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A BRIEF OVERVIEW OF BIOACTIVE COMPOUND RECOVERY FROM MARINE BY-PRODUCTS AND THEIR APPLICATION POTENTIAL

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ABSTRACT

The global expansion of seafood processing industries generates substantial amounts of waste materials from finfish and shellfish, which are often discarded despite their rich biochemical composition. These by-products contain a wide range of valuable compounds, including collagen, chitin, chitosan, enzymes, carotenoids, fatty acids, amino acids, minerals, and vitamins, many of which exhibit functional and biological activities superior to those of terrestrial origin. This review examines recent advances in the extraction and purification of bioactive compounds from marine by-products. The functional properties and applications of these compounds in food, pharmaceutical, nutraceutical, cosmetic, and biomedical industries are discussed, highlighting their growing commercial relevance. Overall, the effective valorization of marine by-products contributes to waste reduction, economic value creation, and the advancement of a circular bioeconomy.

KEYWORDS: Marine By-Products, Extraction, Purification, Finfish, Shellfish, Biological Activity, Food Applications, Sustainability, Health Benefits.

1. INTRODUCTION

Population growth is expected to surpass 9 billion people by 2050 due to demographic increases (Al Khawli et al., 2020). There has been a strong demand for aquaculture production globally to meet the growing need for food. The United Nations Food and Agriculture Organization predicts that global aquatic food production for human consumption will reach 202 million tons by 2030, increasing by 24 million tons from 2020 levels (Department, 2018). Fish processing results in a variety of waste products such as fins, heads, skin, visceral organs, and the digestive system. However, only about 25% of total fish production is utilized in the food processing industry, while the remaining 75% is discarded as waste (Gaikwad and Kim, 2024), amounting to over 20 billion tons of fish tissue globally (Shaw et al., 2022). Notably, approximately 30% of fish processing waste can be recovered as valuable sources of bioactive compounds and protein metabolites (Klomklao et al., 2024). The volume of fish and crustacean processing by-products has risen sharply, which has the potential to be a source of bioactive compounds with distinctive characteristics and economic importance (Klomklao et al., 2024). According to Nurilmala et al. (2020), among these by-products, fish skin accounts for 8–10% of fresh fish weight and 4–5% of filleting waste (Nurilmala et al., 2020) and is particularly rich in collagen and proteins (Barzkar et al., 2025). Consequently, marine by-products are increasingly utilized in industrial, cosmetic, pharmaceutical, and food applications (Xia et al., 2024; Ali et al., 2021). The number of fish by-products depends on factors like age, gender, health, and protein content. These by-products typically contain 15–30% protein, variable lipid levels (0–25%), and 50–80% moisture, depending on the species, age, and season (Kundam et al., 2018, Pateiro et al., 2020). For example, the nutritional value of tuna and other similar fish by-products worldwide reached 7.8 million tons in 2020 and is expected to increase to 25 million tons in 2030 (Sisa et al., 2024). Waste from tuna fish organs produces a proteolytic enzyme with gelatin and antioxidant properties that are in high demand globally (Blanco et al., 2023).

In addition, marine by-products produce high-quality proteinaceous compounds used in the food industry, as marine food often contains healthier nutrients (Ali et al., 2021). Fish by-products quantity relies upon age, gender, healthy body, and proteinaceous material. These by-products comprise 15–30% protein, highly variable lipid levels (0–25%), and 50–80% moisture, depending on species, age, and season. For instance, the tuna fish organs and their waste produce proteolytic enzyme to gelatin and antioxidant properties, making a huge demand in the global market (Blanco et al., 2023). Moreover, shellfish waste is well-known in aquaculture production as a rich source of bioactive compounds like chitin, collagen, chitosan, carotenoids, minerals, lipids, and amino acids (Barzkar et al., 2024g). These valuable bioactive metabolites have numerous applications in pharmaceuticals, cosmetics, nutraceuticals, and biomedical industries (Azelee et al., 2023, Durazzo et al., 2022, Barzkar et al., 2021, Barzkar et al., 2024a). Several studies have been conducted to explore the presence of biologically active metabolites in marine by-products and waste. For instance, the crab shell waste that produces chitin by-products has antioxidant activity (Zhou et al., 2024). Fishmeal and fish oil are the two best bioproducts produced from the valorization process of the fish processing industry. Fish oil is the primary source of long-chain polyunsaturated fatty acids (PUFAs), including eicosapentaenoic acid (EPA), which are considered useful components for the treatment of cardiovascular diseases (Rodrigues et al., 2024). Hence, Marine organism wastes and by-products from the fish processing industry are potential sources of biomolecule supplements. The review examines the application of bioactive compounds derived from ocean waste in various industries, including cosmetics, biotechnology, and pharmaceuticals. It also examines how these compounds can be utilized for sustainable food production. The review emphasizes the importance of utilizing these by-products to minimize waste and foster a more sustainable food system.

2. SEAFOOD PROCESSING AS A SOURCE OF BY-PRODUCT

According to recent estimates by researchers, fishery resources constitute a significant sector of the world economy, annually consisting of 170 million tons of fish, shellfish, shrimp, and other marine life. The processing of fish and seafood produces 25% to 70% of by-products. Such products are heads, bones, scales, viscera, and other parts of seafood, which currently have almost no use (Zhao et al., 2022). Thus, according to a study [26], when cutting whole fish, more than 30-50% of meat, 4-5% of skin, 21-25% of heads, and 24-34% of bones, i.e., about 45% of the fish body remains. Utilization of fish by-products is a promising way to address these problems and maintain sustainable food production (Kumar et al., 2025). The seafood processing industry produces a large number of by-products, which make up around 55% to 65% of the total weight of the yearly catch.

