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Scaling New Depths: Innovations in Fish Collagen Extraction and Biomedical Frontiers Explored

Yuvashree Chandrasekaran[1], S. Jagadeeswari[2], Balakumaran Manickam Dakshinamoorthi[1], D. Rushika Sri[1] and B. Kiran Sharma[1]*

[1]Department of Biotechnology, Dwaraka Doss Goverdhan Doss Vaishnav College (Autonomous), University of Madras, Chennai, Tamil Nadu, India.
[2]Department of Microbiology, Dwaraka Doss Goverdhan Doss Vaishnav College (Autonomous), University of Madras, Chennai, Tamil Nadu, India.

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Collagen is a fibrous protein commonly found in the bodies of human and other animals. It is referred to be the most abundant protein which comprises 30% of animal's overall protein. It is broadly used in diverse applications such as food, pharmaceutical, biomaterials, cosmetics, and biomedical industries. Fish waste is one of the cost-effective sources of collagen. The increasing adoption of marine-based and freshwater-based collagen is driven by their distinctive properties, which include advantages over mammalian-based collagen. These advantages encompass the absence of disease transmission risks, freedom from religious restrictions, cost-effective production, biocompatibility, and enhanced absorption within the human biological system. This review provides an overview of recent research regarding the extraction of collagen from marine and freshwater sources, with a specific focus on fish by-products. It encompasses subjects including the primary sources of fish collagen, pretreatment of fish materials, extraction techniques, collagen characterization, and its wide-ranging applications. More particularly, the study focuses at the procedures used to extract fish collagen, with an emphasis on isolating acid-soluble collagen (ASC) and pepsin-soluble collagen (PSC). Likewise, the fish derived collagen's application in biomedical engineering such as drug delivery systems, tissue engineering, therapeutic applications and cosmetic industry is summarized.

Keywords: Biomedical Applications; Collagen; Characterization; Extraction techniques; Fish waste.

Collagen, a naturally occurring structural protein in mammals, accounts for around 30% of the total protein composition inside an animal's connective tissues.[1,2] Collagen provides structural support and promotes tissue growth by utilizing mechanochemical signalling mechanisms that preserve tissue tensile resilience, firmness and elasticity. It is vital for functions such as movement, regeneration, and overall structural support.[3]

Collagen's distinctive function as a wound repairing substance involves safeguarding and expediting the regeneration process by hindering the absorption and proliferation of pathogens, especially harmful microorganisms.[4] Transforming the waste materials of fish processing like scales, skin, and muscles into collagen can help address the environmental and public health concerns linked to how seafood processors dispose of these materials.

*Corresponding author E-mail: kiransharma@dgvaishnavcollege.edu.in

This will automatically lead to a reduction in improper waste dumping in landfills.[5]

Furthermore, due to the large daily consumption of fish and the yearly creation of approximately 20 million tons of by-products from fish processing, which include components like the head, fins, skin. These materials are often disposed of as 'trash'.[6,7] To address the growing demand for collagen, numerous researchers have been exploring alternative collagen sources, with a particular emphasis on marine sources, including fish by-products. Hence, further research is in progress to investigate various extraction procedures and characterization process of collagen obtained from fish processing by-products.[1,8]

Some of the fishes include *Sardinella longiceps*, *Catla Catla, Cirrhinus mrigala*, Nile tilapia *(Orechromis niloticus)* and silver catfish *(Pangasius sp.)*.[5,9,1,10] Fish collagen offers numerous benefits, including its exceptional safety profile (free from pig-related foot-and-mouth disease, bovine spongiform encephalopathy in cattle, and cow-transmissible spongiform encephalopathy), excellent absorbability, absence of religious restrictions, cost-effectiveness, and biocompatibility. These attributes position fish collagen as a versatile and highly applicable resource in diverse domains such as health foods, cosmetics, and biomedicine.[11,12,13,14,15]

The analysis of purified collagen's amino acid composition indicated the existence of 18 different amino acids, including the relatively uncommon tryptophan, in collagen obtained from carp fish scales.[16] The extracellular matrix is typically described as the noncellular part of tissue, offering crucial biochemical and structural support to its cellular components.[17] Collagen, considered through the lens of materials science, stands out as an exceptionally prevalent polymeric biomaterial extensively employed across diverse domains, spanning from the realms of nutrition and beauty products to pharmaceuticals.[18,19]

Type I collagen, the most common collagen type, acts as a great foundational component for cosmetics and biomaterials. It is generally derived from the dermal tissues of bovine or pig sources.[20] Collagen exhibits varying amino-acid compositions based on its source, resulting in the identification of 28 distinct collagen types to date. The prevalent types are categorized as types I to V and distinguished by their macromolecular structures.

