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Review

Bioactive peptides from by-products of shrimp processing: A review

[1]Rodríguez-Jiménez, J. M. J., [2]Anaya-Esparza, L. M., [3,4]Martínez-Montaño, E., [1]Montalvo-González, E. and [1]*García-Magaña, M. L.

[1]Laboratorio Integral de Investigación en Alimentos, Instituto Tecnológico de Tepic, Av. Tecnológico 2595, Col. Lagos del Country, CP 63175, Tepic, Nayarit, México
[2]Centro Universitario de los Altos, Universidad de Guadalajara, Departamento de Ciencias Pecuarias y Agrícolas, Av. Rafael Casillas Aceves No. 1200, CP 47620, Tepatitlán de Morelos, Jalisco, México
[3]Maestría en Ciencias Aplicadas, Unidad Académica de Ingeniería en Biotecnología, Universidad Politécnica de Sinaloa, Mazatlán, Sinaloa, México
[4]Cátedras CONACYT, Consejo Nacional de Ciencia y Tecnología, Ciudad de México, México

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Abstract

Currently, the mismanagement of marine by-products (head, skin, guts, blood, and bones) is a problem for the seafood processing industry, causing economic losses and environmental problems. Shrimp is a high-protein marine plankton species, and after processing, 45% of the total weight is discarded. Therefore, processes must be developed to recover biomolecules from this waste. Hydrolysis of shrimp by-products is an efficient way to add value to the protein for the extraction of bioactive peptides. The present review focuses on recent research on the use of marine by-products to obtain bioactive peptides, especially those from shrimp waste, and discusses their benefits for human health. Protein hydrolysates from shrimp by-products are a viable and technological strategy to obtain peptides of different sizes and improved antioxidant, anti-hypertensive, anti-inflammatory, and hypocholesterolaemic activities. Therefore, the reuse and valorisation of shrimp by-products by obtaining bioactive peptides is an active research area, with potential applications and beneficial effects for human health, the environment, and the economy. However, further studies are needed to ensure their safe use, and to understand their mechanism of action.

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Introduction

According to the Food and Agriculture Organization (FAO), about one-third of the world's food production is lost or wasted, including seafood (Wang *et al*., 2021). In this context, the prevention of food loss and waste has a positive impact on the environment, and can provide food security for the world's population, and contribute to a circular economy (Ribeiro *et al*., 2022). In addition to prevention, valorisation of food waste is a viable and innovative strategy to reduce food loss and waste, especially from the seafood industry, by obtaining compounds with biological activities with potential applications in the pharmaceutical and food industries (Fraga-Corral *et al*., 2022).

The marine environment is home to a wide variety of organisms that provide a source of food with high nutritional value (Ali *et al*., 2021; AlFaris *et al*., 2022). Unfortunately, seafood processing results in waste (heads, skin, guts, and blood), which is one of the most underutilised biological resources (Djellouli *et al*., 2020). It is estimated that more than 20 million tons of marine by-products are generated annually (Pavlicevic *et al*., 2022). They contain 10 to 20% protein, which can be used to obtain bioactive peptides and essential amino acids that are necessary for the proper functioning of the human body (Zamora-Sillero *et al*., 2018). Therefore, the production of bioactive peptides (BPs) from marine organisms (fish, algae, crustaceans, and sponges) has increased significantly in recent years, mainly from shrimp by-products; they exhibit biological activities for diverse pharmaceutical and industrial applications (Tonon *et al*., 2016; Joshi *et al*., 2020; Nikoo *et al*., 2021; AlFaris *et al*., 2022).

*Corresponding author.
Email: mgarciam@ittepic.edu.mx

Shrimp is marine plankton, and consumed worldwide due to its high protein content (Nikoo *et al*., 2021). According to the world shrimp market, the total production of this crustacean was estimated at 9.4 million tons in 2022 (FAO, 2023). Shrimp constitutes 7% of aquaculture production, and it is considered a fishery product of high economic value (Widiasa *et al*., 2024). By-products such as the head, tail, and cephalothorax, which represent 40 - 60% of the total weight, remain after processing. These by-products must remain as part of a circular economy because they have been shown to have bioactive potential (Tonon *et al*., 2016; Joshi *et al*., 2020; Nikoo *et al*., 2021; 2023). According to da Silva *et al*. (2017), the hydrolysates from shrimp waste are a potential human dietary supplement. Furthermore, some BPs obtained from shrimp waste and by-products by hydrolysis have exhibited angiotensin-converting-enzyme inhibitory effects and antioxidant, anti-hypertensive, anti-inflammatory, antiproliferative, and hypoglycaemic properties (Salampessy *et al*., 2017; Joshi *et al*., 2020; AlFaris *et al*., 2022). In general, shrimp wastes and by-products are valuable raw materials to obtain BPs, and need to be treated as such. The present review thus focuses on novel research on using marine by-products to obtain BPs, particularly those obtained from shrimp waste, and discusses their human health benefits.

Bioactive peptides: Sources and applications

BPs are specific protein fragments characterised by a short amino acid sequence (typically 2 to 20 amino acid residues) obtained after protein hydrolysis, and a molecular weight < 10 kDa (Atef and Mahdi Ojagh, 2017). In general, these short-chain amino acids are inactive within the sequence of the whole protein, but can exert positive effects on physiologic functions (anti-hypertensive, antioxidant, and anti-inflammatory properties) upon proteolysis (food processing or digestion) in a structural-dependent manner; moreover, some BPs can exhibit more than one bioactivity (Du and Li, 2022). They can be produced from different animal and plant protein sources, including bovine blood, gelatine, meat, egg, fish, corn, rice, soybean, pumpkin, sorghum, and amaranth (Singh *et al*., 2014; Lassoued *et al*., 2015; Przybylski *et al*., 2016; Moosavi-Nasab, 2018; Selamassakul *et al*., 2018; Kamal *et al*., 2021). BPs have gained attention in recent years due to their potential pharmaceutical and industrial applications, and lack of toxicity (Atef and Mahdi Ojagh, 2017), as shown in Table 1.

In general, BPs can be obtained from different protein sources (Bhandari *et al*., 2020). Moreover, they can be produced through chemical and biological routes, and each method has its advantages and limitations (Figure 1). Nonetheless, their bioactivity is dependent on the method of synthesis, protein source, amino acid sequence, molecular weight, and degree of purification (Bhandari *et al*., 2020). Chemical methods include acid and alkaline hydrolyses, which are relatively low-cost, and easy practices for producing protein hydrolysates on an industrial scale. However, these methods are challenging to control due to their harsh reaction and

Table 1. Bioactive peptides obtained from different sources.