These by-products consist of fillet remains (15–20%), viscera (12–18%), bones (9–15%), heads (9–12%), scales (5%), and skin and fins (1–3%). Effectively using these materials is crucial for the economic and environmental sustainability of the seafood sector. Fish protein hydrolysates are mainly obtained from fish heads and frames of various species through enzymatic hydrolysis. For example, fish heads and frames have been widely processed with enzymes to create bioactive protein hydrolysates (Morales-Medina et al., 2017, Barzkar et al., 2022). Redfish scales have been treated with acid and alkali to produce collagen peptides with potential nutraceutical uses. Similarly, the viscera of Atlantic cod have been processed with Alcalase to make high-quality fish feed. Crustacean by-products, like shrimp and crab shells, are the main source of chitin and chitosan. These compounds are usually extracted through demineralization using inorganic acids and deproteinization using strong alkalis. Furthermore, squid ink—a mixture of melanin, glycosaminoglycan-like polysaccharides, proteins, enzymes, and lipids—represents another underutilized by-product with potential pharmaceutical and food applications (Fahmy et al., 2013, Morales-Medina et al., 2017, Blanco et al., 2015) (Table 1).

Table 1: Examples of Seafood Processing By-Products.

Source	Species	Byproduct	Ref
Fish	Kingfish, horse mackerel, catshark	Head & frame	(Morales-Medina et al., 2017, Blanco et al., 2015)
	salmon	Backbone	(Wu et al., 2017, Slizyte et al., 2016)
	Atlantic cod, Arctic cod, sardine, catshark	Viscera	(Villamil et al., 2017, Blanco et al., 2015)
	Redfish	Skin/ scale/bone	(Wang et al., 2008)
	Croceine Croaker (*Pseudosciaena crocea*)	scale	(Wang et al., 2013)
Squid	*Doryteuthis singhalensis, Dosidicus eschrichitii Steenstrup,*	Skin//ink/Head	(Veeruraj et al., 2015, Lin et al., 2012)
	Ommastrephes bartrami	Viscera	(Song et al., 2016)
	-	Head	(Sukkhown et al., 2018)
	llex argentinus	Pens	(Vázquez et al., 2017a)
Shrimp	*Penaeus vannamei*	exoskeleton	(Vázquez et al., 2017b)
	Penaeus kerathurus, Litopenaeus vannamei Boone	shell	(Maruthiah and Palavesam, 2017, Hamdi et al., 2017, Gamal et al., 2016, De Queiroz Antonino et al., 2017)
Crab	Blue crab *(Portunus segnis)*	shell	(Hamdi et al., 2017, Oh et al., 2007)

3. BIOACTIVE COMPOUNDS FROM MARINE BY-PRODUCTS

The global aquatic ecosystem is the source of millions of bioactive compounds, and their waste material is used as organic metabolites for various applications (Honrado et al., 2022). Common marine by-products include fish processing waste (e.g., skin, bones, scales, head, viscera, carcasses, and other digestive system organic compounds), shellfish waste, and seaweed residues, which account for more than 60% of total biomass. Fish waste produce high valued compounds when an appropriate process is applied; by-products are bioactive peptides, fatty acids, enzymatic compounds, and other biomaterial organic products like collagen, gelatin, chitin, and chitosan (Borges et al., 2023, Barzkar et al., 2024d). Extraction of bioactive peptides from marine resources is found as an active metabolite and broken down into 3 to 30 amino acids in bioprocessing activities. Bioactive peptides have several properties, such as anti-inflammatory, antioxidant, anti-cancer, immunomodulatory, cytotoxic, anti-hypertensive, and antimicrobial. These properties of bioactive peptides rely on the number, composition, structure, and sequences of amino acids present in them (Cunha and Pintado, 2022). Seafood processing globally generates a significant portion of the total fish catch as by-products. Fish by-products are a valuable source of nutrients and can be used for different industrial purposes. These by-products consist of bioactive compounds, proteins, minerals, lipids, and, with appropriate evaluation methods, can be transformed into valuable products. The worth of these leftovers cannot be overstated. Examination of the heads of Skipjack tuna (*Katsuwonus pelamis*) has revealed their high content of amino acids, fatty acids, and carnosine (Li et al., 2019). Fish scales are known to be poorly biodegradable [31], but their value lies in the presence of collagen, hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$] (Kulikova et al., 2025b, Kulikova et al., 2025a), calcium carbonate, magnesium, phosphorus, and other bioactive compounds (Sari et al., 2025). The collagen and calcium contained in fish bones are essential components for human health. Valuable hydroxyapatite is extracted from fish bones for pharmaceutical applications (Waqar et al., 2025). The study (Muhammad et al., 2016) confirmed the high mechanical strength, thermodynamic stability, and good biocompatibility of fish hydroxyapatite. Fish skin contains collagen and antibacterial biomolecules that protect the body from pathogens [33]. Skin mucus contains antimicrobial components: proteins, lysozyme, immunoglobulin, and lectins [34]. The composition of fish viscera is mainly proteins, and viscera are a valuable source of enzymes and probiotics (Barzkar et al., 2024b). The sources of by-products are feed fish, food fish, and aquaculture. Antarctic krill (*Euphasia superba*) is a valuable source of secondary products (Gunathilaka et al., 2021). Annual *krill* catches are less than 1%, as it is a valuable component of fish, bird, and animal nutrition. It is used to produce krill oil and krill meals. Krill by-products include 12-16% protein and essential amino acids (lysine, valine, leucine and isoleucine, threonine, phenylalanine, methionine). *Krill* proteins are superior to cod proteins in terms of value and biological activity (Kaur and Torrecillas, 2025). Abirami and colleagues obtained chitosan from crab shells for industrial and medical applications (Abirami et al., 2021). Marine waste research is a practical and innovative approach to improve product supply chains. The full utilization of high-quality marine by-products is a promising alternative for the economic efficiency of the fish processing industry, according to the concept of closed-loop biological economy. Table 2 presents the health benefits of biologically active components derived from marine by-products.

