Recent update: collagen extraction from marine resources as a promising natural antiaging

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Abstract. Aging is a natural process that occurs in every human. Aging can be prevented or slowed down through the appropriate and suitable use of collagen as an anti-aging treatment. Collagen is typically derived from raw materials such as pig or cow bones/skin, but recently there have been frequent outbreaks of infectious diseases among livestock, prompting the exploration of raw materials sourced from the sea to address this issue and create promising collagen for anti-aging purposes. The objective of this literature review research is to explore the potential of collagen extracts from marine resources as an anti-aging solution through an examination of relevant literature, which can serve as a reference for future research. A systematic review method was employed by collecting data from various literature sources, including research journals published both nationally and internationally, which discuss various marine resources containing collagen with anti-aging properties. Based on the systematic review, several natural resources containing collagen with anti-aging properties were identified, including sea cucumbers (*Holothuroidea* sp.), milkfish (*Chanos chanos*), tilapia (*Oreochromis niloticus*), jellyfish (*Rhopilema esculentum*), starfish (*Asterias pectinifera*), mackerel (*Decapterus macarellus*), squid (*Todarodes pacificus*), silver carp (*Hypophthalmichthys molitrix*), and blue sharks (*Prionace glauca*).

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1 Introduction

Premature aging is an inevitable physiological process [1]. Skin aging occurs due to intrinsic and extrinsic factors. Intrinsic aging naturally occurs with age, resulting from the slowing of cell renewal processes and changes in hormone production [2]. Extrinsic aging is caused by chronic exposure to light, pollution, ionizing radiation, chemicals, and toxins [3]. The skin is the body part most frequently exposed to external factors [1]. The effects of skin aging include thinning, dryness, reduced elasticity, rough texture, wrinkles, and dark pigmentation. Collagen is one of the essential components of the extracellular matrix that plays a crucial role in maintaining youthful skin [2]. As the primary structural component of the skin, collagen decreases by 1% each year. Therefore, there is high demand for collagen due to its bioactive effects in preventing skin aging [4].

Collagen is the main structural protein and the most abundant protein found in the animal kingdom, constituting nearly 25-30% of the total protein content in the entire body [5]. One of the numerous benefits of collagen is its anti-aging properties [6]. Over the years, most of the available collagen has been extracted from byproducts of cattle and pigs processing industries. However, in recent decades, the use of collagen from these sources has remained limited due to religious restrictions (for Muslims, Jews, and Hindus) and the risk of transmitting diseases such as Bovine Spongiform Encephalopathy (BSE), Transmissible Spongiform Encephalopathy (TSE), and Foot and Mouth Disease (FMD) that have occurred in cattle in recent years. Therefore, there is an urgent need to discover new alternative sources of collagen [4].

Marine resources have garnered significant attention in the last two decades as a safe and abundant alternative source for collagen extraction. Marine collagen (MC) poses a lower risk of infectious diseases and does not raise religious concerns [7]. Additionally, a substantial number of byproducts generated from the fish processing industry, accounting for approximately 70-85% of the total catch weight, has become a primary driver for research aimed at transforming cost-effective byproducts (such as fish skin and scales) into collagen-based products with high added value and minimal environmental impact [7, 8].

Therefore, this literature review is conducted to explore various marine resources and their collagen extractions with anti-aging properties through a literature search, which can serve as references for further research.

1.1 Aging

Aging is the gradual alteration of the anatomical structure of the skin, resulting in a decline in its physiological functions, which occurs as individuals age and due to environmental influences. Skin aging can be attributed to both intrinsic and extrinsic factors. Intrinsic factors include genetics, age, hormones, and ethnicity. Intrinsic signs of aging encompass fine wrinkles, a thinning and increased transparency of the skin due to a reduction in epidermal cells and melanocytes, as well as skin dryness. Extrinsic factors contributing to skin aging comprise exposure to UV radiation, contact with harmful substances, exposure to electronic device light, and lifestyle factors such as an unhealthy diet, sleep patterns, stress, lack of physical activity, and smoking [9].

