrix (ECM) is crucial for maintaining cell integrity and aiding in cell functions like proliferation, differentiation, migration, and adhesion (Fischer et al., 2019; Carvalho et al., 2021). Marine organisms, such as fish, jellyfish, sponges, and other invertebrates, offer a valuable source of collagen that is free from religious restrictions and animal pathogens. This

type of collagen is metabolically compatible and has clear advantages over other sources (Oryan et al., 2018). Fish skin is a popular choice for extracting type I collagen because it’s abundant and not suitable for industrial use. Overall, marine sources of collagen are a safe, convenient, and promising option. The combination of biomaterials and single gene delivery has shown promising potential for tissue engineering. Skin lesions can be slow to heal and may not heal completely, but studies have found that marine collagen from organisms like fish, jellyfish, and sponges can promote wound healing, enhance blood circulation, and prevent infection (Coppola et al., 2020b; Wang, 2021). In addition to these benefits, marine collagen has anti-aging properties that have been demonstrated in mice with osteoporosis (Wang, 2021). It can increase bone mineral density, protect against bone loss and osteoarthritis, induce plastic differentiation, and even improve skin elasticity while slowing the aging process (Wang, 2021). Finally, marine collagen is also used for immobilization and drug delivery within the human body (Mantha et al., 2019).

Marine collagen hydroxylates, have been extracted and refined from the *Chondrosia reniformis* (Pozzolini et al., 2018b). *In vitro* tests were conducted using collagen peptide fragments at a concentration of 50 mg/mL, with cell examination at varying time intervals. The treated cells displayed signs of fibroblast and keratinocyte migration and proliferation, as well as increased wound adhesion between the skin and infected cells compared to the control group. These results demonstrate that marine collagen hydroxylates isolated from *C. reniformis* possess promising wound healing abilities. Similarly, hydrolyzed peptide collagen isolated from the jellyfish *Rhopilema esculentum* has also shown wound healing activity in both *in vitro* and *in vivo* experiments. In one study, collagen peptides were seen to increase cell migration and wound closure in a dose-dependent manner using the scratch-healing method. Additionally, a separate research on injured mice showed that collagen peptides partially promoted wound healing by stimulating chemokines such as  $\beta$ -FGF and TGF- $\beta$ 1, which protect wounds from infection by attracting inflammatory cells that also control the migration of fibroblasts and keratinocytes. Hence, promoting wound healing (Pozzolini et al., 2018b).

The anti-aging industry widely utilizes collagen for skin regeneration, as the aging process negatively impacts the aesthetic

TABLE 3 Rheological properties (Young’s modulus) and relative density of collagen-glycosaminoglycan scaffolds.

Collagen samples	Pore size, $\mu\text{m}$	Relative density, %	Young’s modulus, Pa	Thermal transition temperature, $^{\circ}\text{C}$	Denaturation temperature, $^{\circ}\text{C}$	Isoelectric point	Source
Marine (fish waste)	120 $\pm$ 21	0.062 $\pm$ 0.005	224 $\pm$ 48	32-34	35-37	3.56	(Liang et al., 2014; Wang et al., 2015; Hema et al., 2017)
Marine (waste of molluscs, sponges)	155 $\pm$ 34	0.064 $\pm$ 0.003	230 $\pm$ 22	31-33	30-37	3.5-5.0	(Hema et al., 2017)
Animal (cattle waste)	99 $\pm$ 11	0.049 $\pm$ 0.003	236 $\pm$ 38	40	40	6.0	(Liang et al., 2014; Hema et al., 2017)
Animal (poultry waste)	113 $\pm$ 15	0.060 $\pm$ 0.003	199 $\pm$ 29	52-62	50-70	5.5	(Hema et al., 2017)

TABLE 4 Collagen functions.

Studied material	Collagen functions	Source
Collagen	Therapeutic agents, reparative, skin healing, plastic material, for the treatment of wounds, burns and ulcers, in combination with hyaluronic acid used for disinfection and regeneration of the epithelium, in the treatment of periodontal disease, skin allergies, psoriasis, acne, dandruff, dermatoses, alopecia, inflammatory processes in the joints, softens the edges of postoperative sutures, used in the prevention of cellulite, skin stretch marks, stimulates spontaneous platelet aggregation and is an effective hemostatic, easily forming complexes with many drugs and biologically active substances, production of molded fish products, increased water and fat-holding capacity, gel-forming properties, production of polyfunctional biologically active additives.	(Nomura et al., 2005; Goldring and Otero, 2011; Zhang et al., 2011; Farage et al., 2013; Santos et al., 2013; Yamada et al., 2013; De Luca et al., 2016; Cicciù, 2017; Pullar et al., 2017; Arbex et al., 2018; Brunt and Burgess, 2018; Ito et al., 2018; Tang et al., 2018; Rahman, 2019; Veeruraj et al., 2019; Feng et al., 2020; Luo et al., 2020; Shalaby et al., 2020; Zhao et al., 2020; Bal et al., 2021; Melotti et al., 2021; Meng et al., 2021; Mohd Zaffarin et al., 2021)

