FISH COLLAGEN: MODERN EXTRACTION METHODS, FUNCTIONAL PROPERTIES AND PROSPECTS FOR APPLICATION

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Abstract - Annually, fish processing generates up to 75% secondary waste, which represents a valuable resource for the production of bioactive collagen. With the growing demand for safe and sustainable food ingredients, fish collagen offers a promising alternative to animal-based alternatives, eliminating the risks of zoonotic diseases and cultural and religious restrictions [6, 7, 10]. The aim of this study is to systematize modern methods for extracting fish collagen and evaluate the potential of its bioactive peptides as a functional ingredient for restoring connective tissue and supporting joint health. A critical analysis of the literature (2015–2026) on extraction methods (acid, enzymatic, ultrasonic, and deep eutectic solvents), structural and functional characteristics, and clinical data was conducted. It was found that combined "green" technologies increase the yield of target fractions by 25–40% while preserving >85% of the native structure [9, 16]. Enzymatic hydrolysis produces peptides with a molecular weight of 3–10 kDa, which exhibit high bioavailability and proven activity, including ACE inhibition (IC_{50} ~168–197 μmol/L) and antioxidant and anti-inflammatory effects [4, 5, 12]. Clinical studies confirm the effectiveness of doses of 10–15 g/day for stimulating collagen synthesis in tendons and accelerating post-exercise recovery [3, 14]. Fish collagen is a scientifically proven ingredient for the development of specialized nutritional products. Scaling up requires standardization of molecular weight distribution, validation of pilot technologies, and harmonization of regulatory requirements.

Keywords - Fish Collagen, Bioactive Peptides, Enzymatic Hydrolysis, Molecular Weight Distribution, Bioavailability

I. INTRODUCTION

Fish processing annually generates up to 75% secondary waste in the form of skin, scales, bones, and fins, which are traditionally disposed of or recycled into low-value products [6, 10]. In the context of the global transition to a circular economy and stricter requirements for raw material safety, fish collagen is becoming a strategic alternative to mammalian collagen. Its key advantages include the absence of the risk of zoonotic infection transmission, the absence of cultural and religious restrictions, high bioavailability, and low immunogenicity [7, 8, 10]. The marine collagen market is estimated at >$1.2 billion (2024) with a CAGR of 7–9%, driven by nutraceuticals and cosmeceuticals [10].

Objective of the study

To systematize modern approaches to obtaining fish collagen and its hydrolysates, analyze structural and functional characteristics, assess technological and regulatory challenges, and identify commercialization prospects in the food, nutraceutical, and biomedical industries.

II. MATERIALS AND METHODS

An analysis of scientific publications from 2015–2026 was conducted on extraction methods (acid, enzymatic, ultrasonic, using deep eutectic solvents and supercritical fluids), peptide molecular weight distribution, in vitro/in vivo bioactivity assessments, and industry applications. Data on product yield, native structure retention, amino acid profile, and biocompatibility were compared. The methodological approaches and identified peptide motifs were compared with data on fish collagen to identify universal structural and functional patterns.

III. RESULTS AND DISCUSSION

Traditional methods for producing acid-soluble (ASC) and pepsin-soluble collagen (PSC) are gradually giving way to combined "green" technologies. Comparative analysis shows that enzymatic-physical and solvent approaches can significantly increase the yield of target fractions, reduce energy costs, and minimize the formation of toxic effluents [10, 16].

Ultrasonic cavitation promotes partial unfolding of macromolecules, increasing the accessibility of peptide bonds without critical denaturation of functional centers, which, in synergy with enzymatic hydrolysis, increases the extraction rate by 30–50% compared to classical methods [9, 16]. The use of deep eutectic solvents (DES) and electrochemical hydrolysis of fish scales and skin makes it possible to achieve protein contents of 80–90% with a high proportion of low-molecular fractions [12]. Summary parameters of the extraction methods are presented in Table 1.

	Yield/Efficiency (according to the authors)	
	Moderate–high; long processing time, high reagent consumption	Acetic/Hydrochloric Acid Concentration, Temp., S/L, Time
	Higher than ASC; reduced immunogenicity, structure preservation	Pepsin Type/Concentration,pH2–3, 4–15°C, 12–48h
	Yieldincreaseupto30–50%; Accelerated kinetics	Frequency, Power, Duty Cycle, Synergy with Acid/Enzymes
	High solubilizing capacity; environmentally	HBD/HBA Ratio, Temperature,
	friendly, tunable polarity	Regeneration Capability
Scale, skin (cod, trout, herring)	Protein80–90%; >90%lowmolecularweightpeptides	Current Density, Electrolyte, Alcalase2.5L, Temperature Range

Table 1. Comparative characteristics of fish collagen extraction methods and product yield

Data aggregated from a literature review show that:
- ASC/PSC yield: typically 15–35% of skin/scale dry weight [6, 8];
- denaturation temperature (T_d) of fish collagen: 25–32 °C (depending on the fish species) [14].
- proportion of fractions <5 kDa after enzymatic hydrolysis: 70–95% [3, 12].

Ultrasound and enzyme-assisted extraction increase collagen yield by 25–40% compared to classical acid processing, while preserving >85% of the triple helix, which is critical for biomedical applications [9, 16].