Type I collagen is prevalent in several connective tissues, including these. Type I collagen has a triple-helix structure made of two á1 chains and one á2 chain Within this structure, a linkage between two á chains is termed a â chain, forming a chain dimer, while a linkage among three chains is referred to as a ã chain, forming a trimer.[5,21,22,23,2]

Marine collagen offers a sustainable solution that is safer than mammalian collagen due to the absence of exposure to zoonotic diseases. Additionally, the utilization of discarded fish scales from food processing to extract type I collagen presents an appealing opportunity for efficiently recycling organic resources and reducing waste. Nevertheless, the majority of techniques for extracting type I collagen from fish scales rely on enzymatic processes.[24,25]

Collagen fibres play a crucial role in vertebrate tissues by not only preventing premature mechanical issues but also aiding in the storage, dispersion, and transmission of energy originating from musculoskeletal or externally applied forces. These fibers are crucial in providing structural support to every organ inside the body maintaining the appropriate firmness, elasticity, and strength required for optimal movement, tissue renewal, and the healing process, all of which are achieved through mechanochemical transduction processes.[26]

Exploring the full potential for utilizing waste generated during fish processing is crucial. By embracing reuse practices, we can not only reduce costs but also enhance product nutritional value while minimizing waste emissions and environmental pollution.[4] Research has indicated that fish scales are rich in protein, comprising approximately 70% of their composition, and primarily consist of collagen and keratin, resulting in an important resource with substantial biological significance.[27] Exploring the potential of fish scales presents a promising avenue for generating value-added products and contributing to environmental conservation. Current study focuses on obtaining collagen from the scales of freshwater fish.[28]

The aim of this review is to present a contemporary examination of collagen production

from fish scales, with a particular emphasis on the methods employed for extraction and characterization.

Primary sources of fish collagen

Fish collagen may be derived from a variety of fish by-products, such as fish bones, scales, and skins. These by-products are extensively eaten in many regions of the world, but they also generate a substantial quantity of trash, accounting for 50% to 70% of the original raw materials generated by fish shops and processing plants.[29] The fish derived sources of collagen is given in Figure 1

Fish scales

A substantial quantity of waste is generated in the fish processing industry, with fish scales being a significant contributor. Recent research has indicated that collagen extracted from fish scales exhibits characteristics consistent with Type I collagen, comprising two á1 chains and á2 chain.[30,31,32] Fish scale-derived collagen exhibits effective water absorption at a rate of 13.3% and strong water retention capabilities at 15%, rendering it well-suitable for medical and therapeutic uses.[31] However, since fish scales contain significant amount of calcium, ranging from 16% to 59% of their mineral composition by weight, decalcification must be carried out using ethylenediaminetetraacetic acid (EDTA).[20]

Fish skin

Fish skin typically contains around 70% type I collagen, with variations depending on the species, age and seasonal conditions.[16] Collagen derived from fish skin showcases impressive water retention capabilities, absorbing approximately 6% of its weight when exposed to 63% humidity for 24 hours. Additionally, it poses no irritant risks, making it a suitable choice for use in dermal applications.[33] Aside from the traditional methods of collagen extraction such as Acid Soluble Collagen (ASC) and Pepsin Soluble Collagen (PSC), a different approach for collagen extraction from the skin of fish involves utilizing carbon-dioxide acidified water, a technique previously employed to isolate collagen from Atlantic cod (*Gadus morhua*). Collagen extracted with acidifies water exhibited a total proline-like amino acid content of 151 per 1000 residues, and the extraction yield was 13.8%,[34] while Acid Soluble Collagen (ASC) and Pepsin Soluble Collagen (PSC) method being the classical method.[35]

Fish bones

The collagen derived from fish bones resembles characteristics of type I collagen, comprising two á1 chains and á2 chain.[28,36] Collagen derived from bones of tilapia, catfish, pomfret, and mackerel requires a greater extraction temperature (16.6 æ%C–19.03 æ%C) and a shorter recovery duration (73.16 hours) in comparison to collagen derived from scales and skin of fish. Moreover, it exhibits lower extraction yields (0.64%) when contrasted with collagen obtained from fish skin.[37] In an earlier study, the maximum collagen output attained from fish bones using a 1% pepsin solution was 16.13 mg/mL. Desalting is recommended as a crucial step in bone collagen extraction because of the elevated hydroxyapatite and calcium levels, both of which are eliminated during pretreatment using EDTA or HCl. Nevertheless, it's worth noting that HCl usage can lead to collagen degradation.[38]

Fish cartilage

Collagen from fish cartilage is mostly made up of type II collagen, with smaller amounts of other collagen types like type IX and type XI. For example, type IX and type XI collagen variants have been found in the nasal cartilage of Hoki (*Macruronus novaezelandiae*),[33] the cartilage of *Sphyrna lewini*, *Dasyatis akajei*, and *Raja porosa* included type I collagen.[39] The cartilage yielded collagen type II in it's Acid Soluble Collagen (ASC), collagen type II solubilized with pepsin (PSC) and type II gelatine.[38]