Bioactive peptide	Source	Synthesis method	Bioactivity	Reference
NI	Sardine muscle	Biological	Anti-diabetic	Rivero-Pino *et al*. (2020)
IPVDM	Boarfish	Biological	Anti-diabetic	Harnedy-Rothwell *et al*. (2020)
IPNVAVD	Carp	Biological	Anti-diabetic	Zhang *et al*. (2020)
ATPGDEG	Abalone by-products	Chemical	Antioxidant	Qian *et al*. (2018)
NI	Snook fish	Biological	Antioxidant	Romero-Garay *et al*. (2020)
TYIA	Red algae	Biological	Anti-hypertensive	Cermeño *et al*. (2019)
NI	Mackerel	Chemical	Antioxidant	Asaduzzaman *et al*. (2018)
YSK	Rice bran	Chemical	ACE inhibitory	Wang *et al*. (2017)
CGLP	Chicken hydrolysates	Biological	Anti-hypertensive	Onuh *et al*. (2016)
SNLRPCG	Poultry by-products	Biological	Antioxidant	Wan *et al*. (2016)
Lunasin	Soybeans	Biological	Anti-carcinogenic	Rizzello *et al*. (2016)
PIIVYWK	Blue mussel	Biological	Antioxidant	Park *et al*. (2016)
NI	Croceine croaker	Chemical	Anti-osteoporotic	Chi *et al*. (2015)

NI: no information; and ACE: angiotensin I-converting enzyme.

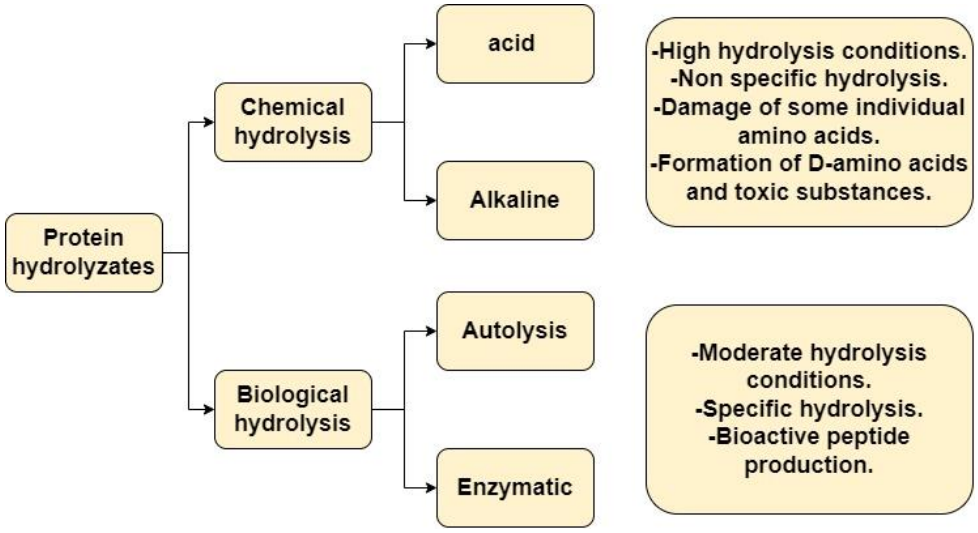

Figure 1. Hydrolysis methods used to obtain bioactive peptides (Zamora-Sillero *et al*., 2018).

cleavage of non-specific peptide bonds, giving a heterogeneous peptide yield and reducing the nutritional quality of products due to damage to their amino acids. Moreover, BPs obtained from chemical methods are not recommended for food applications (Harnedy and FitzGerald, 2012).

On the other hand, biological methods include enzymatic hydrolysis by different proteases (regardless of plant, animal, or bacterial origin) or autolysis (Ali *et al*., 2021). These methods exhibit specific protein hydrolysis (they are easier to control), and moderate experimental conditions without affecting the amino acids, and reducing the formation of by-products (Zamora-Sillero *et al*., 2018). Furthermore, Ghanbari (2019) mentioned that BPs obtained by proteolysis had improved hydrophobicity due to the protein chains unfolding, mainly associated with the exposure of R groups of amino acids, which are very active.

The current trend for obtaining BPs was estimated through a stratified search to understand the tendency to use different protein sources and synthesis methods to produce BPs, and their potential applications. The importance of the protein sources in the production of bioactive molecules formed by different amino acid profiles with potential biological properties is shown in Figure 2.

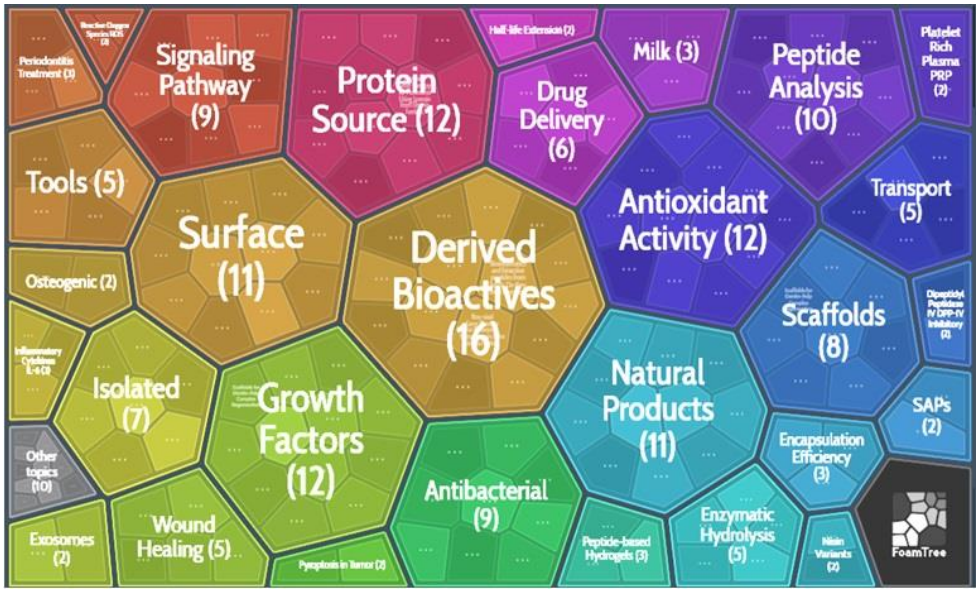

Figure 2. Stratified search clustering to obtain bioactive peptides and their biological activities. The figure was created using Carrot2 software and data were obtained from PubMed database using the search pattern "Bioactive peptides" AND "Applications". Available in https://search.carrot2.org/#/search/pubmed/(Bioactive%20Peptides)%20AND%20(applications)/pie-chart (accessed on 20 March 2024).

Based on the evidence, BPs have human health benefits based on a structural-dependent response (Islam *et al*., 2022). However, some factors have a negative effect on their biological activities, mainly associated with their bioaccessibility in the target tissue, such as the processing conditions, the enzyme used for proteolysis, the size and molecular weight of the resulting peptide, and the protein source (Udenigwe *et al*., 2021). In this context, BPs obtained from marine protein sources have been proposed as a desirable raw material for obtaining BPs for application in the pharmaceutical industry (Harnedy and FitzGerald, 2012; Romero-Garay *et al*., 2020).

Bioactive peptides obtained from marine sources

Marine species, which comprise one-half of the global biodiversity, are rich in biologically active compounds with different structures and potential applications (Ali *et al*., 2021). Some of these compounds are proteinaceous in origin (protein and amino acids) which provide a large range of raw materials for obtaining BPs (Wang *et al*., 2019). Some BPs obtained from marine by-products and their related biological activity or bioactivity are listed in Table 2.

