REVIEW ARTICLE

Marine-Derived Bioactive Peptides: A Comprehensive Review of Molecular Diversity, Therapeutic Applications, and Future Frontiers in Natural Remedies

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Abstract

The marine environment, representing approximately 90% of the Earth's biosphere, serves as an unparalleled reservoir of chemical and biological diversity. This review systematically examines the molecular characteristics and therapeutic potential of bioactive peptides isolated from marine organisms, including fish, sponges, mollusks, and algae. These low-molecular-weight protein fragments, often released during digestion or enzymatic hydrolysis, exhibit diverse biological activities such as antimicrobial, antihypertensive, antioxidant, and antiproliferative effects. Specifically, this paper discusses the role of marine-derived angiotensin-converting enzyme inhibitors in managing hypertension as a safer alternative to synthetic drugs, the potent bactericidal activity of peptides such as arencin-1 and tauramamide, and the emerging field of neuroprotective peptides in treating neurodegenerative disorders. Furthermore, the review explores the mechanism of action of antioxidant peptides in scavenging reactive oxygen species to prevent cellular damage. Despite the promise of these compounds, the transition from laboratory identification to clinical application remains a challenge. This review concludes by identifying knowledge gaps in structure-function relationships and calling for further *in vivo* studies to validate the efficacy of marine peptides as functional food ingredients and pharmaceutical leads.

Key words: Angiotensin-converting enzyme inhibition, antimicrobial peptides, antioxidants, bioactivity, drug discovery, marine peptides, nutraceuticals

INTRODUCTION

The oceans, which make up 90% of the biosphere, cover about 70% of the Earth's surface. Approximately half of the world's biodiversity is found in marine organisms, which have been thoroughly investigated in recent decades as possible sources of new bioactive natural compounds. The oceans are a great source of new chemicals since many bioactive natural products have not yet been extracted, identified, and characterized due to the challenges associated with researching deep water environments. Numerous marine organisms include peptides, which are significant bioactive natural compounds that have been the subject of much study. One important source of novel chemicals is marine creatures. The marine environment's biodiversity and the chemical variety that goes along with it provide an almost limitless supply of novel active ingredients for the creation of bioactive products. This review describes the molecular diversity of various marine peptides and provides information on their biological characteristics and mechanism of action.[1]

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Bioactive chemicals with a wide variety of structures can be found in abundance in marine species. Marine-derived bioactive peptides (BP) have attracted a lot of attention lately due to their many positive health effects. Furthermore, due to their therapeutic potential in the treatment or prevention of diseases, numerous studies have shown that marine BPs can be utilized as antihypertensive, antioxidative, anticoagulant, and antibacterial components in functional foods, nutraceuticals, and medicines.[2]

BPs are present in many foods, with antihypertensive peptides that inhibit angiotensin-converting enzyme (ACE) being the most extensively studied. Although synthetic ACE inhibitors such as Captopril are effective, they can cause adverse effects, including cough, skin rashes, and taste disturbances. These limitations, along with the high prevalence of hypertension and its association with cardiovascular disease and stroke, have increased interest in food-derived ACE-inhibitory peptides for use in functional foods and nutraceuticals. Such peptides have been identified in various plant, milk, and animal muscle proteins, including beef, chicken, pork, and fish.[3]

They are typically said to prevent chronic illnesses, strengthen the immune system, manage stressful situations, regulate blood glucose, control body weight, improve cognitive function, postpone aging or lengthen life expectancy, and more. Nutraceutical products frequently contain BPs. Following gastrointestinal digestion, they are absorbed through the intestine and changed into the active form.[4]

Certain protein fragments that positively affect bodily processes or circumstances and may have an impact on health are known as BPs. There are already about 1500 distinct BPs listed in the "Biop" database.

BPs are short amino acid sequences released from food proteins that exert beneficial physiological effects. Their biological activity depends on their amino acid composition and sequence, and they may exhibit antihypertensive, antioxidant, antimicrobial, antithrombotic, immunomodulatory, opioid, and mineral-binding properties, as well as hormone-like or drug-like effects. Both plant- and animal-derived proteins serve as important sources of these BPs.[5]

Peptides are low molecular weight protein fragments that typically don't exceed 20 kDa. BPs are those that can positively impact humans by modifying certain physiological processes. Peptides are generated either by protein fermentation with appropriate microorganisms or by *in vitro* digestion with appropriate proteases to form a protein hydrolysate; the fermented products and protein hydrolysates contain peptides with different structural and functional properties.[6]

Therefore, this review summarizes the current knowledge on marine-derived BPs, with particular emphasis on their molecular diversity, natural sources, biological activities, mechanisms of action, therapeutic applications, commercially available products, and clinical development. It also discusses the existing challenges, knowledge gaps, and future research opportunities that may facilitate the successful translation of marine peptides into innovative pharmaceutical and nutraceutical products.