Table 2: Marine By-Products and Their Reported Health Benefits.

Source of by-products	Bioactive Compound	Findings	Biological activity	Ref
Catfish (*Clarias gariepinus*) Scales	Chitosan	Yield: 45.56% (dry wt.); moisture 5%; ash 1.26%; pH 7.0; soluble in acetic acid	Antioxidant (DPPH scavenging 15% at 20–100 μM); antibacterial activity against seafood pathogens (*Vibrio parahaemolyticus*, *Vibrio cholerae*, *Staphylococcus aureus*, *Salmonella typhii*, *Escherichia coli*, *Shigella dysenteriae*, MIC 0.5–1 mg/mL); food preservation; wound dressing; antimicrobial textiles	(Gokulalakshmi et al., 2017)
Fish (*Cynoscion acoupa*) skin	Gelatin	Increased skin hydration, collagen, hyaluronic acid, hydroxyproline; modulated EGFR, COL1A2, COL3A1, MMPs, TIMP-1; activated TGF-β/Smad pathway	Modulates collagen synthesis and degradation; antioxidant; anti-inflammatory; improves skin integrity; gut microbiota modulation	(Arpi et al., 2018)
Silver carp (*Hypophthalmichthys molitrix*) skin	Gelatin hydrolysates	At the concentration of 30 mg mL^{-1}, the alcalase hydrolysate exhibited the strongest CA (54.8%), followed by 50.9% for flavourzyme hydrolysate and 16.8% for papain hydrolysate.	Flavourzyme hydrolysates exhibited the highest DPPH scavenging activity (1.2-fold of alcalase, 1.6-fold of papain) and reducing ability (1.2-fold of alcalase, 2.3-fold of papain), while the alcalase hydrolysates demonstrated the highest Fe^{2+} chelating ability. Fish mince treated with the mixture of flavourzyme hydrolysates and sucrose exhibited higher sulfhydryl and salt-soluble protein contents, greater Ca^{2+}-ATPase activity, and better water holding capacity	(Zhang et al., 2021)
Shark skin	Gelatin hydrolysates	15–20 kDa peptides	Antioxidant (DPPH scavenging, IC50 27.39 mg/mL), which is	(Limpisophon et al., 2020)

			greater than ascorbic acid	
Scales of Croceine Croaker fish	Collagen and Antioxidant Collagen Peptides	their amino acid sequences were identified as GFRGTIGLVG (ACH-P1), GPAGPAG (ACH-P2), and GFPSG (ACH-P3). ACH-P1, ACH-P2, and ACH-P3 showed good scavenging activities on hydroxyl radical (IC$_{50}$ 0.293, 0.240, and 0.107 mg/mL, respectively), DPPH radical (IC$_{50}$ 1.271, 0.675, and 0.283 mg/mL, respectively), superoxide radical (IC$_{50}$ 0.463, 0.099, and 0.151 mg/mL, respectively), and ABTS radical (IC$_{50}$ 0.421, 0.309, and 0.210 mg/mL, respectively)	ACH-P3 was also effective against lipid peroxidation in the model system	(Wang et al., 2013)
Squid (*Illex argentinus*) pens	chitin and chitosan	Molecular weights of chitosan ranged from 143 to 339 kDa	Best values for chitosan were 61.0–63.7% of NaOH and 14.9–16.4 h of deacetylation	(Vázquez et al., 2017a)
Tuna dark muscle	Protein by-product hydrolysate	Hydrolyzed using Alcalase; fractionated by ultrafiltration (UF) and nanofiltration (NF)	Tuna dark muscle by-product hydrolysate showed the highest iron chelating activity (75%) compared to other peptide fraction hydrolysates. The nanofiltration permeate showed the highest 2,2-diphenyl-1-picrylhydrazyl (DPPH) and hydroxyl radical scavenging activities (75% and 65%, respectively) The NF retentate (1–4 kDa) that contained antioxidant amino acids such as Tyr, Phe, Pro, Ala, His, and Leu, which accounted 30.3% of the total amino acids, showed the highest superoxide radical and reducing power activities.	(Saidi et al., 2014)
Bigeye Tuna (*Thunnus obesus*) Skin	Collagen	They dissolved very well in dimethyl sulfoxide and distilled water. The pH ranges were 4.60–4.70 and 4.30–4.40 for PSC and BSC, respectively. PSC and BSC were free from As, Cd, Co, Cr, Cu, and Pb.	Pepsin-soluble collagen exhibited significantly higher antioxidant activity than bromelain-soluble collagen, with DPPH radical scavenging activity of 2.62 ± 0.03 µmol AAE/g protein and reducing power of 0.46 ± 0.01 mg AAE/g protein, compared to 1.03 ± 0.03 µmol AAE/g protein and 0.18 ± 0.00 mg AAE/g protein, respectively.	(Devita et al., 2021)
Shrimp shell	Chitin	The biological activities of chitosan-M and chitosan-C, produced through enzymatic and alkaline treatments, respectively, were subsequently assessed.	Chitosan-C, with a lower molecular weight (5,820 g/mol), exhibited higher antioxidant activity. In addition, chitosan-C demonstrated enhanced antitumor activity against bladder carcinoma cells (RT112) and slightly greater antimicrobial activity compared with chitosan-M, which had a higher molecular weight (19,780 g/mol).	(Younes et al., 2014)
Oyster Shell	Calcium	Thermally processed oyster shell powders (TPOS) and	Solubility values were 0.7 mg/g (FCC), 0.5 mg/g (TPOS), 0.4	(Ahn et al., 2025)