In general, BPs have been obtained from diverse marine proteins such as fish, molluscs, crustaceans, algae, and marine by-products (skin, viscera, muscle, trimmings, blood, and shellfish). These BPs have been shown to have anti-hypertensive, antioxidant, anti-inflammatory, anti-allergenic, hypocholesterolaemic, neuroprotector, anti-proliferative, and antimicrobial activities (Du and Li, 2022). Moreover, their chemical structure depends on the method of synthesis and the protein source used (Bhandari *et al*., 2020).

Since the increase in fishing activity, the processing of large amounts of waste such as bones, heads, skin, scales, fins, and viscera that are not usually used has been encouraged. The percentage of by-products depends on the type of marine species (Nikoo *et al*., 2023). Fish produce mainly heads (9.9 - 27%), viscera (6.9 - 14.3%), frame (7.6 - 16.4%), and skin plus scales (4.7 - 7%) (Heu *et al*., 2003; Jeffree *et al*., 2006; Bat *et al*., 2023). Cephalopods produce heads plus tentacles (23 - 25%), viscera (8 - 18%), and skin (3 - 4.2%)(Heu *et al*., 2003; USDA, 2016). Crustaceans produce mainly heads (20 - 54%), liver, legs, shell (7.4 - 7.6%), and tails (1.7 - 2.8%) (Heu *et al*., 2003; Wu *et al*., 2020; Bao *et al*., 2021; Davis *et al*., 2021). Therefore, many researchers have taken on the task of investigating some types of fish by-products, mainly those with high protein content, which could be beneficial for human health. Wang *et al*. (2019) reported that the BPs (Thr-Pro-Glu-Val-His-Ile-Asn-Val-Lys-Phe) obtained from Atlantic salmon (*Salmo salar*) viscera after pepsin hydrolysis exhibited anti-allergic properties in a dose-dependent manner. They found that BPs exerted therapeutic effects on alleviating allergies at a dose of 1 mg/mL, with an 89.40% reduction in the incidence of an allergic reaction associated with inhibition of the release of β-hexosaminidase, and mast cell degranulation in the RBL-2H3 cell model (half maximal inhibitory concentration [IC_{50}] of 1.39 mg/mL). Moreover, Romero-Garay *et al*. (2020) studied protein hydrolysates from snook fish (*Centropomus* spp.) by-products. They found that the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity was 483.21 µM ET/mL, the reducing antioxidant power was 1198 µM ET/mL, and the antioxidant capacity was 38.03 µM ET/mL using the ABTS assay. Therefore, based on these results, it is possible to consider these hydrolysates as potential ingredients in food additives and pharmaceutical products.

A wide variety of research has focused on fish peptides that have anti-diabetic properties. Rivero-Pino *et al*. (2020) produced and characterised anti-diabetic peptides from discarded *Sardina pilchardus* protein using two different endopeptidases (Alcalase 2.4 L and Flavourzyme) with different selectivity, and one exopeptidase to produce hydrolysates with anti-diabetic activity. They used an *in vitro* dipeptidyl peptidase IV inhibition (DPP-IV) assay in different fractions of the hydrolysate to see which fraction was more inhibited. They concluded that the amino acid composition and proteins of the substrate, as well as the enzymatic treatment, are involved in the anti-diabetic peptides released. They found peptides in the range of 800 to 1400 Da; these peptides were four to nine amino acids long. *In vitro* DPP-IV inhibition by peptides from carp (*Cyprinus carpio*) by-products has also been evaluated in culture cell models. In that study, Zhang *et al*. (2020) made hydrolysates with papain, and identified the peptides using liquid chromatography-tandem mass spectrometry (LC-MS/MS). They found that DPP-IV inhibition by papain hydrolysate was not attenuated after gastrointestinal digestion. Ile-Pro-Asn-Val-Asn-Val-

Table 2. Bioactive peptides obtained from marine by-products.

Source	Type of by-product	Peptide sequence	Bioactivity	Reference
Heterocarpus reedi	Heads, shells, and empty tails	NI	Antioxidant	Leiva-Portilla *et al.* (2023)
Charybdis natator	Leg muscle	LGLGAAVLL	Anti-inflammatory	Narayanasamy *et al*. (2020)
Engraulis encrasicolus	Viscera	NI	Anti-inflammatory	Giannetto *et al*. (2020)
Sardine pilchadrus	Muscle	800 - 1400 Da	Anti-diabetic	Rivero-Pino *et al*. (2020)
Cyprinus carpio	Roe	IPNVNVD	Anti-diabetic	Zhang *et al.* (2020)
Salmo salar	Skin	LDKFR	Anti-diabetic	Jin *et al*. (2020)
Centropomus ssp.	Scales and skin	NI	Antioxidant	Romero-Garay *et al.* (2020)
Salmo salar	Viscera	TPEVHINVKF	Anti-allergenic	Wang *et al.* (2019)
Rachycentron canadum	Skin	YAA, AWW, IWWWI	Anti-hypertensive	Lin *et al.* (2019)
Tergillarca granosa	Muscle	MDLFTE	Antioxidant	Yang *et al.* (2019)
Hallotis discus hannai	Processing water	NTPGDEG	Antioxidant	Qian *et al.* (2018)
Meuchenia sp.	Fresh mince	NI	Anti-hypertensive	Salampessy *et al* (2017)
Oreochromis niloticus	Head, skin, trimmings, fins, frames, and visceral waste	< 116 kDa	Antioxidant	Tejpal *et al.* (2017)
Corbicula fluminea	Muscle	VLP, VLL	Hypocholesterolaemic	Lin *et al.* (2017)
Paralichthys olivaceus	Muscle	MEVFVP, VSQLTR	Anti-hypertensive	Ko *et al*. (2016)
Stichopus horrens	NI	CRQNTLGHRTSQTSIAQ	Anti-hypertensive	Forghani *et al.* (2016)
Arctoscopus japonicus	Muscle	ATSHH	Antioxidant	Jang *et al*. (2016)
Benthosema pterotum	NI	PYTDW	Neuroprotector	Chai *et al.* (2016)
Sepia brevimana	Mantle	LNLCCN	Antioxidant	Sudhakar and Nazeer (2015)
Raja clavata	Skin gelatine	IVGRPR	Anti-hypertensive	Lassoued *et al*. (2015)

NI: no information.

Asp peptide increased the inhibition of DPP-IV secreted by Caco-2 cells with no cytotoxicity; they concluded that this peptide may be used as a functional ingredient in food for patients with diabetes. The main objective of a study by Jin *et al*. (2020) was to identify novel DPP-IV inhibitory peptides from Atlantic salmon skin. They used different enzymes (pepsin, papain, trypsin, and Alcalase 2.4 L) to make the hydrolysates. After evaluating these enzymes, they found that the hydrolysate from trypsin showed the greatest inhibitory effect (66.12 ± 0.68%). This protein hydrolysate was separated into three fractions by ultrafiltration; they found that the A_{10} fraction had the greatest inhibitory effect, and the Leu-Asp-Lys-Phe-Arg peptide was identified. Once the peptide was obtained, molecular docking was carried out to observe the interactions that caused DPP-IV inhibition; they found six hydrogen bonds and eight hydrophobic interactions.