LITERATURE SEARCH METHODOLOGY

Literature was searched using PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar between 2000 and 2025. Keywords included "marine peptides," "marine bioactive peptides," "marine natural products," "antimicrobial peptides," "ACE inhibitory peptides," "marine-derived pharmaceuticals," and "marine nutraceuticals." Only English-language peer-reviewed articles were included.

SOURCES OF MARINE BPS

Marine organisms represent an abundant and valuable source of BPs, which have gained considerable attention due to their therapeutic potential against various diseases. The highly diverse and dynamic marine ecosystem contributes to an enormous chemical diversity, providing a continuous reservoir of novel bioactive compounds with promising pharmaceutical and nutraceutical applications.[1] Marine-derived peptides have been isolated from a wide range of organisms, including fish, crustaceans, mollusks, shellfish, marine processing by-products, algae, sponges, tunicates, ascidians, and coelenterates.[2]

These marine resources are particularly rich in structurally diverse organic compounds that exhibit multiple biological activities such as antihypertensive, antioxidant, antimicrobial, anticoagulant, antidiabetic, anticancer, immunomodulatory, hypocholesterolemic, calcium-binding, and appetite-suppressing properties.[3] Due to these beneficial physiological effects, marine BPs are increasingly being explored as functional food ingredients and therapeutic agents.[4]

Among marine organisms, crustaceans have been extensively investigated for their peptide content. BPs isolated from crustaceans are involved in regulating several physiological functions, including heart activity, metabolism, color adaptation, muscle contraction, development, metamorphosis, and reproduction.[5] These organisms therefore serve as unique protein sources for the generation of biofunctional peptides with significant biomedical importance.

Marine algae, particularly macroalgae, have also emerged as an important source of BPs. The high protein content of marine algae, which may reach up to 47% of dry weight depending on the species, has increased scientific interest in

their utilization for peptide production.[6] Macroalgae possess complex metabolic pathways capable of synthesizing a broad range of bioactive compounds, including proteins, linear and cyclic peptides, depsipeptides, amino acid derivatives, and amino acid-like substances.[7]

Although only a limited number of peptides derived from macroalgal proteins have been identified so far, these organisms remain a relatively unexplored source of functional peptides. Marine algal peptides have demonstrated potential health-promoting properties, especially antihypertensive activity, making them promising candidates for the development of functional foods and disease-preventive formulations.[8]

MARINE BIOPEPTIDES WITH DIFFERENT BIOACTIVITIES

Antimicrobial peptides

Antimicrobial peptides are low-molecular-weight bioactive compounds with broad-spectrum activity against bacteria, fungi, viruses, yeasts, and some cancer cells. Their potent biological properties have led to their therapeutic use in conditions such as diabetes, hepatitis C, myeloma, and skin infections, while advances in peptide engineering have improved their stability, efficacy, and cost-effectiveness.[7]

Marine organisms are recognized as valuable sources of antimicrobial peptides, particularly mussels such as *Mytilus edulis* [Figure 1]. Investigations on the hemolymph of untreated and immunocompromised mussels have led to the identification of peptides possessing both antibacterial and antifungal properties. Among these, a novel antifungal peptide with a molecular mass of approximately 6.2kDa and containing 12 cysteine residues has been partially characterized. In addition, two isoforms of a unique cysteine-rich peptide consisting of 34 amino acid residues have demonstrated remarkable bactericidal activity.[8]

Figure 1: Mussels (*Mytilus edulis*)

The purification of a 40-residue antimicrobial peptide from the mesoglea of the scaphoid jellyfish *Aurelia aurita* [Figure 2], originally described by Linnaeus in 1758, has been reported. The isolated peptide, termed aurelin, exhibited potent antimicrobial activity against both Gram-positive and Gram-negative bacterial strains, indicating its potential significance as a marine-derived therapeutic peptide.

Marine polychaete *Arenicola marin*a [Figure 3] is a rich source of antimicrobial peptides. Peptides isolated from A. marina, particularly arenicin, exhibit potent antibacterial activity against both *Staphylococcus aureus* and *Pseudomonas aeruginosa*, highlighting its potential as an effective marine-derived antimicrobial compound.