		citric acid–treated TPOS (TPOSc) exhibited enhanced physicochemical properties and significant antimicrobial activity compared with reference calcium materials (FCC and CCP).	mg/g (TPOSc), and 0.05 mg/g (CCP), while average particle sizes were 476 nm (FCC), 1000 nm (TPOS/TPOSc), and 1981 nm (CCP). SEM, EDS, and XRD analyses confirmed calcium ion release and structural modifications in TPOS and TPOSc. Both samples showed effective antibacterial activity and retained antimicrobial efficacy when incorporated into rice cakes at 0.3 wt%; however, higher concentrations adversely affected textural properties	
Crab (*Serratia marcescens* TNU02) shell	Prodigiosin (PG)	PG demonstrated both DPPH and ABTS radical scavenging capacities.	Of these, the ABTS radical scavenging activity of the PG was higher than the DPPH radical scavenging capacity of the PG, with a max activity of 98.3% (at a tested PG concentration of 4 mg/mL) and 96% (at a tested PG concentration of 8 mg/mL), respectively	(Nguyen et al., 2020)
Salted jellyfish (*Rhopilema hispidum*) umbrella by-products	Peptides	Pepsin hydrolysis (enzyme-to-substrate ratio 3:20, 48 h, 37 °C); peptide purification and synthesis	1.85 ± 0.05 mM TE/mg protein (hydrolysate); 56.07 mM TE/mg protein ABTS: 7.28 ± 0.03 mM TE/mg protein; FRAP: 3.04 ± 0.12 mM $FeSO_4$ /mg protein	(Muangrod et al., 2025)
tuna dark muscle	Peptides	amino acid sequences of the two antiproliferative peptides isolated from papain and Protease XXIII hydrolysates were Leu-Pro-His-Val-Leu-Thr-Pro-Glu-Ala-Gly-Ala-Thr (1206 Da) and Pro-Thr-Ala-Glu-Gly-Gly-Val-Tyr-Met-Val-Thr (1124 Da)	Dose-dependent inhibition of MCF-7 human breast cancer cells was observed, with IC_{50} values of 8.1 μM for papain-derived peptides and 8.8 μM for Protease XXIII–derived peptides.	(Hsu et al., 2011)

3.1. Collagen

There has been an interesting fact that with age, collagen synthesis diminishes in the body, and wrinkles appear on the skin. Therefore, to tackle these challenges, collagen treatment was started earlier, but the collagen source was terrestrial organism by-products, which cause various complications later due to diseases, toxic elements, and invasions. To date, collagen biomolecules extracted from marine organism has drawn huge attention in the global market due to their hundreds of benefits, e.g., less toxicity, disease resistance, easy availability, more validity, lasting impacts, and health benefits in numerous applications (Wang, 2021). Now, particularly the extraction parameters and targeted applications of collagen hydrolysate in tissue engineering, bone remodeling, and skin wrinkles regeneration by the production of liquid matrices. Commercially, collagen derived from marine by-products like fish skin, scale, bone, and fine have made potential applications on a large scale in recent years (Barzkar et al., 2023, Rajabimashhadi et al., 2023, Rigogliuso et al., 2023, Martins et al., 2023, Barzkar et al., 2024f). Collagen extracted from marine by-products is less toxic and plays a vital role in treating degenerative disease, tissue regeneration, drug delivery (*in-vitro* or *in-vivo*) in skin wrinkle treatment, and other aging-related disorders (Barzkar et al., 2023). As far as collagen extraction from marine organisms contributes to ecosystem conservation and advancement in technological solutions (Table 2).

3.2. Chitin

Chitin is one of the important natural biopolymers next to cellulose. Its applications in biomedical and pharmaceutical fields depend on its molecular weight, viscosity, solubility, and pH of compounds. With an increase or decrease in the molecular weight of chitosan, its solubility changes for different applications (Vanathi). Chitin compounds, with their N group, reveal exceptional characteristics such as non-toxicity, film- and fiber-forming properties, absorption of metallic ions, solute concentration or deferment, and biological activities (Prihanto et al., 2024). Chitin is present in nature in three forms, i.e., alpha, beta, and gamma, which are extracted from shell of shrimps and crabs. All these types of chitins are insoluble in solvents, due to which their applications are limited. Instead of this, the deacetylated form of chitin, chitosan, is soluble in acidic and alkaline solutions; therefore, different techniques are applied for the functionalization and application of chitins (Trung et al., 2020).