Extraction methods of collagen

The process of collagen isolation commences with preparation, advances to the extraction stage, and culminates in the recovery phase.[2] The process of collagen production includes pretreatment, extraction, separation, purification, and characterization,[40] which is expressed as a flowchart of collagen extraction procedure in Figure 2. Pretreatment procedures, comprising cleaning, washing, and size reduction are required before extraction to reduce the contamination of the samples.[32]

Pretreatments involving both acidic and alkaline solutions are frequently employed in the fish processing industry to eliminate non-collagenous compounds like proteins, fats, and

pigments, thereby enhancing collagen purity, while simultaneously optimizing collagen yield and quality.[42] Acidic pretreatment is a suitable method for materials that are raw containing collagen with less cross-links because it enables the controlled breaking of noncovalent bonds at specific temperatures. This process involves immersing the raw materials in an acidic solution. In contrast, pretreatment with alkaline solutions is commonly employed to break down the intermolecular and intramolecular cross links found in dense and tough raw materials, aiming to eliminate non-collagenous components.[41,42]

Treating collagen derived raw materials such as scales or skin is essential prior to their utilization.[43] NaOH is a popular choice for alkaline pretreatment due to its exceptional swelling characteristic, which enhances the collagen by maximizing the rate of mass transfer inside the tissue matrix.[44] Besides, to prevent environmental pollution, it is crucial to carefully choose a suitable method for pre-treating raw materials, ensuring the minimal production of excess waste liquid and the formation of reagent residues in collagen.[1]

The demineralization process, often known as pretreatment, is an important step in enhancing the efficacy of collagen extraction. This technique is employed when extracting collagen from raw materials naturally containing minerals, such as scales and bones. During the demineralization process, ethylenediaminetetraacetic acid (EDTA) is utilized to facilitate the removal of these minerals.[42]

Collagen extraction has been performed through various techniques, including chemical extractions involving strong acids and alkalis, thermal extractions, and other innovative non-conventional methods.[45] The choice of extraction method significantly influences both quantity and quality of the resultant collagen.[10] An example of collagen extraction commonly employs acid and enzymes as the primary method.[46,10,47,48] A comparative study is done on extraction procedure and types of collagens of various species and represented collectively in Table 1.

Acid-soluble collagen (ASC) extraction procedure

Acid Solubilized Collagen (ASC), represents a specialized collagen variant obtained exclusively through acid-based extraction methods. The interaction between acid and collagen effectively breaks the cross-links inside the collagen helix, thereby elevating the quality of the extracted collagen. Consequently, researchers have continuously investigated the application of