Tunichromes are tiny peptides found in a number of tunicate species that include one or more units produced from dehydrodopa. *In vitro* crosslinking capabilities are inherent when tunichromes derived from *Ascidia nigra* [Figure 5] hemocytes are incubated under oxidative circumstances. In addition, three tunichromes (An-1, An-2, and An-3) have been identified from *A. nigra* blood cells. When it comes to the gram-positive human pathogen *Enterococcus*

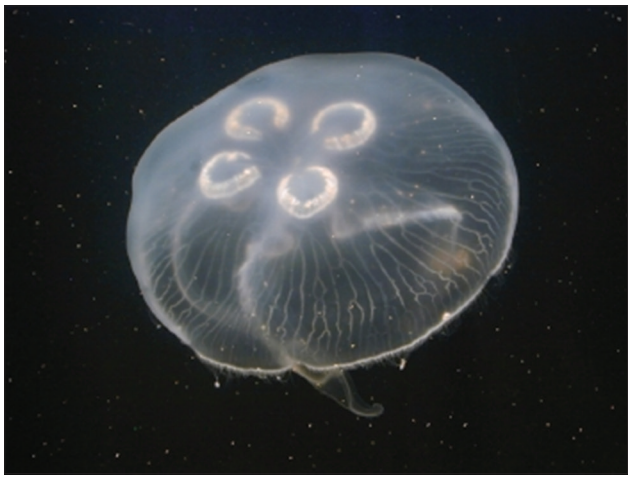

Figure 2: Scyphoid Jellyfish (*Aurelia aurita*)

Figure 3: Polychaete (*Arenicola marina*)

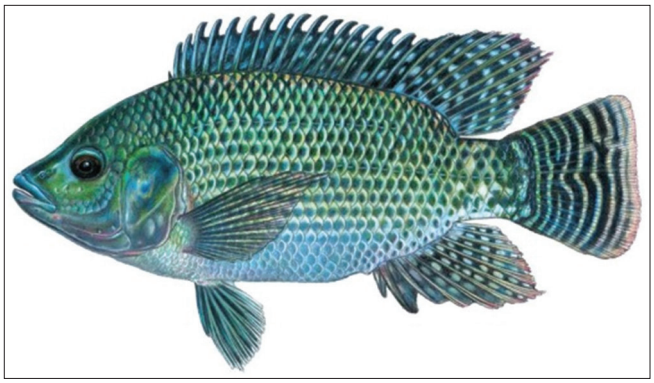

Figure 4: Tilapia (*Oreochromis mossambicus)*

Figure 5: *Ascidia nigra*

Figure 6: Giant mud crab (*Scylla serrata*)

Figure 7: Red sea sponge (*Theonella swinhoei*)

spp., tunichromes exhibit strong (minimum inhibitory concentration [MIC] = 0.1 μg/mL), comparatively selective action.

Marine-derived bioactive peptides have also been isolated from *Oreochromis mossambicus* (Tilapia) [Figure 4], which has been extensively investigated for its antioxidant peptide hydrolysates. Scygonadin is an anionic antimicrobial peptide that was recently discovered in the seminal plasma of gigantic mud crabs (Scylla serrata) [Figure 6]. This molecule inhibited the growth of *Micrococcus luteus* and exhibited no homology to any other protein in databanks. Scygonadin shown action against Streptococcus pyogenes (MIC = 25–50 μg/mL), *P. aeruginosa* (MIC = 12.5–25 μg/mL), *S. aureus* (MIC = 50–100 μg/mL), and *Escherichia coli* (MIC = 25–50 μg/mL).[9]

A new antimicrobial peptide with 55 amino acid residues was extracted from *Mytilus coruscus* hemolymph using reverse-phase high-performance liquid chromatography. The biological characteristics of a peptide called NKLP27, which is produced from tongue sole (*Cynoglossus semilaevis*) NK-lysin, were investigated in this work. The 27 amino acids that make up NKLP27 have minimal sequence similarity to known NK-lysin peptides. Both Gram-positive and Gram-negative bacteria, including common aquaculture pathogens, are susceptible to the bactericidal action of NKLP27.[10]

The polar percentage of the Red Sea sponge (*Theonella swinhoei*) organic extracts [Figure 7]. Theonellamide G, a novel bicyclic glycopeptide, was obtained through successive chromatographic separations and ultimate HPLC purification of the strong antifungal fraction. Theonellamide G. demonstrated potent antifungal efficacy against both amphotericin B-resistant and wild strains of *Candida albicans*.[11]