The dermis layer is a crucial part of the skin that plays a vital role in maintaining skin elasticity and softness [10]. When collagen production in the dermis layer decreases, as occurs with aging and due to environmental factors, the skin can become dry and lose its elasticity. One of the factors that can lead to reduced collagen production in the skin's dermis layer is excessive exposure to sunlight [7]. UV radiation from the sun can increase the levels of free oxygen radicals (ROS) in the skin, which, in turn, can cause oxidative stress to the skin tissues. This results in damage to the extracellular matrix (ECM) of the skin [11].

Damage to the ECM directly contributes to the skin aging process and is responsible for the increased activity of enzymes such as collagenase, elastase, and tyrosinase. Activation of these three enzymes leads to a decrease in elastin and collagen levels in the skin, causing it to lose its elasticity, strength, and the development of wrinkles [12].

Therefore, efforts need to be made to prevent and slow down skin aging, one of which is through the use of cosmetic products. The use of cosmetic products is one option to avoid skin aging because it can improve skin texture and function [13]. One available solution to address skin aging is the use of anti-aging products. Anti-aging products work to inhibit skin damage and have the ability to reduce signs of aging on the skin [14]. Cosmetic products designed for anti-aging purposes have proven their benefits in reducing wrinkles, blemishes, and skin discolorations caused by pigmentation [15].

1.2 Collagen

Collagen is an abundantly present structural protein in the animal kingdom, and in the human body, it contributes to approximately 30% of the total protein [16]. Collagen plays a crucial role as the main component of the extracellular matrix that forms the skin, bones, ligaments, cartilage, and tendons [17]. There are nearly 28 types of collagens that can be classified based on differences in their molecular chains [18]. More than 85% of the collagen in the human body is of type I, while other types of collagens include type II, III, and IV. Collagen itself is a trimer consisting of three α polypeptide chains. The structure of type I collagen is characterized by a double helix and is rich in glycine, proline, and hydroxyproline residues [17]. Collagen provides a number of health benefits, including [19]:

- Plays a role as an aid in the digestion process.
- Exhibits anti-aging properties.
- Contributes to weight loss.
- Supports joint and bone health.
- Enhances athletic performance by increasing muscle mass.
- Improves sleep quality.
- Strengthens the health of hair, nails, and teeth.

Natural collagen is originally produced in the body by fibroblast cells. However, the body's ability to produce collagen can decrease with age and due to unhealthy lifestyles. Therefore, there is a need for collagen intake from external sources. The raw materials commonly used for this are usually extracted from mammals and poultry. However, concerns about infectious diseases such as Bovine Spongiform Encephalopathy (mad cow disease) and bird flu have raised questions about the safety of collagen from these sources [20]. Therefore, there is a need for new alternatives in the form of collagen sources derived from marine resources. Extracting collagen from marine sources not only addresses concerns of religious significance but also offers unique benefits [18].

1.3 Mechanisms of Antiaging in Collagen

Collagen has numerous applications in the cosmetics industry, especially in its role as an anti-aging ingredient. Collagen can penetrate into the skin layers and continuously form a colloid system on the skin's surface, resulting in a smooth and soft skin sensation. Considering collagen's capabilities, it can be used as an ingredient in cosmeceutical-based cosmetic products with anti-aging purposes [21].

2 Collagen from Marine Sources with Potential Anti-Aging Activity

Table 1. Collagen from marine sources with potential anti-aging activity

Marine Resources	Source of Collagen	Collagen Yield	Anti-Aging Activity Test	Ref.
Sea cucumber (*H. leucospilota*)	Body wall	7.92%	Antityrosinase and antielastase activity	[22]
Milkfish (*C. chanos*)	Scale	19.96 g of 300 g dry sample weight	Measurement of the water content and oil content of the skin	[1]
Tilapia (*O. niloticus*)	Bone	41.5%	Measurement of moisture, pore size, blemishes and number of wrinkles	[23]
Tilapia (*Oreochromis sp.*)	Skin	-	Observation of skin superficial characteristics, histopathological observation, determination of moisture content, Hyp content, and SOD content	[24]
Jellyfish (*R. esculentum*)	Umbrella	50 mg	Antityrosinase	[25]
Starfish (*A. pectinifera*)	All parts	3.8%	Measurement of reduction in MMP expression	[26]
Mackerel (*D. macarellus*)	Skin	6.39±0.97% (pepsin-soluble collagen)	Antiglycation and antityrosinase activity	[27]
Squid (*T. pacificus*)	Outer skin and inner skin	75.4% and 68.9%	Antityrosinase and antielastase	[28]
Silver Carp (*H. molitrix*)	Skin	-	Measurement of inhibition of MMP-1 secretion	[29]
Blue Shark (*P. glaucia*)	Cartilage	-	Measurement of moisture, sebum, texture and blemishes	[30]