3.3. Chitosan

Chitin is an insoluble compound in all basic solvents, e.g., water, organic solvents, and mild or basic solutions (Liang et al., 2018). To improve solubility, the acetyl group in chitin has been eliminated by deacetylation and changed into chitosan for better performance. This process is achieved by an enzymatic method commercially because of low cost and the best production systems (Ozogul et al., 2021). Therefore, chitosan has a wide range of applications, such as preserving the microbial and sensory qualities of refrigerated catfish products in the food industry (Karsli et al., 2021). Chitosan can be produced from residues of various marine organism by-products, such as lobster and krill shells, heads, and backbones. The yield varies depending on the source, ranging from 15–30% in crabs to 30–40% in shrimp. To separate the protein and carotenoids from the extract of chitin, the enzymatic fermentation process from scrimps shell after removing calcium from it, or by hydrolysis of protein by-products for chitosan production. Now chitosan has inviolable properties such as antimicrobial, antifungal, antioxidant, anti-cancerous, and anti-inflammatory. About chitosan extracted from marine by-products, there is a high level of anticancer activity shown in human ovarian cancerous cells (Kumari et al., 2017, Srinivasan et al., 2018, López-Pedrouso et al., 2020).

3.4. Carotenoids

Carotenoids are an important organic compound present in marine seafood and waste of marine organisms like crustaceans, shrimps, lobsters, fish, crabs, krill, and crayfish. Common natural components of carotenoids are beta-carotene, lutein, zeaxanthin, and astaxanthin extracted from fish processing waste (Ashraf et al., 2020). The astaxanthin is the main carotenoid seemed as a red-pigment in fish and shrimp organisms in marine life. Astaxanthin is applied in various roles as an antioxidant and as a food supplement in fish feed. Astaxanthin is extracted from crustaceans, shrimps, crabs, lobsters, and shell of prawns by organic solvent extraction, i.e., green solvent methods like the degradation of crustacean and shrimp shells processing wastes. For instance, maximum concentration of protein carotenoids, i.e., astaxanthin presents in crustaceans and shrimp shell waste and has potential application as antioxidants, anti-inflammatory, antihypertension, and also contributes as a coloring agent in aquafeed as well as functional compounds in the cosmetic and food industry (Trung et al., 2020, Parjikolaei et al., 2017, El-Bialy and Abd El-Khalek, 2020, Ozogul et al., 2021).

3.5. Gelatin

Gelatin has an excellent contribution in health and well-being of lives, extracted from fish processing, and has increased attention in aquaculture industries for their utilization in cosmetic, pharmaceutical, biomedical, and food industries (Ranasinghe et al., 2022). Gelatin is a moderately hydrolyzed composition of collagen protein crafted from fish head, skin, viscera, and bones in recent years. Gelatin extracted from fish by-products has low risk of disease transmission, eco-friendly because being extracted from fish waste and less costly instead of bovine and porcine prepared from terrestrial organism and has potential application as in existing literature discussed by researchers, gelatin as a renowned marine by-product for tissue regeneration, as well as a valuable pharmaceutical ingredient with various types of biological activities, such as antioxidant activity (Derkach et al., 2020, Alves et al., 2022). Types of marine gelatin by-products and their antioxidant activity are summarized in Table 3. More than 80% of gelatin composition is composed of non-polar amino acids such as glycine, valine, proline, and alanine (Shavandi et al., 2019). Lin et al. (2011) used pepsin digestion to produce gelatin hydrolysates, which they used as a source of natural antihypertensive chemicals from squid skin. Based on molecular weight, the hydrolysates were divided into three peptide fractions: 6–10 kDa (HSSG-I), 2–6 kDa (HSSG-II), and <2 kDa (HSSG-III). With an IC_{50} value of 0.33 mg/mL, the smallest fraction (HSSG-III) exhibited the greatest angiotensin-I-converting enzyme (ACE) inhibitory activity in vitro. HSSG-III was given orally to renovascular hypertensive rats (two-kidney, one-clip model) for 30 days in order to verify its impact on living systems. When compared to untreated hypertensive controls, the treated rats' arterial blood pressure significantly decreased. These findings highlight squid skin as a promising functional food or nutraceutical ingredient for blood pressure management by showing that low-molecular-weight peptides produced from squid skin gelatin have significant antihypertensive effects and substantial ACE-inhibitory action (Lin et al., 2012).

Table 3: Antioxidant Activity of Gelatin Derived from Marine By-Products.