Antiviral peptides

Marine sponges are among the earliest multicellular invertebrates and represent a rich source of bioactive natural products. Approximately 8,000 sponge species are known from marine and freshwater habitats, producing diverse secondary metabolites as chemical defenses against pathogens and predators. More than 5,300 natural compounds have been identified from sponges and their associated microorganisms, highlighting their significant potential in drug discovery.[12]

Compounds isolated from the marine sponge *Tethya crypta* [Figure 8]. Their discovery subsequently contributed to the development of two important therapeutic agents, Ara-C (cytarabine), an anticancer drug, and Ara-A (vidarabine), the first antiviral drug derived from a marine source. However,

its clinical use and commercial availability were later discontinued due to its lower efficacy and higher toxicity compared to newer antiviral agents such as acyclovir (Zovirax).[13]

Mycalamide A and B were isolated from a New Zealand sponge belonging to the genus Mycale, and their *in vitro* antiviral activity was documented in 1988 and 1990, respectively. It was discovered that the crude extract with 2% mycalamide A was effective against the A59 coronavirus. In addition, the Type I polio and herpes simplex viruses were suppressed by mycalamide A.[14]

Theopapuamides A–C demonstrated potent antifungal activity against both wild-type and amphotericin B-resistant strains of *C. albicans* at concentrations of 1–5 µg/disk. In addition, these compounds exhibited cytotoxic effects against HCT-116 human colon cancer cells, with IC_{50} values ranging from 2.1 to 4.0 µg/mL. The findings highlight the strong anti-*C. albicans* and anticancer potential of theopapuamides isolated from marine sponge sources.[14]

Cytotoxic peptides

Marine-derived cytotoxic and antitumor peptides exhibit remarkable diversity in terms of molecular size, amino acid composition, and structural complexity. Based on their structural characteristics, these peptides are generally classified into four major categories: linear peptides, linear depsipeptides, cyclic depsipeptides, and marine protein hydrolysates. The unique structural features of these compounds contribute significantly to their biological and pharmacological activities.[15]

In recent years, extensive research has focused on the isolation, structural characterization, and pharmacological evaluation of marine cytotoxic peptides. A number of these compounds have demonstrated potent *in vitro* and *in vivo* anticancer activity against various human cancer cell lines, highlighting the immense therapeutic potential of marine BPs in oncology research and drug development.

Figure 8: Marine sponge (*Tethya crypta)*

Antioxidative activity

Antioxidants protect cells from oxidative damage caused by reactive oxygen species (ROS), which can damage DNA, proteins, and lipids and contribute to chronic diseases, including cancer. By reducing oxidative stress, antioxidants help prevent genetic alterations associated with carcinogenesis and support cellular protection.[16]

Marine-derived BPs, particularly fish protein hydrolysates obtained from sources such as tilapia, have demonstrated considerable antioxidant potential. These peptides exhibit the ability to scavenge ROSs and effectively reduce ferric ions, thereby minimizing oxidative damage within biological systems. Such properties indicate their potential application as natural antioxidant agents in functional foods and pharmaceutical formulations.[16]

The antioxidant efficacy of marine protein hydrolysates has been found to be comparable with that of protein hydrolysates derived from other sources. For instance, enzymatic hydrolysates of casein have shown a remarkable capacity to scavenge ROSs. Similarly, soy and wheat protein hydrolysates have also demonstrated significant DPPH radical scavenging activity. These findings suggest that marine BPs may serve as promising natural antioxidants with potential therapeutic and nutraceutical applications.[16]

Antioxidant activity has been demonstrated in protein hydrolysates obtained from the skin gelatin of flying squid (*Ommastrephes bartramii*, Figure 9), tuna (*Thunnus spp*., Figure 10), and jumbo flying squid (*Dosidicus gigas*). These gelatin-derived peptides are rich in hydrophobic amino acids, which contribute to their strong antioxidant properties and emulsifying capacity.[15]

It has been demonstrated that the muscle hydrolysates of horse mackerel (*Magalapsis Cordyla*) [Figure 11] and croaker (*Otolithes ruber*, *Nemipterus japonicus*, and *Exocoetus volitans*) [Figure 12] exhibit antioxidant activity by scavenging free radicals and ROSs.[15]

Protein hydrolysates from umbrella collagen from jellyfish (*Rhopilema esculentum*) and protein isolates from Channel

Figure 9: Flying squid (*Ommastrephes batramii*)

Figure 10: Tuna (*Thunnus* spp.)