Efforts have also been made to obtain fish protein hydrolysates with anti-hypertensive activity by inhibiting the activity of the angiotensin-converting enzyme (ACE). Lin *et al*. (2019) have focused on the use of cobia fish (*Rachycentron canadum*) skin by-products to obtain protein hydrolysates with anti-hypertensive activity. Hydrolysis was carried out using Protamex and protease N for 5 h to obtain hydrolysates PX-5 and PN-5, respectively. The soluble protein content was 612 and 270 mg/g for PX-5, and 531 - 400 mg/g for PN-5. Four peptide sequences were identified: Tyr-Ala-Ala, Ala-Trp-Trp, Ile-Trp-Trp, and Trp-Ile, from which IC_{50} values for ACE of 11.5, 9.40, 0.51 and 26.80 µM, respectively, were obtained. In another study, Ko *et al*. (2016) obtained BPs from fish (*Paralichthys olivaceus*) muscle by pepsin hydrolysis with anti-hypertensive properties. They reported that the oral administration of BPs (Met-Glu-Val-Phe-Val-Pro and Val-Ser-Gln-Leu-Thr-Arg) in male spontaneously hypertensive rats (> 210 mmHg) at a dose of 40 mg/kg of body weight induced a significant reduction in systolic blood pressure (after 6 h), similar to that observed in a group treated with captopril (40 mg/kg body weight). According to the authors, BPs acted as a competitive and non-competitive inhibitor of ACE (IC_{50} of 79 and 105 µM, respectively), reducing blood pressure. Moreover, a similar ACE inhibitory effect by BPs obtained from enzymatic hydrolysis of fresh leatherjacket (*Meuchenia* sp.) mince has been reported, mainly associated with the hydrophobicity of the C-terminal amino acid residue, and its affinity with the active site of ACE (Salampessy *et al*., 2017).

There is a wide variety of research that refers to other types of bioactivities of peptides from fish by-products. Giannetto *et al*. (2020) reported *in vitro* and *in vivo* biological activities of protein hydrolysates from anchovy (*Engraulis encrasicolus*). Treatment with these hydrolysates exerted significant protection against lipopolysaccharide (LPS)-induced inflammation. RAW 264.7 cells decreased the expression of proinflammatory mediators such as COX-2, and inhibited the nuclear translocation of NF-$_k$B through I_KB-α. Supplementation with anchovy hydrolysates in the diet of ApoE knockout mice downregulated proinflammatory cytokines such as tumour necrosis factor-alpha (TNF-α), interleukin (IL)-1α, IL-1β, and IL-6 in the aorta and heart tissues, and modulated the expression of oxidative stress-related genes, showing that these hydrolysates can have a beneficial role with antioxidant and anti-inflammatory activities.

There are also reports of other types of marine by-products from molluscs with various bioactivities. Qian *et al*. (2018) isolated the peptide Asn-Thr-Pro-Gly-Asp-Glu-Gly (752 Da) from boiled abalone (*Hallotis discus hannai*) by-products that were fractionated using an ultrafiltration membrane system (< 1 kDa); it was shown to have antioxidant activity against free radicals (DPPH, hydroxyl, peroxyl, and superoxide radicals), reactive oxygen species stress, and DNA damage in H_2O_2-treated RAW 264.7 macrophages. The ACE inhibition pattern proved to be non-competitive. This peptide was shown to have an anti-hypertensive effect based on the measurements made after oral administration in spontaneously hypertensive rats (10 weeks old, male, SHR/Hos, SPF, 180 - 240 g body weight), compared with commercial captopril. Similarly, Forghani *et al*. (2016) reported that the oral administration of BPs (obtained from *Stichopus horrens* by enzymatic hydrolysis using Alcalase) in normotensive rats (angiotensin I injected) at a dose of 400 mg/kg body weight reduced systolic blood pressure (from 104 to 94 mmHg) associated with the ACE inhibitory effects of BPs. In addition, Lassoued *et al*. (2015) found that the peptide (Ile-Val-Gly-Arg-Pro-Arg) obtained after hydrolysis of thornback ray (*Raja clavata*) skin gelatine exhibited an ACE inhibitory effect *in vitro* (IC_{50} of 170 and 27.9 µM, respectively) and antioxidant activity by the DPPH radical scavenging

test (IC_{50} of 1.98 and 21.19 mg/mL, respectively). Moreover, these authors mentioned that the sequence in the peptide could have contributed to the ACE inhibitory activity and antioxidant activity. Narayanasamy *et al*. (2020) evaluated the anti-inflammatory properties of BPs (Leu-Gly-Leu-Gly-Ala-Ala-Val-Leu-Leu) obtained after hydrolysis of marine crab (*Charybdis natator*) leg muscle. They reported that BPs exhibited potent anti-inflammatory activity in an LPS-stimulated RAW264.7 cell line (cell viability of 81% at 50 µg/mL) without toxic effects. Moreover, a decrease in COX-2 was observed in a concentration-dependent manner, indicating the potential use of BPs as an anti-inflammatory agent. In addition, Lin *et al*. (2017) reported that freshwater clam muscle is a potential raw source of BPs with hypocholesterolaemic properties. They showed that BPs (Val-Leu-Pro and Val-Leu-Leu) obtained after gastrointestinal digestion (*in vitro*) inhibited cholesterol micelle formation, associated with their ability to bind to bile acids, avoiding reabsorption of bile acids in the ileum, which promotes a reduction in the blood cholesterol levels.

Based on the literature, marine by-products have been recognised as a proteinaceous source to obtain BPs with diverse biological activities for improving human health. In this context, shrimp by-products are a valuable source of BPs that could be used for pharmaceutical and industrial applications.

Bioactive peptides obtained from shrimp by-products

Aquaculture by-products have generated great interest for the production of protein hydrolysates with biological activities, including different species of shrimp by-products. Some bioactive peptides from shrimp by-products and their peptide sequences are shown in Table 3.

The BPs obtained from different shrimp species come from the exoskeleton, head, processing water, and shrimp appendix. The peptides presented have different molecular weights and different numbers of amino acid residues in the peptide chain. The structure of the peptide depends directly on the method of hydrolysis, whether chemical or biological.

Biological activities of bioactive peptides obtained from shrimp by-products

As discussed in the preceding sections, marine sources, particularly shrimp by-products, could be used as a protein source to obtain BPs that are associated with diverse biological activities (antioxidant, anti-hypertensive, anti-inflammatory, and hypocholesterolaemic properties) for pharmaceutical and industrial applications.

Antioxidant activity

The antioxidant activity of BPs may be the result of specific scavenging of the radicals formed during peroxidation, scavenging of oxygen-containing compounds, or their metal-chelating capacity (Xiong, 2010). Peptide antioxidant activity depends on the presence and position of amino acids in the peptide chain (Bechaux *et al*., 2019). Properties modified during enzymatic hydrolysis include hydrophobicity, primary structure, amino acid composition, and spatial conformation (Elias *et al*., 2008).