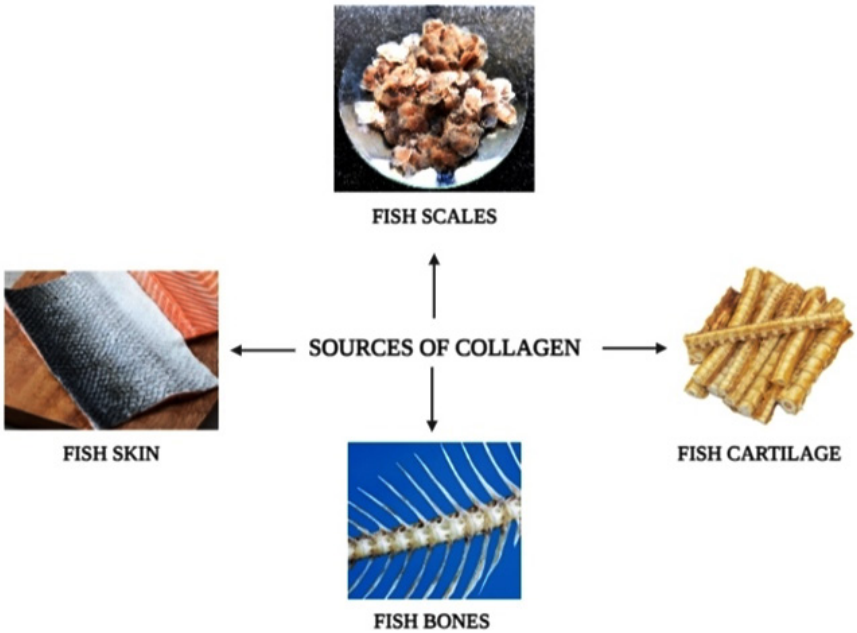

Fig. 1. Collagen origins from fish environments

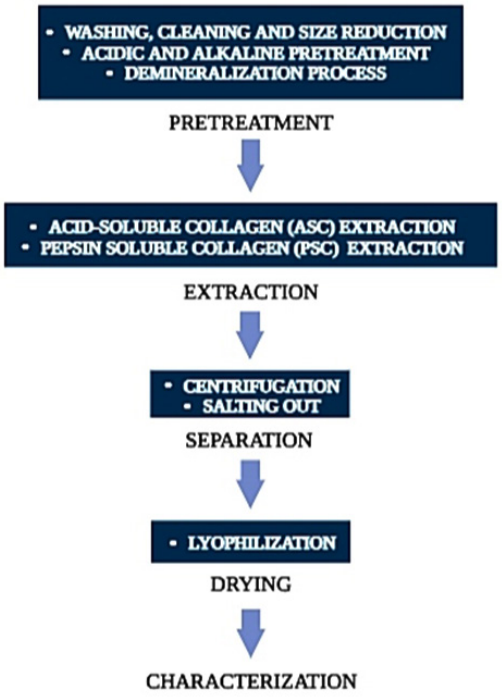

Fig. 2. Process of Fish derived collogen extraction

diverse acidic agents to optimize the efficiency, purity, and yield of collagen extraction.[10] The acid extraction solution, with concentrations ranging from 0.5 M to 1 M, allows for the breaking of both intramolecular and intermolecular crosslinks while maintaining the integrity of the collagen chains.[43]

Pepsin Soluble Collagen (PSC) Extraction Procedure

Another commonly employed technique for collagen extraction involves the utilization of Pepsin Soluble collagen (PSC) extraction, wherein pepsin is introduced into the extraction method.[49] The PSC extraction method has been fine-tuned by optimizing three crucial parameters: achieving the highest PSC extraction efficiency entailed employing a pepsin concentration that was 1389 U/g, maintaining a ration of solids-liquids of 1:57, and a hydrolysis duration of 8.67 hours. These maximized parameters produced an impressive PSC extraction yield of 84.85%.[50]

Consequently, numerous research endeavours have incorporated an enzymatic pre-treatment involving pepsin to enzymatically break down the telopeptide ends of collagen chains,

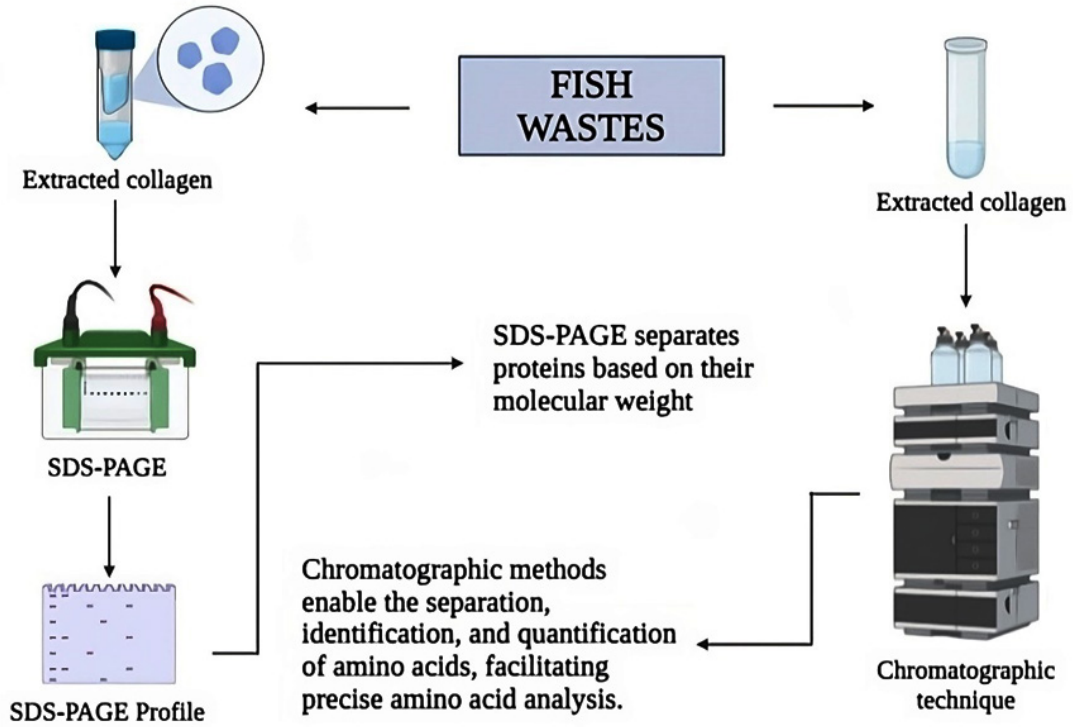

Fig. 3. Characterization of extracted collagen thourgh SDS-PAGE and Chromatographic method.