Source of Gelatin By-product	Processing Method	DPPH Activity	Lipid Peroxidation Inhibition	Other Antioxidant Activity / Notes	References
Jellyfish	Enzymatic hydrolysis (trypsin + Properase E); ultrafiltration (SCP1–SCP3)	-	-	SCP2: strongest hydroxyl & H_2O_2 scavenging; SCP3: highest reducing power & superoxide scavenging; high hydrophobic amino acids	(Zhuang et al., 2010)
Brown cannonball jellyfish (*Stomolophus meleagris*)	Alkaline extraction + heat + dialysis	-	-	ABTS scavenging IC_{50} = 0.42 ± 0.10 mg/mL	(Esparza-Espinoza et al., 2023, Barzkar et al., 2024h)
Blue shark (*Prionace glauca*) skin	Protamex hydrolysis; Sephadex G-15 fractionation	Fraction III IC_{50} = 0.57 mg/mL	-	Hydroxyl radical IC_{50} : Fraction III = 2.04 mg/mL; comparable to glutathione; peptides Gly-Tyr, Glu-Gly-Pro, Gly-Pro-Arg, Tyr important	(Weng et al., 2014)
Skipjack tuna (*Katsuwonus pelamis*) bone	Thermal extraction (80 °C, 90 °C, 100 °C)	-	-	Strongest DPPH, hydroxyl, and ABTS activity at 80 °C; high glycine & proline; smoother microstructure and stable gel network at lower temperatures	(Rao et al., 2025)

4. METHODS OF EXTRACTION OF BIOACTIVE COMPOUNDS FROM MARINE BY-PRODUCTS

There are several novels, green, and sustainable conservative methods for the extraction and purification of bioactive compounds from marine waste at various levels. The best stimulated extraction method is supercritical, microwave-assisted extraction, and enzymatic hydrolysis, which are considered the most beneficial as compared to conventional methods (Al Khawli et al., 2019) (Table 4).

Table 4: Isolation, Extraction, and Purification of Bioactive Compounds from Marine By-Products.

Bioactive Compounds	Source	isolated by	Extraction Method	Purification Techniques	Utilization/ Applications	Ref
Collagenase	Fish waste (a mixture of haddock, herring, ground fish, and flounder)	Tris-buffer system	Precipitation using ammonium sulfate (40% - 80%)	Gel-filtration chromatography using Sephadex G-100	-	(Daboor et al., 2012, Barzkar et al., 2024c)
Peptides (ACE-inhibitory)	seaweed pipefish *(Syngnathus schlegeli) muscle*	-	Enzymatic hydrolysis: papain, alcalase, neutrase, pronase, pepsin, trypsin	Alcalase hydrolysate fractionated by FPLC on Hiprep 16/10 DEAE FF anion exchange column (Fr1–Fr4)	Fraction Fr3-II showed highest ACE-I inhibition (IC50 0.62 mg/mL); non-cytotoxic to on human lung fibroblast cell line (MRC-5 cells)	(Wijesekara et al., 2011)
Peptides (antioxidative & ACE-inhibitory)	Thornback ray (*Raja clavata*) muscle	enzymatic hydrolysis	alcalase 2.4L (DH: 22%), neutrase 0.5L (DH: 11%), B. subtilis A26 (DH: 18%), R. clavata crude alkaline protease (DH: 15%)	RP-HPLC (symmetry C_{18} column), MALDI-TOF/TOF	ACE inhibition: TRMH-A26 and TRMH-Neutrase ~87% at 5 mg/mL; hydrolysates show strong antioxidative and ACE inhibitory potential	(Lassoued et al., 2015)

Peptides (CCK-stimulating)	fish muscle Blue whiting (*Micromesistius poutassou*) and brown shrimp (*Penaeus aztecus*) head	STC-1 cell assay for CCK release	Enzymatic hydrolysis (pH-stat method) under controlled pH, temperature, and stirring; enzyme inactivation (90 °C, 20 min); centrifugation (7000 g, 30 min); freeze-drying; filtration (0.22 μm)	Size exclusion chromatography (Toyopearl HW-40F) for MW fractions F1–F9 (7000–<300 Da) - SEC-FPLC (Superdex Peptide column) for MW confirmation - Membrane processes (ultrafiltration & nanofiltration) for industrial enrichment - Most active fraction: F6 (1000–1500 Da)	Stimulated CCK release in STC-1 cells dose-dependently Maximal activity: FPH B 90.8 pM CCK (purification factor 1.5), FPH C 145 pM CCK (purification factor 1.8) Undigested protein or amino acid mixtures had a minimal effect	(Cudennec et al., 2008)

4.1. Conventional Extraction Methods

This is the traditional way of separating bioactive compounds from marine by-products and waste from marine organisms such as fish skin, scale, shrimp shell, and other by-products. The processes include Soxhlet, hydro-distillation, and soaking with alcohol, but there are some drawbacks because of time and energy consumption, along with solvent extraction being used, which can cause ecosystem degradation. Furthermore, conventional methods of bioactive compounds extraction from marine by-products are very sensitive to various parameters like pH, temperature, and substrate concentration. Thus, novel extraction techniques have drawn significant attention in recent years (Trung et al., 2020, Abhari and Khaneghah, 2020).