Hydrophobic amino acids (Pro, Ala, Gly, Leu, Ile, Met, Trp, Phe, and Val) have been shown to affect lipid molecules, and promote peptide techno-functional properties, including peptide solubility and scavenging of various free radicals (OH and NH_2) in peptide side chains (Nikoo *et al*., 2023). In contrast, aromatic amino acids (Tyr, Trp, and Phe) may have chelating properties due to the presence of imidazole, indole, and phenolic groups (Venuste *et al*., 2013; Duan *et al*., 2014; Rodríguez-Jiménez *et al*., 2023). These amino acids may enhance antioxidant activity because the amino acid groups are capable of free radical inactivation by hydrogen atom transfer, sequential proton loss by electron transfer, and single electron transfer followed by proton transfer (Lončar *et al*., 2021).

Latorres *et al*. (2018) reported that white shrimp protein hydrolysates presented antioxidant activity that was dependent on the composition and size of the peptides. Hydrolysates with the highest peptide chain showed the highest antioxidant power for DPPH radical scavenging and reducing power; hydrolysates with a shorter peptide chain showed higher antioxidant power for 2,20-azinobis (3-ethylbenzothiazolin sulfonic acid) as a radical scavenger. All hydrolysates showed a dose-dependent antioxidant capacity. Yuan *et al*. (2018) optimised hydrolysis using oriental shrimp (*Fenneropenaeus chinensis*) shell waste to obtain peptides to inhibit α-amylase. The optimum conditions were a liquid/solid ratio of 13 mL/g, time of 4.1 h at 50°C, enzyme concentration of 5.4%

Table 3. Bioactive peptides obtained from shrimp by-products.

Common name	Scientific name	Origin	Synthesis method	Hydrolysis condition	Peptide sequence	Reference
Pacific white shrimp	*Litopenaeus vannamei*	Head and exoskeleton	Biological	pH 8.0, 30°C, 0.5 h, 1 g of substrate and 100 µg/mL of *B. karatas*; pH 7.5, 40°C, 0.5 h, 0.5 g substrate and 100 µg/mL enzyme extract from *B. pinguin*; and pH 7.0, 37°C, 1 h, 1.5 g substrate and 100 µg/mL enzyme bromelain	NI	Rodríguez-Jiménez *et al.* (2023)
Kuruma shrimp	*Marsupenaeus japonicus*	Head	NI	NI	NI	Zhou *et al.* (2023)
Red shrimp	*Solenocera crassicornis*	Head	Biological	Pepsin (2500 U/g) for 4 h at 37°C	NI	Jiang *et al.* (2020)
Pacific white shrimp	*Litopenaeus vannamei*	Cephalothorax, shells, and pleopods	Biological	Initial pH (~7.1) using gradual autolysis (40 - 60°C, increasing 5°C/30 min) for 180 min in a temperature-controlled water bath	NI	Karimi *et al.* (2020)
Shrimp	*Oratosquilla woodmasoni*	Muscle waste	Biological	Thermolysin (70°C, pH 8) and pepsin (37°C, pH 2)	DGVAA	Joshi *et al.* (2020)
Shrimp akiami	*Acetes japonicus*	Whole shrimp	Biological	NI	DSVNFPVLHGL, FLVGQENTPILK	Anh *et al.* (2020)
Asian tiger shrimp	*Penaeus monodon*	Shell	Chemical	NI	NI	Sukmawati *et al.* (2019)
Pacific white shrimp	*Litopenaeus vannamei*	Cephalothorax	Biological	Alcalase 1%(pH 8, 60°C, 2 h)	NI	Sinthusamran *et al.* (2019)
White shrimp	*Litopenaeus vannamei*	Cephalothorax	Chemical	NI	KNPEQ	Leduc *et al.* (2018)
Oriental shrimp	*Fenneropenaeus chinensis*	Shell	Biological	5.4% (w/w), liquid-solid ratio of 13 mL/g, 4.1 h, 50°C, pH 7.0 with different enzymes	<4 kDa peptides	Yuan *et al.* (2018)
Shrimp	*Pandalopsis dispar*	Waste	Biological	Protamex at 18%, 24 h, pH 8	DVLFH	Li-Chan *et al.* (2016)
White shrimp	*Litopenaeus vannamei*	Shell waste	Biological	Alcalase (74,688.9 U/g), 55°C, 4 h, pH 7	<5 kDa peptides	Feng *et al.* (2016)

Common name	Scientific name	Origin	Synthesis method	Hydrolysis condition	Peptide sequence	Reference
White shrimp	*Litopenaeus vannamei*	Leg	Biological	Extract from giant catfish viscera, porcine trypsin, and Alcalase, 50°C, pH 8 for 3 h	NI	Ketnawa *et al.* (2016)
Shrimp	*Parapenaeus longirostris*	Head, cephalothorax, shell and appendix	Biological	Alcalase (1000 U/g) at 50°C for 30 min	NI	Sila *et al.* (2014)
Northern shrimp	*Pandalus borealis*	Dry shell	Biological	NI	FWY, FSY	Gildberg *et al.* (2011)
Izumi shrimp	*Plesionika izumiae omori*	Whole shrimp	Biological	0.1% (w/w) Protease S (Amano Enzyme, Nagoya, Japan) at 50°C for 2 h, pH 6.5	VWYHT, VW	Nii *et al.* (2008)
Brown shrimp	*Penaeus aztecus*	Head	Chemical	NI	NI	Cudennec *et al.* (2008)
Northern mauxia shrimp	*Acetes chinensis*	Whole shrimp	Biological	Fermentation with *Lactobacillus fermentum* SM 605 (2%, v/v) was inoculated to 0.5 L of modified MRS medium (10% shrimp slurry, 2% glucose, 0.5% sodium acetate, 0.2% diammonium hydrogen citrate, 0.2% K_2HPO_4, 0.058% $MgSO_4 \cdot 7H_2O$, 0.025% $MnSO_4 \cdot 7H_2O$, 0.1% Tween-80)	DP, GTG ST	Wang *et al.* (2008)
White shrimp	*Litopenaeus vannamei*	Cephalothorax	Chemical	NI	NI	Binsan *et al.* (2008)
Northern mauxia shrimp	*Acetes chinensis*	Whole shrimp	Biological	*Bacillus* sp. SM98011 (4000 U/mL) pH 7, 50°C for 5 h	FCLVRP, IFVPAF, KPPETV	He *et al.* (2006)

NI: no information.