Table 1. Comparison of extraction methods of fish derived collagen and its collagen type across distinct species

Fish species	Source	Extraction method	Type of collagen	References
Nile tilapia (Oreochromis niloticus)	Skin	acid-soluble collagen (ASC) and pepsin-soluble collagen (PSC)	Type I	1
Silver carp (Hypophthalmichthys molitrix)	Scales	acid-soluble collagen (ASC) and pepsin-soluble collagen (PSC)	Type I	4
Carp (*Cyprinus carpio*)	Bone	acid-soluble collagen (ASC)	Type I	28
Silvertip shark (*Carcharhinus albimarginatus*	Cartilage	acid-soluble collagen (ASC) and pepsin-soluble collagen (PSC)	Type II	31
Channel Catfish (Ictalurus punctatus)	Skin	acid-soluble collagen (ASC) and pepsin-soluble collagen (PSC)	Type I	43
Bigeye tuna (*Thunnus obesus*)	Bone	acid-soluble collagen (ASC) and pepsin-soluble collagen (PSC)	Type I	49
Giant croaker (Nibea japonica)	Skin	pepsin-solubilised collagen (PSC)	Type I	50
Bighead carp (Hypophthalmichthys nobilis)	Fins	pepsin-solubilised collagen (PSC)	Type I	52

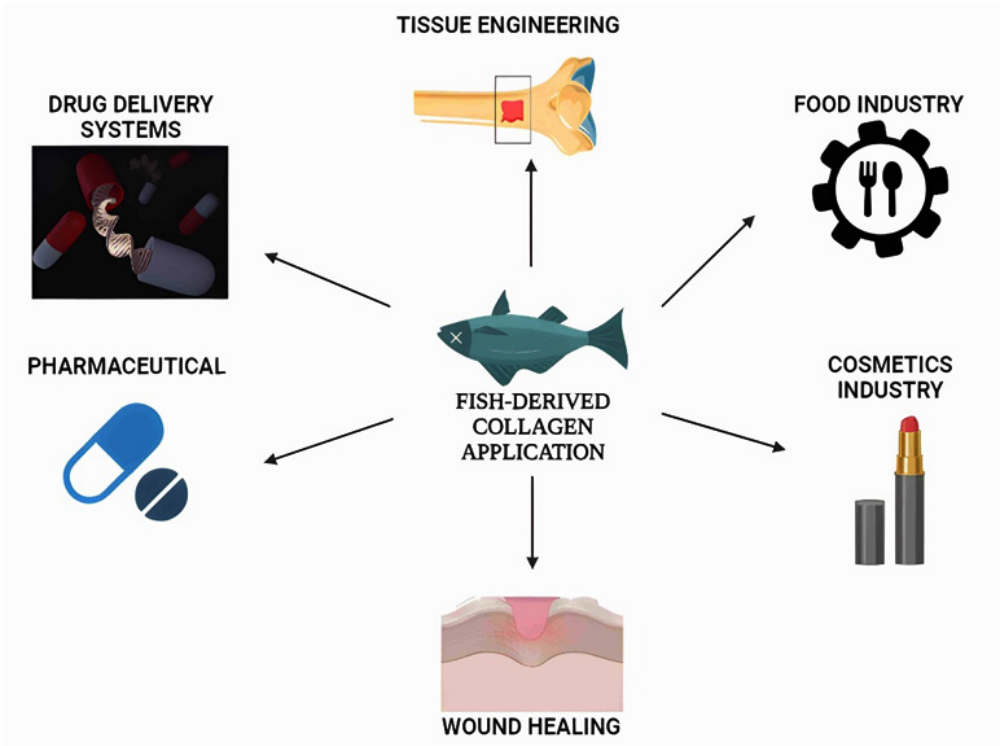

Fig. 4. Fish derived collagen in diverse applications

Table 2. A comparative findings of characterization methods of extracted collagen through various studies