4.2. Advanced Extraction Technologies

The advanced extraction techniques are gaining more attention and interest on a commercial scale to enhance the marine by-products properties for industrial and medical purposes. The different techniques, such as enzymatic hydrolysis, supercritical fluid extraction, microwave-assisted extraction, ultrasound-assisted extraction, and pressurized solvent extraction, for marine bioactive compounds, for instance, protein biomolecules, fish oil (lipopolysaccharides), and marine waste enzymes, for various applications (Abhari and Khaneghah, 2020). The enzyme-assisted extraction is a non-thermal, non-toxic, and eco-friendly method for retrieving bioactive compounds from marine matrices (Kadam et al., 2013). The enzymatic hydrolysis is mostly performed with the help of an enzyme solution mixture (Tonon et al., 2016), such as a foreign enzyme involved in the extraction, to enhance the activity. Supercritical fluid extraction is broadly appraised as a green methodology that has been comprehensively claimed as the extraction of bioactive compounds from marine by-products at different levels (Herrero et al., 2015). This technique is carried out by fluid utilization and keeping the temperature at peak levels, and other parameters like density and viscosity are normally at liquid and gaseous states. These parameters and characters make the smooth penetration of supercritical fluid into solid biomolecules. Usually, carbon dioxide is used as a solvent in this method as it protects the extracts from external environmental damage (Cikoš et al., 2018, del Pilar Sánchez-Camargo et al., 2017).

4.3. Purification of Bioactive Compounds from Marine By-products

The extraction of bioactive compounds from marine by-products has provided valuable solutions to various real-world challenges in different areas of life. To ensure optimal performance and long-term preservation, marine by-products are subjected to extraction, purification, and enzymatic hydrolysis to enhance their biological activities (Barzkar et al., 2023). Various techniques, such as Ultrafiltration, Ethanol precipitation, Ammonium sulphate precipitation, thin-layer chromatography, and Ion exchange chromatography, are employed for purifying bioactive compounds from seafood by-products (Navarro-Peraza et al., 2020, Barzkar et al., 2023). Preparative column chromatography and high-performance liquid chromatography are used for separating and purifying bioactive substances from marine by-products in both forward and reverse directions. The structure and size of these compounds are analyzed using NMR spectroscopy techniques, including Hydrogen (1H), carbon-13, correlation spectroscopy (COSY), nuclear Overhauser effects spectroscopy (NOESY), TOCSY, HSQC, HMBC, Mass spectroscopy, and tandem spectroscopy. Chemical modifications are utilized for extracting additional bioactive by-products from marine microorganisms (Barzkar et al., 2024e). A table detailing the extraction and purification of bioactive compounds from marine by-products and waste is provided below (Table 4).

5. MARINE BY-PRODUCTS AS A SOURCE OF HIGH-VALUE, NUTRITIOUS FOOD INGREDIENTS

The growth of fish processing has led to significant amounts of fish by-products, which can represent up to 55% of the total weight. Converting these wastes into high-value products, particularly for aquaculture fish feed, presents substantial potential (Ghalamara et al., 2024). However, this practice can devalue the products and incur waste management costs. To add value, alternatives such as food ingredients and high-value biomolecules are being explored, including the production of protein hydrolysates yielding bioactive peptides (Stori et al., 2002). These peptides have shown positive effects in studies on rats concerning skin and bone health and weight control, with potential benefits for humans as well. Additionally, incorporating lipids from by-products into foods or supplements offers further revalorization options (Nirmal et al., 2021). Leftover fish parts can be used to make nutritious products like fish burgers and nuggets. Research shows that using these leftovers to make mechanically deboned and dried meat results in a high-quality product. Some studies have also looked at adding this meat to traditional pasta and gluten-free pasta, finding it to be high in protein and unsaturated fatty acids, with minimal changes in taste (Marengoni et al., 2009). In the bakery, a type of biscuit was made with up to 40% edible fish meal, yielding high biological value protein contents of 15.52% and 22.5% fat, mainly unsaturated fat (Bakare et al., 2020). The dried exoskeletons of shrimps contain chitin and chitosan. Chitosan helps to fight various pathogens in the human body and contributes to the preservation of food. Dried shrimp cephalothorax contains lipids, unsaturated fatty acids, astaxanthin, β-carotene, palmitic acid, and oleic acid. All of the above-mentioned bioactive ingredients derived from shrimp by-products are raw materials for producing high-added-value products such as seasoning, bread, crackers, fortified drinks, pastes, detergents, and cheese (Abuzar et al., 2023). A research study found that adding Pangas processing waste protein isolates to sausages improved their nutritional composition and functional properties. Increasing the isolate levels boosted the protein content, reduced fat, and made the product lighter. Adding 10 g of isolates per 100 g of sausages improved their cooking yield and emulsion stability, but higher levels had negative effects on gel strength and folding characteristics. The sensory attributes were not significantly affected, and the overall acceptability remained high. The study concluded that adding 10 g of Pangas protein isolate per 100 g of sausages is optimal for improving functionality without compromising quality (Surasani et al., 2020). Yin et al. (2021) found that xanthan gum (XG)–modified fish gelatin (FG) can effectively replicate the rheological properties of porcine gelatin in low-fat stirred yogurt. A XG: FG ratio of 1:99 (w/w) closely matched the storage modulus of porcine gelatin in milk gels, while XG-modified FG improved water-holding capacity and consistency and produced a more homogeneous gel structure. Yogurts containing XG-modified FG showed similar viscosity, pseudoplasticity, and thixotropic behavior to those formulated with porcine gelatin, indicating its potential as a suitable mammalian gelatin replacement (Yin et al., 2021). In another study, Singh et al. (2021) reported that supplementation of semolina pasta with pangas protein isolates significantly enhanced protein digestibility and improved textural properties without adversely affecting overall sensory acceptability. Pasta containing 5 g/100 g isolates exhibited optimal firmness and toughness, while higher inclusion levels increased fish flavour intensity, indicating 5 g/100 g as the most suitable supplementation level (Singh et al., 2021) (Table 5).