(w/w), and pH of 7.0. Under these conditions, the α-amylase inhibitory ratio was 43.4%. These hydrolysates had the ability to scavenge diphenyl hydranizyl free radicals, reduce iron(III), and inhibit lipid peroxidation. The molecular weight of the shrimp hydrolysates was less than 4 kDa, and the content of amino acids was high (278 mg/g). These hydrolysates could be useful and potentially high-value products. In another type of shrimp, Sila *et al*. (2014) generated peptidic fractions of carotenoproteins from shrimp (*Parapenaeus longirostris*) by-products by enzymatic hydrolysis using Alcalase (0.5 M EDTA) to see if the peptidic fractions had biochemical and antioxidant properties. The peptidic fraction of carotenoproteins (PFCP; Pro-Phe-Cys-Pro) comprised 80.8 ± 0.21% protein, 1.13 ± 0.08% chitin, 14.4 ± 0.14% ash, 2.74 ± 0.3% lipid, and 1.08 ± 0.02 μg total carotenoid/g of sample, and had high percentage of essential amino acids such as arginine, lysine, histidine, and leucine. PFCP showed excellent solubility, and possessed interfacial properties which were governed by their concentrations. The antioxidant activity of PFCP at different concentrations was evaluated using four *in vitro* antioxidant assays, including the DPPH radical method, reducing power, chelating effects assay, and β-carotene bleaching. That study suggested that Pro-Phe-Cys-Pro could be good source of natural antioxidants and peptides with interesting functionalities. Similarly, Binsan *et al*. (2008) extracted antioxidant peptides from cephalothorax of white shrimp (*Litopenaeus vannamei*). They demonstrated ABTS and DPPH radical scavenging activity, as well as ferric-reducing activity with different water/ethanol mixtures (1:1, 1:2, and 2:1). The results of ABTS and DPPH with water extract increased linearly as the concentration increased. Antioxidants from white shrimp by-products could be promising as novel natural antioxidants for nutraceutical applications. Furthermore, Joshi *et al*. (2020) reported that the peptide (Asn-Gly-Val-Ala-Ala) obtained from shrimp (*Oratosquilla woodmasoni*) waste presented antioxidant activity by the ABTS and DPPH methods; however, the effect was concentration dependent. In accordance with Ambigaipalan and Shahidi (2017), the antioxidant activity of BPs can be influenced by their hydrophobicity/hydrophilicity, amino acid sequence, degree of hydrolysis, and molecular weight. Similarly, the peptide derived from *O. woodmasoni* muscle has high amount of total hydrophobic amino acids in its structure, which could improve the antioxidant capacity of the peptide (Ambigaipalan and Shahidi, 2017).

Anti-hypertensive activity

Anti-hypertensive peptides act in reducing arterial blood pressure by inhibiting the action of ACE-I. This enzyme is able to catalyse the conversion of angiotensin I to the active vasoconstrictor angiotensin II, and can inactivate a vasodilator (bradykinin), thus resulting in an increase in blood pressure (Lee and Hur, 2017). Therefore, ACE inhibition has become the main target in the treatment of hypertension (Himaya *et al*., 2012). Although several synthetic ACE inhibitors such as enalapril, alacepril, or lisinopril are effective antihypertensives, they have been reported to have side effects, including an inflammatory response, dry cough, taste disturbance, skin rash, or angioneurotic oedema (Intarasirisawat *et al*., 2013). Therefore, food-derived ACE inhibitory peptides are being considered as an alternative because of the structure-activity relationship of food-derived products. ACE inhibitory peptides have not been established. However, ACE inhibitory peptides generally contain zinc-binding ligands, a hydrogen bond donor, and a carboxyl-terminal group. Furthermore, ACE activity could be inactivated by the presence of hydrophobic amino acids in the C-terminal tail by alteration of the ACE catalytic site (Kang *et al*., 2003). In their investigation, Joshi *et al*. (2020) isolated peptides from shrimp (*O. woodmasoni*) muscle waste using thermolysin and pepsin to characterise ACE-I inhibition and the antioxidant response. They found that a degree of hydrolysis of 12 was observed, and the maximum ACE-I inhibition activity occurred at 2 and 5 h (73.51 ± 0.25% and 68.93 ± 0.23%) for both enzymes. Although the best thermolysin hydrolysate was ultra-filtrated with membrane, the 10 - 3 kDa fraction showed ACE-I inhibition activity (IC_{50}, 0.47 mg/mL). That fraction was purified by ion exchange chromatography and gel filtration chromatography. They found a pentapeptide sequence (Asn-Gly-Val-Ala-Ala) with a molecular weight of 431 Da using LC-MS/MS with antioxidant activity and ACE-I inhibition (77.09 ± 2.18%). Consequently, this peptide must be investigated further before being considered an alternative as a nutraceutical and functional food. Feng *et al*. (2016) prepared hydrolysates from white shrimp (*L. vannamei*) shell waste to purify ACE inhibitory peptides. They

reported that the hydrolysates had ACE inhibitory activity of 67.07% at optimal hydrolysis conditions of Alcalase (60°C, pH 9.5, 25 g/L substrate, and 4000 U/g of enzyme), whereas neutral protease hydrolysates showed ACE inhibitory activity of 84.04% at optimal hydrolysis conditions (50°C, pH 7.0, 25 g/L substrate, and 2000 U/g of enzyme). These results showed that neutral protease was the better option to produce ACE inhibitory peptides from shrimp by-products; in that sense, the peptides obtained from shrimp waste could be beneficial as anti-hypertensive compounds. Gildberg *et al*. (2011) made hydrolysates from northern shrimp (*Pandalus borealis*) to evaluate the inhibitory activity of ACE-I, and the identification of two peptides. They measured ACE-I inhibitory by two different methods: incubation of ACE from rabbit tissue, and applying Hippuryl-His-Leu as a substrate. Both methods showed better *in vitro* ACE inhibitory activity (IC_{50}, 0.075 and 0.035 mg/mL) than previously reported hydrolysates. These tri-peptides, Phe-Thr-Tyr (IC_{50}, 275 and 59 μM) and Phe-Ser-Tyr (IC_{50}, 7.7 and 2.2 μM) were found in the hydrolysate. The authors also fed spontaneously hypertensive rats with 60 mg hydrolysate/kg body per day, and recorded positive *in vivo* results. More *in vivo* studies are needed to verify the anti-hypertensive potential; good results regarding *in vitro* ACE inhibitory activity suggested that the protein hydrolysate from northern shrimp could be a candidate for nutraceutical application. On the other hand, the anti-hypertensive activity is related to very short peptide sequences (less than nine amino acids), which include glycine, tyrosine, valine, phenylalanine, isoleucine, arginine, or asparagine (Amado *et al*., 2016). In another study, Nii *et al*. (2008) isolated two peptides from whole izumi shrimp by high-performance liquid chromatography (HPLC); their amino acid sequences were Val-Trp-Tyr-His-Thr and Val-Trp. These peptides were given to rats in a single oral dose of 1 mg peptide/1 mL of distilled water by intubation. Control rats were given captopril. The peptides showed a decrease in blood pressure in mice. The antigenicity and allergenicity of these hydrolysates were very low. These findings revealed that the ACE-I enzyme could be inhibited by peptides from izumi shrimp in spontaneously hypertensive rats. Similarly, Wang *et al*. (2008) produced peptides by fermentation of an underutilised shrimp (*Acetes chinensis*) species with *Lactobacillus fermentum* SM 605 to inhibit the ACE-I enzyme. They found that the minimum IC_{50} value (3.37 ± 0.04 mg/mL) was reached by the response surface methodology with the following parameters: fermentation time, 24.19 h; incubation temperature, 38.10°C, and pH 6.12. These were the optimum parameters to hydrolyse the shrimp. Three ACE inhibitory peptides were purified by ultrafiltration, gel filtration, and reverse-phase HPLC. Their amino acid sequences (Asp-Pro, Gly-Thr-Gly, and Ser-Thr) were identified by mass spectrometry, with IC_{50} values of 2.15 ± 0.02, 5.54 ± 0.09, and 4.03 ± 0.10 μM, respectively. Compared with other types of digestion, such as protease digestion, fermentation is an easier and cheaper method to produce ACE inhibitory peptides from this shrimp. He *et al*. (2006) analysed peptides from protease-hydrolysed shrimp (*A. chinensis*) to investigate if they could inhibit ACE-I. They used ultrafiltration, gel permeation chromatography, and reverse-phase HPLC to obtain five peptides with ACE inhibitory activity; their sequences were recognised by their amino acid composition and molecular weight analysis. Phe-Cys-Val-Leu-Arg-Pro, Ile-Phe-Val-Pro-Ala-Phe, and Lys-Phe-Phe-Glu-Thr-Val were uncommon ACE inhibitory peptides. They had IC_{50} values and recoveries in solid basis of shrimp of 12.3, 3.4, and 24.1 μM, and 30, 19, and 33 mg/100 g, respectively. In addition, the Lineweaver-Burk plots for the uncommon ACE inhibitory peptides showed that they were competitive inhibitors. *A. chinensis* hydrolysates probably had ACE inhibitory activity even when they were digested *in vivo*, and these peptides could be good prospects for treatment of hypertension.