Figure 11: Horse mackerel (*Magalapsis cordyla*)

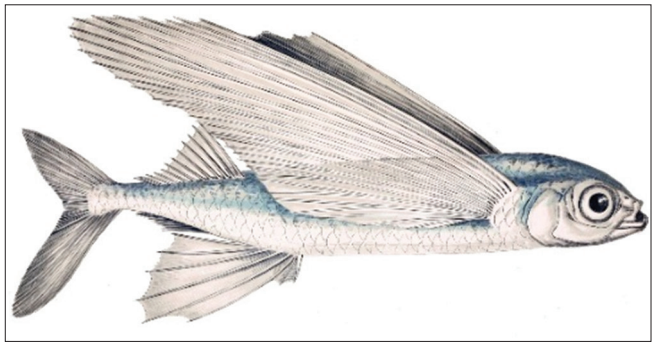

Figure 12: Blue flying fish (*Exocoetus volitans*)

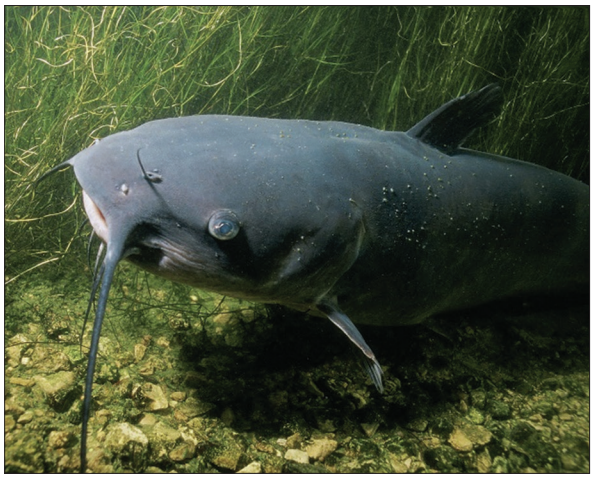

Figure 13: Channel catfish (*Ictalurus punctatus*)

catfish (*Ictalurus punctatus)* [Figure 13] have demonstrated antioxidant activity according to several techniques.[15] Muscle hydrolysates obtained from *Nemipterus japonicus* (Japanese threadfin bream) [Figure 14] have demonstrated significant antioxidant activity by scavenging free radicals.

Enzymatically produced flying squid gelatin hydrolysate exhibited strong antioxidant activity, surpassing butylated hydroxyanisole and α-tocopherol in DPPH radical scavenging. Its antioxidant potential is attributed to amino acids such as histidine, tyrosine, proline, alanine, and leucine, with activity influenced by specific amino acid sequences, histidine content, and peptide hydrophobicity.

Antiproliferative activity

By preventing protein synthesis *in vitro*, didemnin depsipeptides are lethal to cancer cell types. Given the association between inhibiting protein synthesis in cell lysates and in human adenocarcinoma MCF-7 cells, it is hypothesized that Didemnins' binding to the ribosome-EF-1α complex may decrease protein synthesis. Research using Jaspamide in the human leukemia cell line HL-60 showed that nanomolar quantities of this depsipeptide enhanced polynuclear cells and inhibited cell proliferation.[15]

Nevertheless, very little research has been done on the antiproliferative properties of marine proteins. On MCF-7/6 and MDA-MB-231 cell lines, hydrolysates from three blue whiting, three cod, three plaice, and one salmon were found to be substantial growth inhibitors. In BALB/c mice, an enzymatic protein hydrolysate of oysters demonstrated potent immune-stimulating effects by inhibiting the growth of transplantable sarcoma S180 in a dose-dependent manner.

It is also necessary to isolate and identify the particular peptide sequences that are in charge of the antioxidative and anticancer activities. Low molecular weight peptides are thought to have more molecular mobility and diffusivity than large molecular weight peptides, which seems to promote interactions with components of cancer cells and boost anticancer efficacy. However, a study on the mechanism of action found that peptide hydrophobicity modification is essential in combating cancer cells. However, more research is required to understand how the antiproliferative peptides affect the cell cycle of both normal and altered cells, how the BPs are structured, and how these activities are studied *in vivo*.[15]

ACE inhibitory peptides

Hypertension results from increased peripheral vascular resistance, largely mediated by the renin–angiotensin system. ACE converts angiotensin I to the vasoconstrictor angiotensin II, which also promotes aldosterone release and sodium and water retention, leading to elevated blood pressure. Although ACE inhibitors are effective antihypertensive agents, their adverse effects have driven interest in natural and food-derived ACE-inhibitory peptides.[16]