Table 5: Marine By-Products Used in Food Applications.

By-product Source	Bioactive Compound	Food application	Ref
Thunnus tonggol fish Head	Omega-3–rich triglycerides (PUFA, MUFA, SFA fractions)	Production of value-added omega-3 fish oil using supercritical CO_2 fractionation for nutraceutical and functional food applications	(Ferdosh et al., 2016)
hoki (Johnius belengerii) fish bone	Oligophosph opeptide	Nutracutical with a potential calcium-binding activity.	(Jung et al., 2005)
Oyster shell	Calcium	Nanopowdered oyster shell (NPOS), Zn-NPOS used as calcium fortification in milk tablets without adverse effects on texture or sensory quality	(Lee et al., 2016)
Oyster shell and egg shell by-products	Calcium	Bread fortification (functional bakery product)	(Alsuhaibani, 2018)

Fish skin by-product (*Rastrelliger kanagurta*, Indian mackerel	Fish oil is rich in polyunsaturated fatty acids (PUFA), particularly ω-3 fatty acids	Nutraceutical and functional food applications	(Sahena et al., 2010)
Fish skin waste	Gelatin hydrolysate	Ice cream stabilizer and emulsifier; improves texture, overrun, melting, and drip time	(Tekle et al., 2025)
skin of squid (*Doryteuthis singhalensis*)	Collagen	Food and nutraceutical	(Veeruraj et al., 2015)
Tuna dark muscle	Peptides	Useful ingredients in food and nutraceutical applications	(Hsu et al., 2011)
Squid head	Protein hydrolysate	flavored-functional ingredient in foods	(Sukkhown et al., 2018)

6. PROSPECTS AND RESEARCH DIRECTIONS

Due to the increasing global population and its demands, there is a growing need for bioactive compounds in various industrial sectors worldwide. The utilization of marine by-products and waste aligns with the United Nations' sustainable development goals, as it helps lower disease risks and environmental waste challenges. This practice is particularly in line with the UN Millennium Development Goals and supports the sustainable development agenda for 2050. According to the World Economic Forum, over 3 billion people rely on seafood for a significant portion of their animal protein intake, while about 600 million people depend on fisheries and aquaculture for their livelihoods. As global seafood consumption continues to rise, there is a growing concern about waste generated from fisheries, which poses environmental, economic, and social problems. The processing of fish and seafood results in a substantial number of by-products, which can be repurposed to create protein hydrolysates and other compounds with potential nutraceutical and pharmaceutical uses, as well as high-quality fish feed. The food industry can improve the taste of protein hydrolysates by using methods like extraction, enzymatic debittering, and blending with additives. However, food processing can affect the bioactivities of peptides and produce compounds with potential health risks. Incorporating peptides into high-fiber food may reduce negative effects, but more research is needed to optimize methods. The effectiveness of bioactive peptides is currently limited, so more human trials and research are needed to unlock their potential health benefits for treating chronic diseases. However, researchers and marine scientists face challenges in extracting bioactive compounds from marine biodiversity on a large scale. The potential of bioactive compounds from marine by-products in various industries is being highlighted in recent research, and advanced technologies are improving the utilization of food waste and by-products for sustainable industrial development.

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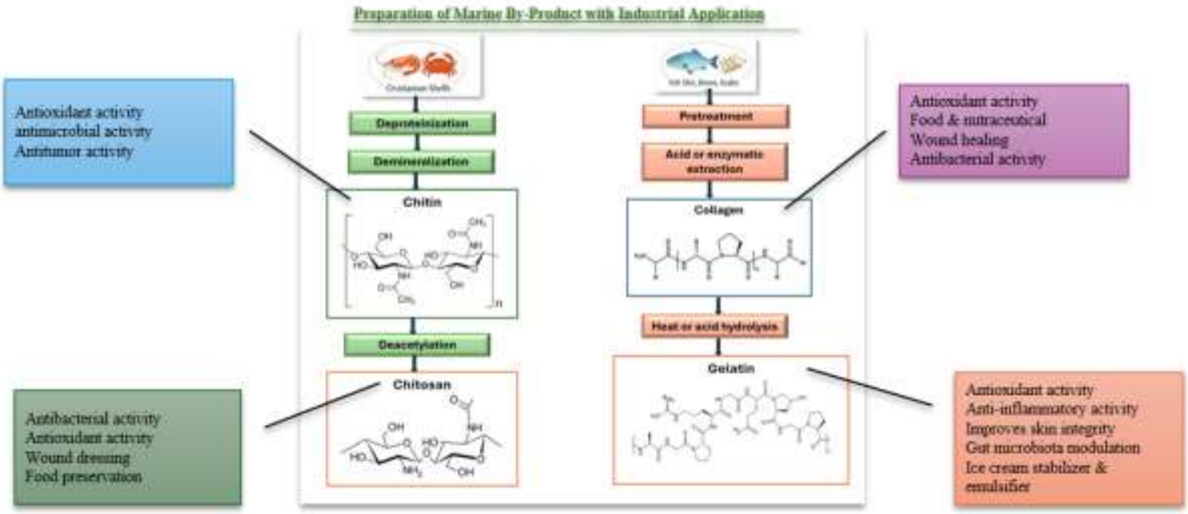

Graphical Abstract