Anti-inflammatory activity

Nirmal *et al*. (2020) mentioned that inflammation is the protective physiologic response of the body against harmful external stimuli such as pathogens, free radicals, and dead cells. Anti-inflammatory compounds suppress the activity of proinflammatory cytokines such as NF-α, IL-1, and IL-6 (Cahú *et al*., 2012). Astaxanthin extracted from the head of *L. vannamei* was observed for an inflammatory response in rat alveolar macrophages induced by phorbol myristate and LPS (Cahú *et al*., 2012). Astaxanthin at 43.5 μg/mL was not only non-cytotoxic, but also increased cell viability to 168%. Astaxanthin reduced the formation of superoxide and nitric oxide free radicals by inhibiting TNF-α extracted from the cephalothorax of *L. vannamei* by solvent extraction (Gómez-Guillén *et al*., 2018). The

induced LPS-treated lipid RAW 264.7 showed reduced nitric oxide production compared with controls. The anti-inflammatory effect of lipids was related to the properties of antioxidants (Gómez-Guillén *et al*., 2018). Astaxanthin was obtained from the shell of Asian tiger shrimp using the solvent extraction method with methanol (1:10), and had anti-inflammatory activity on erythrocyte membrane stability. Treated red blood cells showed dose-dependent stability in the erythrocyte membrane; a concentration of 1000 ppm showed the highest anti-inflammatory activity (Sukmawati *et al*., 2019). The anti-inflammatory properties of shrimp lipids containing astaxanthin, α-tocopherol, and polyunsaturated fatty acids were associated with their antioxidant capacity due to their molecular structure, the presence of hydroxyl, and the ketone group (Santos *et al*., 2012; Gómez-Guillén *et al*., 2018). In another study, Jiang *et al*. (2020) studied low molecular peptides from the head of red shrimp (*Solenocera crassicornis*) to see the ameliorative effect against cyclophosphamide-induced hepatotoxicity in mice. They found that peptide treatment dose-dependently normalised the biochemical markers, hepatic index, and total enzyme content in cyclophosphamide-induced hepatotoxicity in mice. The results of western blotting suggested that peptides significantly restored the levels of endogenous antioxidants (CAR, T-AOC, GSH-Px, SOD, and MDA levels) by activating the Nrf2 antibody. These findings suggested that red shrimp peptides could regulate some antibodies, and reduce the oxidative stress and inflammation in cyclophosphamide hepatotoxicity.

Hypocholesterolaemic activity

Unlike some studies that have evaluated the presence of hypocholesterolaemic activity in protein hydrolysates and/or fish peptides and molluscs (Lin *et al*., 2017), to our knowledge, there are very few reports on the presence of this bioactivity in hydrolysates or peptides obtained from muscle or by-products of crustaceans such as the white shrimp, *L. vanammei.* In an *in vivo* study, Halder *et al*. (2013) reported hypocholesterolaemic activity in male albino rats fed for four weeks with a diet supplemented with fermented shrimp-shell hydrolysate; however, the anticholesterolemic activity was attributed to an effect produced by the presence of chitin and chitooligosaccharides rather than the peptides present in the hydrolysate. To consider that these peptides have hypocholesterolaemic or hypolipidemic activity, they must have the ability to reduce the concentration of lipids and/or lipoproteins in the blood, which in turn prevents the accumulation of high levels of cholesterol in the blood vessels (Chai *et al*., 2016). It has been reported that some peptides could interfere with the formation of lipid and sterol-transporting micelles, which in turn interferes with the absorption of cholesterol by the intestinal epithelium, and favours its excretion through the faeces (Silva Afonso *et al*., 2018). Also, hydrophobic peptides can bind bile salts, preventing their reabsorption in the ileum, which leads to a reduction in blood cholesterol levels (Lin *et al*., 2017).

Food applications

Anh *et al*. (2020) evaluated and characterised peptides from *Acetes japonicus* using Flavourzyme on enzymatic hydrolysis. The results showed that under the optimal hydrolysis conditions for this enzyme (pH 5, 50°C, E:S ratio of 27.4 U/g protein, and hydrolysis time of 4.8 h), the hydrolysate displayed maximal iron-binding capacity of 177.7 μg Fe^{2+}/g protein with 38.77% of essential amino acids. The hydrolysate underwent ultrafiltration to fractions of molecular weight 1 - 3 kDa lower than disodium ethylenediaminetetraacetate (Na_2EDTA). From this fraction, they found two peptides, Asp-Ser-Val-Asn-Phe-Pro-Val-Leu-His-Gly-Leu (1083.53 Da) and Phe-Lys-Val-Gly-Gln-Glu-Asn-Thr-Pro-Ile-Leu-Lys (1372.77 Da), which were identified utilising nano-ultra-HPLC-MS/MS, as well as their *de novo* spatial structures and interaction with ferrous ion simulated by PEP-FOLD 3. The peptides exhibited some functional activities: solubility, heat stability, foaming and emulsifying properties, and oil and water holding capacity. The peptides could be used as an iron chelator, which could shield the human body from iron-deficient-related disorders, or as a functional hydrolysate with some food applications. Leduc *et al*. (2018) induced myotropic activity in European seabass (*Dicentrarchus labrax*) assisted by hydrolysates from shrimp (*L. vannamei*) by-products. They isolated shrimp hydrolysates using chemical hydrolysis and purification processes such as reverse-phase HPLC with an intestinal *in vitro* assay, then recognised the sequence of a pentapeptide (Lys-Asn-Pro-Glu-Gln) with Edman degradation, and showed that it did not have homology with another mycotrophic peptide. They studied the *in vivo* effect