aspects of the skin structure. Collagen and elastane fibers are responsible for maintaining skin elasticity, mechanical strength, and general structure (García-Quintero and Palencia, 2021). Marine collagen is known for its antioxidant properties as it can protect skin cells from harmful free radicals and oxidants that damage cell membranes, DNA, and macromolecules, which contribute to skin aging (Carvalho et al., 2020b). To prevent oxidative stress, antioxidant enzymes such as superoxide dismutase and glutathione peroxidase play a crucial role by inhibiting free radicals and other dangerous oxygen species. Acid-soluble collagen isolated by Chi et al (Balitaan et al., 2020). demonstrated the antioxidant activity of three collagen peptides and also showed its protective effect against other radicals. Additionally, collagen peptides (ACH-P1, P2, P3) were studied for their effects on oxidation and the formation of oxidative particles. The results showed that lipid peroxidation was significantly reduced compared to controls due to decreased uptake, which is a measure of oxidation. Collagen peptides exhibit similar effects as effective antioxidants in preventing oxidative damage (Balitaan et al., 2020).

Marine collagen biopharmaceuticals have the potential to promote cartilage regeneration, in addition to improving skin and bone health. Osteoarthritis is a condition that lacks regenerative ability and is characterized by joint pain and stiffness due to cartilage degeneration. The exposure of subchondral bone further lowers the quality of life for those with OA (Harley et al., 2008; Sinthusamran et al., 2013). However, studies have shown that marine collagen can induce chondrogenic differentiation and potentially facilitate cartilage regeneration (Sionkowska et al., 2020). Researchers like Raabe et al. have found that hydrolyzed fish collagen and growth factor TGFB1 can stimulate protein and collagen fiber synthesis, while fish collagen has been shown to induce chondrogenic differentiation (Gómez-Ordóñez and Rupérez, 2011).

Bourdon et al. conducted a study on fish skin and cartilage chondrocytes to analyze the impact of three collagen hydrolysates (Wang, 2021). A particular experiment revealed that concentrations of 0.5, 50, and 100 µg/mL of collagen hydrolyzate increased collagen I and collagen II levels. Additionally, the use of collagen resulted in decreased expression of protein markers such as Htra1, Mmp103, Adamts5, and Cox2. These markers are known to be associated with OA development (Rahman, 2019). In another study by Ohnishi et al., rabbits injected with a combination of fish collagen peptides

and glucosamine showed protection against cartilage damage while the control group developed OA (Townsend and Gannon, 2019). Although glucosamine and fish collagen peptides have some individual protective effects against OA, their combined effect provides the greatest protection (Chen et al., 2019; Townsend and Gannon, 2019; Geahchan et al., 2022). Collagen has also been found to have bifunctional properties (Allouche et al., 2020). The bifunctional properties of marine collagen are summarized in Table 5.

## Collagen in functional foods

It is essential to improve the existing technology of collagen materials with different functions, the role of collagen in nutrition, create original products, engage in unconventional development, and maximize the conversion of collagen-rich resources into functional products. A significant share of collagen proteins is contained in subproducts of the I and II categories; the latter have long been considered of low value and were used in food production to a limited extent. Collagen is of particular interest and potential in strengthening the meat industry's raw material base, providing animal protein, developing waste-free environmentally friendly technologies, increasing biological value, aesthetic appearance of products, reducing losses, and maximizing and rational use of meat raw materials (Bourdon et al., 2021).

At the moment, collagen-containing meat products with a variety of technical and physiological properties that stimulate the digestive process, absorb toxins and radioactive substances, and provide high performance, technical, and rheological properties of food products are being produced (Bourdon et al., 2021). The ability of collagen to bind many toxins is relevant in the field of deep processing of collagen raw materials with separation of target components, and theoretically justified and effective technical solutions are still insufficient. The most important challenge facing the food industry is to provide not only affordable food products to all segments, but also to maximize the functionality of these products. In this sense, functional foods should absorb and/or inhibit negative environmental factors affecting the human body by binding and releasing them. One of the most aggressive negative factors is heavy metal ions and radionuclides (Ferrario et al., 2020).