Characterization Methods	Fish Species	Illustrated Findings	References
	Scomber japonicus	Bones and skin are primarily composed of type I collagen, featuring a molecular structure consisting of two identical á1-chains and one á2-chain, arranged in a heterotrimeric configuration.	6
FTIR	*Hypophthalmichthys molitrix*	The FTIR spectra indicated that both ASC and PSC were likely structured in their native triple helical conformation.	4
	Sardinella longiceps	The FTIR spectra analysis of ASC and PSC, extracted from sardine scales, skin, and muscles, revealed the distinct presence of various functional groups across a broad range of wavelengths (4,000–400 cm^{-1}).	5
	Solea solea	The fish skin exhibited three distinct -chains: (á1)2, á2 chains (M.W. 118,116 kDa), in addition to a single â chain (M.W. 200 kDa).	60
SDS-PAGE	*Oreochromis niloticus*	The skin showcased comparable protein profiles, featuring á1 and á2 chains weighing around 123 and 113 kDa.	1
	Hypophthalmichthys molitrix	Both the ASC and PSC demonstrate the presence of á1 and á2 chains, suggesting that the collagen found in silver carp scales is consistent with type I collagen.	4
	Chitala ornata	The collagen samples derived from skin displayed notable triple-helical structural characteristics.	47
Circular	*Hypophthalmichthys molitrix*	The CD spectra of ASC and PSC closely resemble each other, exhibiting a peak of rotation at 220 nm and a trough at 197 nm. This pattern mirrors the characteristic spectrum associated with the collagen triple-helix structure.	4
Dichroism	*Acipenser schrenckii*	The CD spectra of collagen revealed a distinctive pattern: a peak rotation at 221 nm, a trough at 198 nm, and a consistent crossover point around 213 nm. This pattern is a typical characteristic of collagen's triple helical conformation.	32
	Hypophthalmichthys molitrix	The analysis of collagen derived from scales unveiled the dominance of collagen type I, boasting a significant 34% glycine and low level of proline (Pro) and hydroxyproline (Hyp).	4
Chromatography	*Silurus triostegus*	Reverse phase HPLC analysis revealed a distinct array of protein peaks within the PSC samples in contrast to the ASC and type I collagen standard samples. This variation is likely attributed to the process of pepsin hydrolysis.	67

	Pterygoplichthys pardalis	A comprehensive analysis revealed the presence of16 amino acids. Notably, glycine emerged as the predominant amino acid in both ASC and PSC samples, constituting 28.3% and 27.9% of the total composition, respectively.	68
	Lates calcarifer	The skin exhibited a maximum temperature limit of 33.33°C, accompanied by a "H value of 0.860 J/g.	66
DIfferential Scanning	*Cyprinus carpio*	An endothermic peak was observed at 116°C on the DSC diagram, indicating a heat absorption of 3.7 J/g.	16
Calorimetry	*Acipenser schrenckii*	The DSC pattern revealed that the temperature at which the material started to change (Tm) was 120.23°C for ASC and 118.80°C for PSC.	32

thus enhancing the ease of proteins extracted from the residual matrix.[40,51] Additionally, a prior study documented the extraction of collagen from several tissues of bighead carp, including scales, skins, fins, bones. This extraction process involved treatment with a 0.1 M NaOH and a solution that was alkaline, followed by the use of PSC.[52]

Collagen Characterization Methods

Analysing the structural properties of isolated collagen provides a meaningful connection between its characteristics and the obtained results. Various methods can be employed to evaluate marine collagen. With a particular emphasis on its structure and morphological properties. Various approaches can be employed for the evaluation of marine collagen, whether it's in a liquid or solid state, to examine its structural, chemical, and morphological characteristics.[2] A schematic representation of few characterization methods are shown in Figure 3.

FT-IR Studies

The Fourier transform infrared (FTIR) technique serves as a valuable tool for assessing collagen's presence, chemical composition, and type recognition. Furthermore, it enables comparisons of collagen compositions obtained through various extraction methods and exploration of how isolation techniques impact collagen composition.[53,31,6] Fourier transform infrared (FTIR) spectroscopy stands out is a popular method for investigating the secondary structure of proteins during collagen characterization.[54] FTIR spectroscopy holds significance as it unveils the absorption wavenumbers spanning from 500 to 4000 cm^{-1} within the spectrum.[55]

The FTIR spectra of collagens derived from seabass scales through both PSC and ASC extraction methods were studied. Their findings revealed that the extracted collagen is type I, and that the treatment processes did not cause any damage to the functional groups within the collagen's triple helix structure.[6] Complementary research utilized FTIR spectra to analyse the composition of PSCs obtained from mackerel (*Scomber japonicus*) bones and skin. Their investigation unveiled that mackerel bones and skin predominantly comprise type I collagen, which is a molecular structure composed of two identical á1-chains and one á2-chain, forming a heterotrimeric configuration.[56]

SDS-PAGE Technique

SDS-PAGE, (Sodium dodecyl sulfate polyacrylamide gel electrophoresis), is a technique used to separate proteins and protein fragments according to their sizes. This technique helps to determine the molecular weight of collagen.[57] Collagen type I peptides exhibit a versatile structure, composed of three alpha chains that can vary in composition depending on the specific type of collagen. For instance, in type I collagen, the arrangement comprises two alpha 1 chains and one alpha 2 chain, whereas in type II collagen, three alpha 1 chains are present. Furthermore, the assembly and post-translational modifications give rise to dimers (â-chains) or trimers (ã-chains), as observed in SDS-PAGE analysis. Fish collagen

typically follows a similar pattern with two alpha 1 chains and one alpha 2 chain.[58,59] A study discovered that the collagen extracted from sole fish skin (*Solea solea*) consisted of three distinctive -chains: $(á1)_2$, á2 chains (M.W. 118, 116 kDa), along with a single â chain (M.W. 200 kDa).[60]