of the peptide by feeding low-meal diets with the hydrolysate to European seabass (*D. labrax*), and they observed an *in vitro* effect on isolated intestine perfused with shrimp hydrolysates. This confirmed that in *vitro*, the Lys-Asn-Pro-Glu-Gln CKK-mimetic peptide stimulated contraction of intestine in concentrations in the range of 1 - 10 µM, and for > 10 h at a concentration of 100 µM. Cudennec *et al*. (2008) obtained peptides from crustacean (*Penaeus aztecus*) by-products to stimulate cholecystokinin release in STC-1 cells. They made brown shrimp peptides by enzymatic hydrolysis under controlled conditions (pH, temperature, and stirring speed). The partial purification of CCK-stimulating peptides produced crustacean hydrolysate with molecular weight ranging between 1000 and 1500 Da. For industrial utilisation of shrimp peptides as potential appetite-suppressive products, further studies will be needed on rats (*in vivo*) and humans (clinical) to confirm the effects of the peptide on satiety. The bioactive properties recorded in an *in vitro* analysis of hydrolysates and peptides obtained from white shrimp by-products indicated their potential for application in the food, pharmaceutical, and cosmetic sectors; however, to date, there are still limited reports of investigations. Regarding the food industry, studies in recent years have evaluated the use of BPs to improve the functional, sensory, and stability properties of edible films (Montero *et al*., 2019). On the other hand, protein hydrolysates obtained from white shrimp by-products, which have been found to be rich in peptides with antioxidant capacity (Latorres *et al*., 2018; Nikoo *et al*., 2021), or even peptides (Latorres *et al*., 2021), have the potential to be used as additives to extend the shelf-life of food products, preventing deterioration due to oxidative processes, mainly lipid oxidation (Olatunde *et al*., 2021). In another sector of the food industry, the use of BPs derived from shrimp by-products has potential in bread-making. Some pioneering studies have been reported by Sinthusamran *et al*. (2019). By including white shrimp cephalothorax protein hydrolysates in a paste formulation, they observed improvements in the nutritional value and sensory properties of biscuit. Karimi *et al*. (2020) found that the addition of shrimp hydrolysates favoured the growth of lactic acid bacteria, which allowed greater fermentation of the dough and an improvement in the quality and shelf-life of the bread. Another example was reported by Montero *et al*. (2019); they incorporated nanoliposomes with low-molecular-weight BPs (antioxidants, antihypertensives, and antidiabetics) obtained from shrimp by-products, and encapsulated in sodium caseinate films. They observed an improvement in the solubility, adhesiveness, and palatability of the films. Examples of pharmaceutical applications of peptides obtained from shrimp by-products include their use in the making of films with liposomes with structural characteristics, organoleptic properties (mainly a very favourable taste perception), and high solubility, creating great potential for use in the sublingual delivery of drugs or other bioactive compounds (Montero *et al*., 2019). The presence of antimicrobial activity in some peptides obtained through enzymatic hydrolysis of shrimp by-products makes them an option for the development of natural antibiotics rather than synthetic drugs in the fight against different pathogens (Gu *et al*., 2023). Some antimicrobial peptides obtained from haemolymph of *L. vannamei* have shown antibacterial activity against Gram-negative bacteria (*Vibrio parahemolyticus*, *V. fluviales*, *V. alginolyticus*, *Escherichia coli*, and *Aaeromonas hydrophila*) and Gram-positive bacteria (*Staphylococcus aureus* and *Streptococcus pyogenes*), as a consequence of serious damage to the cell wall, and efflux of intracellular contents (Yang *et al*., 2018). Another pharmaceutical use of BPs obtained from enzymatic hydrolysis of shrimp by-products is blood pressure control due to the fact that they show ACE inhibitory activity. Examples include different potential ACE inhibitory BPs obtained from enzymatic hydrolysis (trypsin, Alcalase, Protamex, and Savinase) of by-products (heads, shells, cephalothorax, among others) from the processing of different species of penaeid shrimp (Wan *et al*., 2016; Ambigaipalan and Shahidi, 2017; Joshi *et al*., 2020). Li-Chan *et al*. (2016) used shrimp (*Pandalopsis dispar*) waste to make hydrolysates as a source of β-secretase inhibitors. They isolated Asp-Val-Leu-Phe-His peptide using Protamex enzyme; the IC_{50} was 92.7 µM, and the molecular weight was 629 Da. These results suggested that β-secretase inhibitory peptides from shrimp waste could be used as a medicine for Alzheimer disease, and could be used to make functional foods. In addition, recent studies have reported that red shrimp peptides had an effect on the autoimmune system, improving it substantially (Zhao *et al*., 2023).

Challenges and perspectives of bioactive peptide usage

Peptides from marine by-products have been investigated over the years, and several important bioactivities have been found. However, much remains to be explored and developed. In addition, many peptides with potential beneficial effects on human health have been isolated, as well as for application in the industrial field. Despite the numerous applications of hydrolysates from seafood processing residues in the food industry, Siddik *et al*. (2021) described some limitations related to the raw materials and processing conditions. These limitations include:

i. Composition of seafood processing by-products varies from batch to batch in the manufacturing process, and the resulting variable nutritional composition may create challenges in the production of a consistent end product.
ii. Raw materials with high fat content are highly perishable, susceptible to oxidation, and contain microorganisms that contribute the release of putrid odour.
iii. Heterogeneity of hydrolysates comprises a diverse range of peptides with different molecular sizes, hydrophobic nature, and surface properties.
iv. Hydrolysates from marine by-products are generally processed at high temperature to inactivate protease action; this may result in the destruction and racemisation of amino acids.

On the other hand, certain aspects should be evaluated before extracting BPs such as endogenous protease activity, polyphenol oxidase activity, shell softness, and the presence of antibiotic residues from crustacean by-products (Davis *et al*., 2021; Farag *et al*., 2023).

Contamination of shrimp with heavy metals (arsenic, cadmium, chromium, lead, and mercury) has become a global crisis as a result of the discharge of all kinds of pollutants into the oceans by various industries (agricultural, pharmaceutical, and technological), affecting the marine biota (Farag *et al*., 2023), especially shrimps; their bodies can accumulate a large amount of heavy metals (Sinkkonen and Paasivirta, 2000), causing digestive, cardiovascular or central nervous system risks for humans (de Almeida Rodrigues *et al*., 2022). Therefore, different analytical techniques must be used to identify heavy metals, antibiotics, or any other type of biotoxins to ensure the safety of using this type of by-product to produce BPs.

More studies should be done on bioactive compounds derived from marine by-products and processing of by-products in terms of nutritional and functional applications for human health (Ozogul *et al*., 2021). The nutritional value, the bioavailability of nutrients, the yield of their production, the physicochemical properties, and the interaction of BPs with other ingredients must be determined; innovative approaches to easy-to-perform extraction methods are required, taking into account current legislation and security issues.

Conclusion

Peptides derived from by-products of various shrimp species are attracting the attention of the pharmaceutical and food industries. BPs have been produced from different forms of hydrolysis, either chemical or enzymatic; the latter has been proven to be the safest for the pharmaceutical and food industries. Similarly, several biological activities have been found in shrimp hydrolysates, such as ACE inhibitory, antioxidant, anti-inflammatory, hypocholesterolaemic activities, and other applications such as the generation of shrimp by-product films. However, there is still a range of opportunities and knowledge to be discovered in relation to the use and exploitation of these by-products in the future.

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