Native fish collagen retains a triple helix enriched in glycine, proline, and hydroxyproline, which is critical for biomedical applications, but limits its solubility and thermal stability at physiological temperatures [3, 14]. Controlled hydrolysis (including the use of enzymatic membrane reactors) allows for the production of peptides with a specified molecular weight distribution (3–10 kDa), optimal for oral bioavailability and cellular penetration [3, 5, 12]. Ultrasonic and enzymatic modification partially preserves the secondary structure, improving solubility and functional and technological properties (emulsification, gelation, water retention) [8, 9]. Data on structural characteristics are presented in Table 2.

		MWD of hydrolysates	Effect on functional properties
	Partial denaturation; helix loss at high temperatures/pH	Broad distribution, high-molecular-weight aggregates	Decreased bioactivity, requires additional purification
Enzymatic Hydrolysis (Alcalase, Flavorzyme, Pepsin)[3,12]	Controlled cleavage, helical fragment retention	Dominantfraction3–10 k Da (>80%)	Increased solubility, bioavailability, ACE hibition
	Cavitation-induced partial un folding; reversible changes	Narrower distribution, improved dispersion	Accelerated extraction, preservation of Functional groups
		Target fractions(e.g.,<5 kDa)	Optimized for nutraceutical delivery, consistent quality
	Moderate structural rearrangement, peptide fragmentation	62–98%of fractions<10kDa (tissue dependent)	High antioxidant activity, applicable in functional foods

Table 2. Preservation of native structure and molecular weight distribution (MWD) of hydrolysates

Fish collagen is characterized by a high content of hydroxylysine and a low content of aromatic amino acids, which reduces immunogenicity and eliminates the risk of zoonotic transmission [7, 14]. Bioactive peptides released during hydrolysis exhibit pronounced antioxidant, antihypertensive (ACE inhibition), antibacterial and wound-healing activities [5, 15]. Comparative studies show that specific sequences such as Gly-Ala-Arg and Gly-Pro-Met-Gly-Pro-Arg-Gly have high inhibitory activity against ACE (IC_{50} ~168–197 μmol/L) and effective neutralization of free radicals [4, 5]. The biocompatibility of collagen scaffolds has been confirmed in tissue engineering; however, the insufficient mechanical strength and thermal instability of native forms require the development of composite materials, cross-linking, and nanostructured systems [10, 14]. The amino acid profile and biocompatibility parameters are summarized in Table 3.

Parameter	Characteristics	Significance for Practical Application
Amino acid profile	High Gly, Pro, and Hyp content; low aromatic AA content; presence of hydroxyly sine	Low immunogenicity, stimulation of collagen synthesis, compliance with cultural and Religious norms[3,7, 14]
Bioactive peptide sequences	Gly-Ala-Arg, Gly-Pro-Met-Gly-Pro-Arg-Gly, hydrophobic clusters	ACE inhibition(IC_{50}~168–197 μmol/L), antioxidant and anti microbial activity[4,5,15]

Biocompatibility and safety	Non-zoonotic, hypoallergenic, biodegradable, contains cell-Adhesion motifs	Scaffolds fort issue engineering, wound dressings, controlled drug delivery systems [7, 8,14]
Limitations and optimization options	Thermal instability(<30–35°C),low mechanical strength, inter batch variability	Requires cross-linking, nano composite creation, standardized purification(UV filtration, chromatography)[10,14,16]

Table 3. Amino acid profile and biocompatibility of fish collagen

Despite the proven clinical efficacy of doses of approximately 12 g/day for relieving osteoarthritis symptoms, increasing bone mineral density, and protecting articular cartilage [3], large-scale commercialization faces challenges in MMR standardization, validation of "green" methods at the pilot level, and harmonization of regulatory requirements (EFSA, FDA) [5, 10]. Integration of feasibility study (TEA) and life cycle assessment (LCA) is a prerequisite for the transition from laboratory research to industrial production [10, 16].

In turn, the lack of standardized clinical trial protocols, inconsistent molecular weight distribution data, and an insufficient number of full-scale LCA/TEA assessments hinder the transition from laboratory development to industrial scale [10, 14]. In the US, hydrolyzed collagen is recognized as GRAS, in the EU it is being assessed by EFSA as a novel food/functional ingredient and in this regard, harmonization of requirements remains a key barrier to the global release of products, in particular fish collagen [10, 14]. Promising areas include the use of nanotechnology and the creation of composite materials to enhance biocompatibility, the transition to pilot production with feasibility studies and life cycle assessments (LCAs), the harmonization of regulatory requirements [9, 10, 14, 16], and the development of standardized nutraceutical formulations with a proven mechanism of action [7, 9, 14]. Promising areas of development include the integration of nanotechnology.

IV. CONCLUSION

Fish collagen and its bioactive peptides represent a highly valuable raw material for the bioeconomy and sustainable development. The synergy of "green" extraction methods, in-depth study of structure-functional relationships, and the transition to validated pilot production will ensure the market entry of safe, clinically validated products with proven efficacy in the food, cosmetic, and biomedical industries.

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