Circular dichroism

On a similar note, with other proteins, one can evaluate collagen's secondary structure, binding properties, and folding characteristics using circular dichroism (CD), a technique that relies on measuring the distinct right and left circularly polarized light absorption.[61,62] By integrating CD spectroscopy with complementary techniques like rheology, we can unlock valuable insights into the type I collagen fibril's secondary structure and the collagen fibril signals development, ultimately advancing our understanding of collagen-based biomaterials.[2] It is demonstrated that employing an ultrasound-assisted extraction method on collagen from crown featherback (*Chitala ornata*) skin resulted in collagen samples exhibiting distinctive triple-helical structural features, as evidenced by CD spectrometry.[47]

Chromatography

Chromatographic techniques can be employed to separate, identify, and quantify amino acids for the purpose of amino acid analysis.[63] Collagen type I is renowned for its richness in the amino acids like glycine, alanine, proline, and hydroxyproline.[64]

For instance Wu *et al.,* demonstrated that the amino acid analyses of extracted collagen obtained from silver carp (*Hypophthalmichthys molitrix*) scales using PSC and ASC methods revealed the presence of collagen type I with a substantial 34% content of glycine and a relatively low level of amino acid content, specifically 20% consisting of proline (Pro) and hydroxyproline (Hyp).[4]

Differential scanning calorimetry (DSC)

Elevated temperatures lead to the unfolding of collagen molecule structures, and the maximum transformation and collagen's denaturation temperature can be determined by quantifying the calorimetric energy flux.[6] Differential scanning calorimetry (DSC) is used to analyse the collagen thermo behaviour. When temperature rises during DSC analysis, collagen gradually absorbs heat, eventually reaching a species-specific threshold temperature where it begins to undergo structural unfolding.[65] The depicted findings of collagen through characterization methods are illustrated in Table 2. The collagen extracted using pepsin, known for its elevated Hyp content, exhibited a peak denaturation temperature of 39.32°C and a corresponding enthalpy change ("H) of 0.91 J/g. In contrast, the collagen isolated with acid demonstrated slightly lower values, with a denaturation temperature of 38.17°C and a "H of 0.72 J/g.[6] In another study, it was found that the Hyp content in the skin of seabass (Lates calcarifer) reached 79 residues per 1000 residues. The skin demonstrated a maximum temperature threshold of 33.33°C, along with a "H value of 0.860 J/g.[66]

An Overview on the Application of Fish Collagen in Various Fields

Fish derived collagen has received research attention for biomaterial applications due to its solubility in water, safety, versatility, biodegradation, ease of extraction, and minimal immunogenicity.[69,70] The biocompatibility and biodegradability characteristics of fish atelocollagen make it a suitable choice for scaffolds in regenerative medicine.[71] The various collective applications are shown in Figure 4.

Utilizing type I collagen from fish as a compostable spacer and scaffold proves highly effective in mimicking the natural extracellular matrix. This replication facilitates the spatial organization of cells, offers environmental cues, and allows for site-specific cellular control.[72,73,74]

Fish collagen has been evaluated as a scaffold for achieving tissue engineering objectives.[75,76] Incorporating fish collagen in situ may promote the formation of hard tissue, serving not just as both a framework for implanted cells and a nutritive component.[67] Furthermore, various types of collagens, obtained through different techniques, have been shown to be instrumental in promoting the regeneration of dental tissue, underscoring their potential for use in biomedical applications aimed at restoring tooth tissue.[76,77]

Moreover, they play a vital role in drug delivery systems, including their use in ophthalmology through collagen shields, facilitating protein delivery via pills and mini-pellets, controlling transdermal administration

with gel formulations in combination with liposomes, and facilitating gene delivery through nanoparticles.[78,79,80,81,82,83]

In an effort to enhance the allopurinol efficacy as a pharmaceutical agent for addressing gout and elevated uric acid concentration in the human body, a pH-sensitive hydrogel by utilizing fish scale-derived collagen and carrageenan was prepared as a drug delivery system.[84] The application of this hydrogel resulted in enhanced drug bioactivity and favourable changes in the drug's physical characteristics when exposed to simulated body fluids. Notably, the release of drug rate was much slower, ranging from 1.5 to 6.7 times more gradual than the control sample.