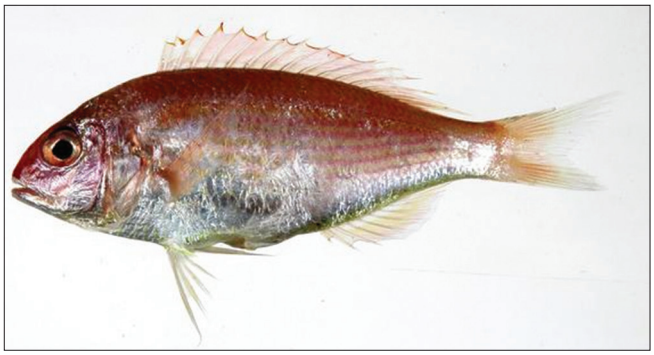

Figure 14: Japanese threadfin bream (*Nemipterus japonicus*)

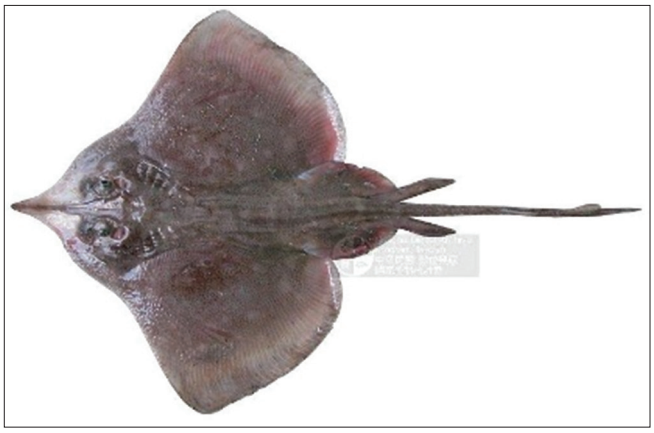

Figure 15: Skate (*Okamejei kenojei*)

Figure 16: Club tunicate (*Styela clava)*

Alcalase, flavorzyme, neutrase, and protamex were used to hydrolyze the skin gelatin of skate (*Okamejei kenojei*) [Figure 15]. ACE inhibitory activity was reported to be highest in the alcalase hydrolysate. Protease was then used to further hydrolyze the alcalase hydrolysate, which was then separated using an ultrafiltration membrane system. Bioactive peptides isolated from the marine tunicate *Styela clava* [Figure 16] have shown promising angiotensin-converting enzyme (ACE) inhibitory activity. Ultimately, MVGSAPGVL (829 Da) and LGPLGHQ (720 Da) were found to be the two peptides responsible for ACE inhibitory activity. The isolated

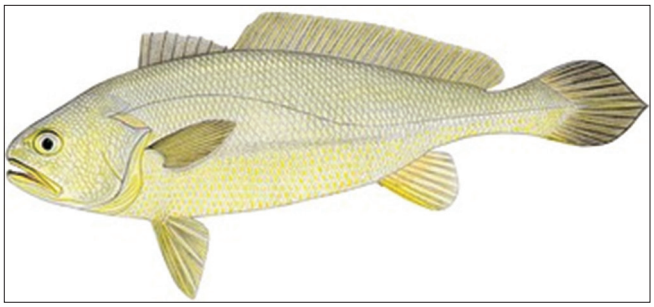

Figure 17: Croceine croaker (*Pseudosciaena crocea*)

peptides' capacity to scavenge free radicals was assessed in human endothelial cells.[17,18]

Cytoprotective peptides

The health benefits of antioxidants are widely recognized. They shield the body from ROS, which cause oxidative damage to DNA, proteins, and membrane lipids. ROS is thought to accelerate the development of Type II diabetes by reducing insulin sensitivity and harming the pancreatic β-cells that produce insulin.[19,20] In actuality, cancer and death can arise from oxygen metabolism and the harmful chemicals that follow. The field of cancer prevention is seeing an increase in interest in medically relevant antioxidants, and efforts to mitigate the damage produced by ROS are becoming more widely accepted as the foundation for innovative therapeutic methods.[21]

According to certain epidemiological research, including antioxidants in the diet may help prevent the development of cancer.[22] It has been suggested that consuming antioxidants, such as carotenoids, can lower the incidence of head and neck cancer. Patients with Alzheimer's disease (AD) have significant deposits of amyloid β-peptide (Aβ) in their brains. In AD brain regions where Aβ is prevalent, free-radical oxidative damage, specifically of neuronal lipids, proteins, and DNA, is widespread. These findings may be related, according to a recent study, and it is hypothesized that oxidative stress caused by Aβ causes neurodegeneration in the AD brain. According to this theory, free-radical antioxidants prevent Aβ from causing neuronal lipid peroxidation, protein oxidation, and DNA oxidation.[23]