In this regard, an essential condition for increasing the functionality of food products is the inclusion of active

TABLE 5 Bifunctional properties of marine collagen.

No.	Collagen properties		Source
1	Bioactive	Functional	(Ahmed et al., 2020b; Allouche et al., 2020; Asaduzzaman et al., 2020; Haq et al., 2020; Suarez-Jimenez et al., 2020)
2	Antimicrobial	Gelling and water-binding properties	
3	Antioxidant	Surface charge (hydrophilicity or hydrophobicity)	
4	Antihypertensive/ACE inhibitor activity	Film forming ability	
5	Animal species identification	Applications for microencapsulation	
6	Wound-healing	Rheological properties and thermostability	
7	Chondroprotectors	Emulsifying, foaming, colloid-stabilizing, brightening properties	

components that are biologically neutral in relation to intra- and intercellular biochemical processes of the human body while also possessing a pronounced ability to at least sorb, and at most bind in low or non-dissociating complexes of polyvalent metal ions and radionuclides, demonstrating selectivity of action. To ensure the immune and physiological state of the organism in all spheres of life activity, including unfavorable and chronic conditions, it is necessary to create special, preventive, therapeutic, and generally strengthening nutrition, ingredients, biopreparations, and other products (Zhuang et al., 2009).

When assessing the use of food additives and ingredients based on modified collagen in meat product technology, dietary fibers and their connective tissue are also the most logical way to enrich food products, and the expansion of sources for their selective isolation in the form of isolated preparations of a given functionality for further use in the production of enriched products should be recognized (Ferrario et al., 2020).

## Collagen for skin regeneration

Tissue engineering and regenerative medicine is a rapidly growing interdisciplinary field that integrates materials science, biotechnology, medicine, cell biology, pharmacology, and chemistry to repair damaged tissues and organs (Aziz et al., 2016; Geahchan et al., 2022). The widely accepted concept of tissue engineering and regenerative medicine includes three major components: the selection of suitable stem cells, the identification of signaling pathways for repair or regeneration of specific tissues or organs (Chi et al., 2015). Biomass is a key component for the production of scaffolds. The use of appropriate biopreparations improves adhesion, migration, proliferation, and differentiation of stem cells, increasing their ability to repair and regenerate damaged tissues and organs (Caruso et al., 2020).

Among all natural polymers, collagen is one of the most studied and widely used in clinical practice. Major biomedical applications involving collagen include biomaterials development, tissue engineering, absorbable surgical threads, hematopoiesis, and

burn/wound treatment. To address societal ethical and nutritional concerns and the risk of spreading animal diseases such as bovine spongiform encephalopathy and foot-and-mouth disease, the scientific community is exploring the potential of using marine collagen as a substitute for mammalian collagen (Gauza-Włodarczyk et al., 2017). Another important argument in favor of using marine collagen is that collagen accounts for approximately 75% of the total weight of fish, indicating the abundance of this type of collagen (Raabe et al., 2010). During processing, approximately three-quarters of the fish, including skin, fins, bone system, and head, are discarded (Ito et al., 2018). Seafood is also an important source of valuable organic and inorganic materials used in various industries such as nutrition, cosmetics, regenerative medicine, and pharmaceuticals. Marine collagen applications include but are not limited to tissue engineering, wound dressing, cosmetics, and drug delivery (Ohnishi et al., 2013). Numerous studies have shown that hydrolyzed fish collagen exhibits biological activities such as regenerative, antioxidant, immunomodulatory, antibacterial, anti-inflammatory, and angiotensin-converting enzyme inhibitor.

## Collagen in cosmetics

Collagen has a wide range of applications. It is widely used in cosmetic, pharmaceutical, medical, and food industries because of its high biocompatibility, non-toxicity, and biodegradability (Hu et al., 2021). Collagen is a key component of many cosmetic formulations because of its moisturizing properties. Because the cosmetic industry is always looking for new and effective products, the source of collagen is an important research question (Dhatchayani et al., 2020). The potential of marine collagen was discovered about 70 years ago during the study of marine sponges (Gómez-Guillén et al., 2011). The research contributed to the study of structural and physicochemical features of collagen of marine origin.