In a separate study, hydrogel microneedles were created using crosslinked collagen derived from fish scales via an altered lower temperature press technique, and these microneedles were successfully loaded with ferrous gluconate.[85] Researchers aim to target the delivery of drugs to particular body tissues or organs, with the goal of mitigating substantial issues such as low bioavailability, instability, poor solubility, and inadequate absorption.[86]

The process of bone regeneration is a multifaceted physiological phenomenon, encompassing both the creation and breakdown of bone tissue.[87] A primary objective within the field of tissue engineering involves the restoration of impaired, infected, or tissues and destroyed organs by employing permeable, biocompatible, and naturally degradable scaffolds.[88,89,90,91]

Usage of marine collagen in creating scaffolds has been investigated for its potential to promote osteogenic activity in the context of bone tissue engineering applications.[2] Hoyer *et al.,* used the combination of salmon skin collagen and hydroxyapatite to fabricate scaffolds tailored for bone regeneration. They harnessed the biomimetic mineralization principle as the foundation for their approach. In addition to its impressive mechanical elasticity, these scaffolds demonstrated remarkable absorbent qualities along with a well-established network of interconnected pores. This architecture facilitated the adhesion and proliferation of human Mesenchymal Stem Cells (hMSCs), making it a promising platform for fostering osteogenic differentiation.[92]

A collagen fibril using collagen extracted via the swim bladder of Bester sturgeon fish was successfully developed. They created hydrogels utilizing a double network structure. These double network hydrogels displayed outstanding mechanical characteristics, and the hydrogel exhibited excellent mechanical properties *in vivo*. As a result, they claimed that this hydrogel offers promise for applications such as artificial cartilage.[93] A chitosan-collagen composite scaffold, incorporating collagen derived from tilapia scales, was engineered for the explicit aim of facilitating oral mucosa regeneration.[94]

In an attempt to enhance the wound healing process using a skin engineering approach Hu *et al.*, undertook a study. They assessed the wound repair potential of marine derived collagen peptides produced from Nile tilapia skin (*Oreochromis niloticus)* through both *in vitro* and *in vivo* experiments. The marine derived collagen peptides they synthesized primarily consisted of polypeptides. Their findings from both *in vitro* and *in vivo* experiments indicated that the collagen extracted from Nile tilapia had the potential to promote and accelerate the wound-healing process.[95]

Collagen is of significant importance in the biomedical field because of its biocompatibility, biodegradability, and enhanced capability to permeate lipid free surfaces. Its biological uses are numerous, primarily because collagen has the unusual capacity to self-organize and create cross-linked collagen fibres, which exhibit remarkable strength and stability.[96,97]

Numerous studies have established that collagen hydrogels stand out as prime materials for wound dressings. Their effectiveness stems from their three-dimensional structure, closely resembling the natural moisture of the extracellular skin environment.[98] Marine collagen has the potential to serve a dual purpose as both a dressing for wounds and a medication carrier. To illustrate, curcumin was incorporated within fish scale-derived collagen, along with Hydroxy methylcellulose nanogel, for applications in wound healing.[99]

Analogously, collagens are increasingly acknowledged for their remarkable biological effects and significant potential for application in the cosmetic industry. As new generations pursue novel beauty and youth-maintenance goals

while continually seeking safe and cost-effective ingredients, proteins of marine, particularly marine derived collagens, are currently emerging as outstanding functional components for the cosmetic sector.[100,79,80,101] Within the cosmetic industry, marine collagen is sourced from the skin of cold-water fishes such as cod, haddock, and salmon.[102,103] Furthermore, it is also made from scales of fish by procedures such as decalcification and enzymatic hydrolysis.[104]

In the food sector, the core purpose of food packaging is to safeguard and maintain the quality of food, chiefly by shielding it from oxidative and microbial deterioration. This is achieved by improving the packaging's barrier and mechanical properties, which, in turn, extends the food's shelf life. Fish collagen has also garnered increasing attention for its capacity to introduce innovative and intelligent attributes to traditional packaging solutions.[105,106,107,108]

CONCLUSION

Collagen sourced from marine and freshwater environments, especially fish collagen, is increasingly acknowledged for its value owing to its easy accessibility, minimal transfer of disease risk, absence of religious restrictions, and the potential for larger collagen yields. Progressive research and development in the extraction and application of fish collagen from aquatic sources makes it a promising and sustainable alternative to conventional collagen sources like bovine or porcine collagen. Consequently, by-products of fish are emerging as a favoured option for collagen extraction. The choice of extraction method significantly influences collagen quality and quantity, with acid-soluble and pepsin-soluble collagen methods yielding high results. The implications of several fish derived collagens in biomedical industries, therapeutic, cosmetic industry, food, biomaterials are noteworthy. Therefore, it is desirable to focus research on developing environmentally sustainable and cost-efficient approaches for collagen synthesis.

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Conflict of Interest

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All authors contributed equally to this work.

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