Hydrolysate peptides from oysters (*Crassostrea talienwhanensis*) were examined for their antioxidative potential [Figure 18]. Following subtilisin hydrolysis, an orthogonal design and a hydroxyl radical scavenging reaction were used to assess the yields of the peptides that were soluble in trichloroacetic acid-soluble and the antioxidant activity of the resultant hydrolysate.[24,25]

Enzymatic hydrolysis of gelatin from Japanese flounder skin produced the antioxidant peptide Gly-Gly-Phe-Asp-Met-Gly (582 Da), which effectively scavenged intracellular ROS, protected DNA, proteins, and lipids from oxidative

Figure 18: Oysters (*Crassostrea talienwhanensis*)

Figure 19: Japanese flounder (*Paralichthys olivaceus)*

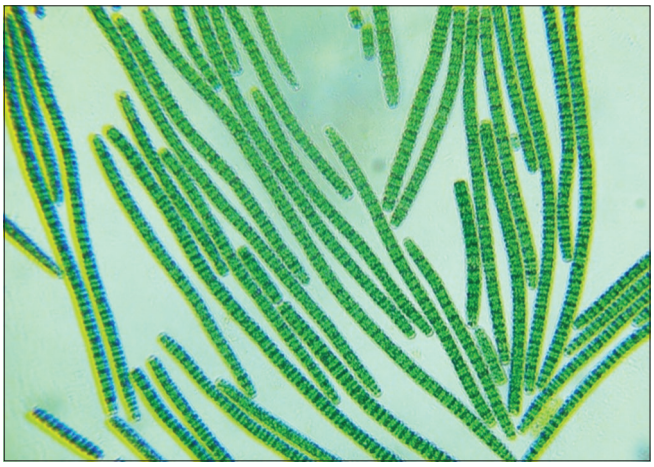

Figure 20: *Spirulina maxima*

damage, and enhanced endogenous antioxidant enzymes such as glutathione, catalase, and superoxide dismutase. These findings highlight Japanese flounder skin as a valuable source of antioxidant BPs.[26] Antioxidant peptides derived from the skin gelatin of *Paralichthys olivaceus* (Japanese flounder) [Figure 19] effectively scavenge reactive oxygen species and protect against oxidative damage.

Cardiovascular protective peptides

Marine BPs contribute to cardiovascular health through anticoagulant and antiplatelet activities. A 12.01 kDa protein, named YAP, isolated from yellow fin sole (*Limanda aspera*), inhibited activated coagulation factor XII (FXIIa) and reduced platelet aggregation by targeting platelet integrins, demonstrating its potential as a cardiovascular protective peptide.[27] Peptides isolated from *Pseudosciaena crocea* (Croceine croaker) [Figure 17] have exhibited antioxidant and cytoprotective properties.

Two BPs, P1 (LDAVNR; 686 Da) and P2 (MMLDF; 655 Da), isolated from enzymatic hydrolysates of *Spirulina maxima*, exhibited anti-atherosclerotic activity by suppressing inflammatory mediators (MCP-1 and IL-6), reducing endothelial adhesion molecule expression, inhibiting monocyte adhesion, and decreasing intracellular ROS generation.[28,29] Enzymatic hydrolysates of *Spirulina maxima* [Figure 20] have yielded bioactive peptides with anti-atherosclerotic and cardiovascular protective activities.

Immunomodulatory peptides

BPs can be released from dietary proteins through fermentation, with fish proteins representing an important yet underutilized source. Marine-derived peptides exhibit anti-inflammatory and immunomodulatory activities; for example, thalassospiramides A and D inhibit nitric oxide production, while peptides from chum salmon and shark proteins enhance immune responses by stimulating lymphocyte proliferation, natural killer cell activity, and T-cell function.[30,31]

Neuropeptides

They can be used as a safe, natural substitute for opioid medications, which are typically linked to addiction, tolerance, and dependency. Hagfish have been found to have the gonadotropin-releasing hormone, which boosts pituitary gonadotropin output.[32,33]

There have been reports of proopiomelanocortin-derived hormones (such as corticotropin, melanotropin, etc.) from snakeskin gourami (*Trichopodus pectoralis*) [Figure 21][34] and a neuropeptide in marine annelid (*Platynereis dumerilii*) [Figure 22].[35]