2.1 Sea cucumber (*Holothuria leucospilota*)

The study Addillah et al. [22] utilized anti-tyrosinase and anti-elastase activity tests to determine the anti-aging activity of sea cucumber collagen. The results showed that in the anti-tyrosinase activity test, the IC50 value was 1.20 mg/mL, while in the anti-elastase activity test, the IC50 value was 125 µg/mL. Collagen isolated from sea cucumbers exhibited weak anti-tyrosinase activity and moderate anti-elastase activity.

2.2 Milkfish (*Chanos chanos*)

The anti-aging activity of collagen from milkfish scales in the study by Wahid et al. [1] was assessed by measuring the moisture and oil levels in the skin using a skin analyzer. This study formulated the collagen obtained into a cream preparation with concentrations of 5%, 6%, and 7%. The results of the moisture (moist) and oil level activity tests for preparations with concentrations of 5%, 6%, and 7% demonstrated anti-aging effects in improving skin conditions, with significance values for each concentration obtained (P>0.05), indicating no significant differences among the concentrations, although visually, the 7% concentration showed effectiveness in skin moisture levels. Therefore, it can be concluded that the cream containing 5% milkfish scale collagen (*Chanos chanos*) already possesses anti-aging effectiveness in improving the condition of the back of the hand skin of volunteers during 4 weeks of treatment, with an average change in moisture levels from 12.03% in week 0 to 26.98% in week 4, and an average change in oil levels from 18.03% to 24.53%.

2.3 Tilapia (*Oreochromis niloticus*)

The anti-aging activity of collagen cream derived from tilapia fish bones in the study by Ginting et al. [23] was assessed through measurements of moisture (moist), pore size, the presence of blemishes, and the number of wrinkles on human skin. This research analyzed the anti-aging effectiveness using collagen cream from tilapia fish bones with various concentrations, but the concentration that showed the best anti-aging effectiveness was 3.5% compared to other cream formulas and a comparative cream (Ponds cream). The application of this cream provided a moisture level of 50.2%, categorized as "moist," with a recovery percentage of 24.7%, a reduction in pore size of 21.5%, a decrease in the number of blemishes by 22.1%, and a reduction in the number of wrinkles by 22.2%. Furthermore, in a study conducted by Pu & Qu et al. [24], collagen from tilapia fish skin was administered in low, moderate, and high doses to a group of rats. The research results revealed an increase in dermis thickness with a denser structure, along with a significant elevation in water content, Hyp levels, and SOD activity. This effectively mitigated the skin aging process. The anti-aging effect of tilapia fish skin collagen correlated positively with the dosage administered.

2.4 Jellyfish (*Rhopilema esculentum*)

The anti-aging activity of jellyfish umbrella collagen in the study by Zhuang et al. [25] was evaluated through anti-tyrosinase activity. This research conducted anti-tyrosinase activity tests on several different fractions, namely HF-1 (>3000 Da), HF-2 (1000~3000 Da), and HF-3 (<1000 Da). The study results indicated that HF-2 exhibited an inhibitory effect of over 50% at a concentration of 5 mg/ml. Therefore, it can be concluded that HF-2 has the ability to inhibit tyrosinase activity. This suggests that HF-2 derived from jellyfish umbrella collagen hydrolysate may serve as a potential new natural inhibitor in the pharmaceutical and food industries.

2.5 Starfish (*Asterias pectinifera*)

The anti-aging activity of collagen from starfish (*Asterias pectinifera*) in the study by Han et al. [26] was assessed through the measurement of MMP (Matrix Metalloproteinase) expression reduction. The research results showed that in comparison to MMP-1 expression levels under control conditions without collagen peptides (indicating 100%), there was a decrease in MMP-1 expression levels in cells treated with nanoliposomes containing collagen peptides (less than 100%), specifically around 40%. More importantly, nanoliposomes containing collagen peptides extracted from *Asterina pectinifera* demonstrated a more significant reduction in MMP-1 expression compared to nanoliposomes containing collagen peptides from pig and fish meat, which only experienced about a 10% reduction. These results indicate that nanoliposomes containing collagen peptides from *Asterina pectinifera* have excellent potential as anti-aging agents.