Skin is a tissue composed mainly of type I, III, and V collagens. The predominant type of collagen in the skin is type I (Tang et al., 2022). Studies have shown that this type of collagen is identical to



marine collagen (Ito et al., 2018). Thus, marine collagen is the most popular source of collagen in the cosmetic industry. Studies on collagen from tilapia skin have shown that it has typical properties of type I collagen, along with acid-soluble collagen (ASC) and pepsin-soluble collagen (PSC). ASC has a dissociation temperature of 36.1°C and PSC has a dissociation temperature of 34.4°C (Tang et al., 2023). Acid-soluble collagen isolated from the skin of the fathead minnow (*Hypohalftalmichthys molitrix*) contained type I collagen as shown by SDS-PAGE (Mukherjee et al., 2023). Column chromatography confirmed three chains:  $\alpha_1$ ,  $\alpha_2$  and  $\alpha_3$ . The amount of collagen in Atlantic salmon (*Salmo salar* L.) corresponds to types I and V (Caddeo et al., 2017). Circulating dichroism (CD) raised the circulation temperature of salmon collagen to 27°C. A study of collagen content in cod also confirmed the presence of type I and type V collagens (Cossu et al., 2018). Experiments on adult bigeye snapper (*Priacanthus tayanus*) tissues (skin and bone) revealed two different types of  $\alpha$ -chains,  $\alpha_1$  and  $\alpha_2$  in the form of type I collagen. The electrophoretic spectra of bigeye snapper skin and bone are very similar (La Noce et al., 2014). Both ASC and PSC were derived from hybridized fungi and confirmed by SDS-PAGE and FTIR. The dissociation temperatures of ASC measured by circular dichroism (CD) and differential scanning calorimetry (DSC) were 26.8°C and 26.5°C, respectively. Natural immature collagen is in great demand for cosmetic and biomedical purposes. However, since the temperature of fish collagen is low, there is a limitation to emulsification by heating water and oil. Hydrolyzed collagen is used in many cosmetic products because it can be used as an emulsion with a high emulsification temperature while maintaining the moisturizing properties of collagen (Das et al., 2021).

## Conclusion

Collagen is a type of protein that makes up 30% of the body's total protein and can be found in various tissues like bones, teeth, skin, blood vessels, intestines, and cartilage. A recent study reviewed the current knowledge about collagen isolated from marine organisms and discussed its potential applications. Due to its reliability, low antigenicity, and biodegradability, collagen is commonly used in various industries such as pharmaceuticals, food, biopharmaceuticals, and cosmetics. The article also provides an overview of the physico-chemical properties of marine collagen and the best methods for extracting it from marine organisms. These methods have been found to have positive effects on health and relieve symptoms caused by chronic diseases. If aquaculture can find a solution to the availability of collagen, waste disposal can be integrated into the processing of raw materials to solve production waste problems. One potential direction for advancing marine collagen technologies is manufacturing certified skincare products.

There are many biologically active substances found in marine organisms that can be utilized in the pharmaceutical and cosmetic industries. Research is currently advancing into the numerous applications of collagen derived from these organisms. The main source of marine collagen extractions are fish (skin, bones, scales, swim bladders, and cartilages), mollusks (mesogloea, muscle

organ), marine invertebrates: jellyfish (dome, muscle tissue), sea cucumber (body walls), sea urchin (hard cover, connective tissue), polyps, octopus, and squid (muscle, tentacles, skin).

Marine collagen is a biomaterial that is water-soluble, metabolized, and easily obtainable. A literature review has shown that marine collagen is a versatile substance that can aid in treating skin lesions of varying severity and delay the aging process. Collagen has proven to stimulate the migration of keratinocytes and fibromuscular tissue, as well as cutaneous angiogenesis in both cases. Studies have also demonstrated that marine collagen and its derivatives are useful in preventing and treating osteoporosis and osteoarthritis, as well as other bone diseases. This is attributed to the fact that collagen promotes bone mineral density, mineral deposition, and inhibits the development and spread of osteoporosis. The advantages of marine collagen over terrestrial sources were discussed along with its potential biotherapeutic properties for skin and bone injuries. In keeping with the growing trend of replacing synthetic agents with more natural ones, collagen has found new applications as emulsifiers, foaming agents, colloidal stabilizers, hydrogels, clarifiers, biodegradable packaging materials, microencapsulating agents, and bioactive peptides. Furthermore, using fish processing waste to produce marine collagen for use in cosmetics has an environmental benefit by reducing their environmental impact as they are one of the food industry's strategic environmental components.

Furthermore, the functional properties of marine collagen hydrolysates are focused on the production of bioactive peptides with a number of biological activities (antioxidant, antibacterial, and chondroprotective). On the other hand, the great development of modern analytical methods allows for a deeper characterization of marine collagen properties, and its application for species identification may be of particular interest.

## Author contributions

Conceptualization, writing and original draft preparation: NB. Original draft preparation: SS, OB. Editing: BAVM, STJ. All authors have read and agreed to the published version of the manuscript.

## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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