2.6 Mackerel (*Decapterus macarellus*)

The anti-aging activity of collagen from mackerel skin in the study by Herawati et al. [27] was evaluated through antiglycation and antityrosinase activities. In this research, *D. macarellus* PSC (Partially Soluble Collagen) demonstrated the ability to inhibit glycation reactions by up to 50% at a concentration of 239.29 ppm. However, after collagen was hydrolyzed into HC (Collagen Peptides), the concentration required to achieve the same level of inhibitory activity significantly decreased to 68.43 ppm. Therefore, in hydrolyzed form, the inhibitory activity against glycation was higher than that of intact collagen. A similar trend was observed in the antityrosinase activities of PSC and HC from *D. macarellus*. The antityrosinase activity of *D. macarellus* PSC could inhibit tyrosinase activity by 50% at a concentration of 234.66±0.185 ppm. In this case, the antityrosinase activity of HC increased threefold compared to the PSC activity of *D. macarellus*, with an inhibition rate reaching 50% at a concentration of 79.35±0.5 ppm. Overall, these findings indicate that mackerel skin collagen has the potential as a material with anti-aging properties that can be further explored for use in the pharmaceutical and cosmetic industries.

2.7 Squid (*Todarodes pacificus)*

The anti-aging activity of collagen from the outer and inner parts of squid skin (*Todarodes pacificus*) in the study by Nam et al. [28] was evaluated through anti-tyrosinase and anti-elastase activity tests. In this research, inhibition of tyrosinase activity was tested on peptide fractions at five different concentrations. The results showed that the F3 fraction in both hydrolysates had the ability to inhibit tyrosinase activity, although its ability was significantly lower compared to L-ascorbic acid (positive control). Additionally, the testing of elastase inhibition activity on peptide fractions was carried out at three different concentrations. The research findings indicated that the F2 and F3 fractions in both hydrolysates had significantly higher elastase inhibition capabilities compared to the F1 fraction, although their elastase inhibition activity remained lower than that of urosolic acid (positive control).

2.8 Silver Carp (*Hypophthalmichthys molitrix*)

The results of measuring the inhibition of MMP-1 secretion by silver carp skin collagen polypeptide (SCSCP) in the study by Haung et al. [29] showed that SCSCP at a concentration of 10 mg/mL exhibited a high level of activity in combating DPPH and eliminating hydroxyl radicals. Meanwhile, at a concentration of 0.1 mg/mL, SCSCP significantly improved the survival of UVB-exposed L929 cells and inhibited the production of MMP-1 in L929 cells after UVB exposure. These findings indicate that SCSCP has the potential as a skin anti-aging agent with the ability to eliminate DPPH and hydroxyl radicals as well as inhibit MMP-1 production.

2.9 Blue Shark (*Prionace glauca*)

The study Lu et al. [30] employed 11 different concentration variations in testing anti-aging activity. Anti-aging activity was assessed through measurements of moisture, sebum, skin texture, and blemishes. Sample F11 resulted in improvements in skin moisture levels, skin texture, and skin color pattern. Additionally, Sample F11 was also effective in regulating skin oil production. Over a period of 10 and 20 minutes of use, Sample F11 demonstrated a reduction in skin wrinkles. Based on these positive results regarding skin quality and function, a cosmetic gel formulation containing collagen hydrolysate from P. glauca could be a promising choice for skincare applications.

3 Conclusion

Based on the above journal review, we can conclude that collagen can be sourced not only from livestock but also from marine resources. Marine resources containing collagen can be found in sea cucumbers, milkfish, tilapia, jellyfish, starfish, mackerel, squid, silver carp, and blue sharks. The type of animal that contains the most collagen from marine sources is Squid (*Todarodes pacificus*) in the outer skin and inner skin. Collagen derived from these marine sources is also considered safe and has been researched for its anti-aging properties over the past few years. Therefore, it can be considered an alternative source of collagen in the cosmetics industry.

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