Proteins and peptides appear to have a neuro-protective effect through directly interacting with a variety of cellular and molecular targets through enzyme/ion channels.[36] In many nations, *Hippocampus trimaculatus* [Figure 23] is one of the most traded seahorse species for use in traditional medicine. A peptide produced from *H. trimaculatus* has

Figure 21: Snakeskin gourami (*Trichopodus pectoralis)*

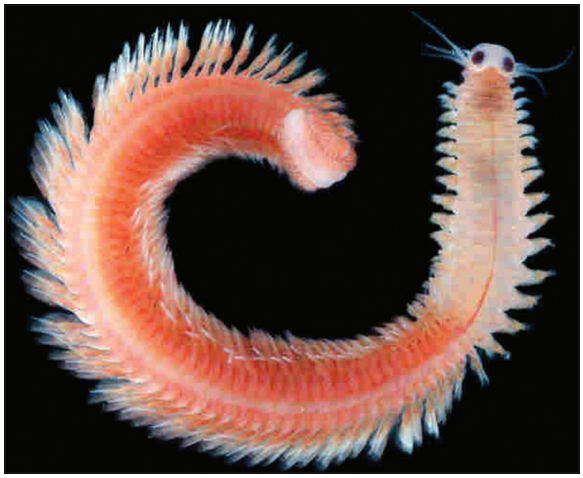

Figure 22: Marine annelid (*Platynereis dumerilii*)

Figure 23: Sea horse (*Hippocampus trimaculatus*)

been shown to have neuroprotective properties against amyloid-β42 (Aβ42) toxicity, which is a key factor in the pathophysiology of AD.[37]

Rat cholinergic neuronal death caused by Aβ1–42 was successfully prevented by fucoidan isolated from *Fucus vesiculosus* [Figure 24]. Pretreatment with fucoidan inhibited caspase-3 and caspase-9 activation. The terminal phases of neuronal apoptosis have been proposed to be mediated by caspase-9 and

Figure 24: Fucoidan (*Fucus vesiculosus*)

Figure 25: Algae (*Bryothamnion triquetrum)*

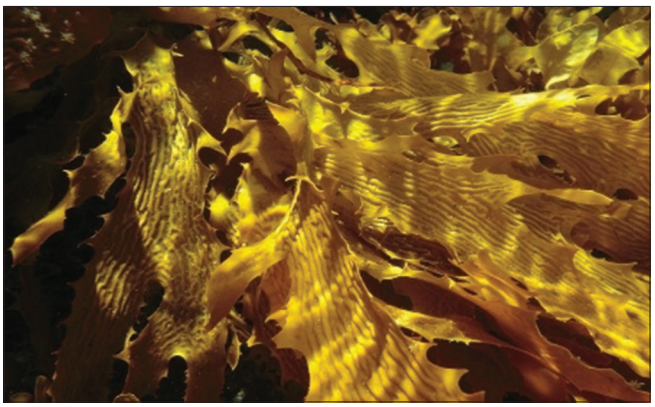

Figure 26: Brown algae

caspase-3. Two of the key elements of the apparatus in charge of apoptosis are caspase-9 and caspase-3. Thus, fucoidan's capacity to prevent caspase-9 and caspase-3 from activating suggests that apoptotic inhibition is the primary mechanism by which fucoidan inhibits neuronal death. Apoptosis may be detrimental in neurodegenerative disorders, and neurodegenerative diseases may be lessened by focusing on this process.[38,39]

Table 1: Marine peptide products in market and clinical trials[42-53]

Compound	Category	Marine source	Therapeutic/commercial application	Current status
Ziconotide	Natural marine peptide	ω-conotoxin isolated from *Conus magus*	Used as a potent analgesic agent for pain management	Approved by the FDA
Brentuximab vedotin	Semi-synthetic derivative	Derived from dolastatin-10 obtained from *Dolabella auricularia*	Employed in cancer chemotherapy	FDA approved
Glembatumumab vedotin	Synthetic derivative	Developed from dolastatin-10 of *Dolabella auricularia*	Investigated for anticancer activity	Under Phase I/II clinical evaluation
Katsuobushi oligopeptide	Natural peptide product	Pentapeptide produced from dried bonito hydrolysate	Utilized for antihypertensive benefits	Commercially available as a nutraceutical
Dermachlorella	Natural oligopeptide extract	Extracted from *Chlorella vulgaris*	Applied in cosmetic formulations as a skin-firming and toning ingredient	Marketed as a skincare product
Plitidepsin	Naturally occurring depsipeptide	Obtained from *Aplidium albicans*	Investigated for anticancer therapy	In Phase I/II clinical studies
HTI-286	Synthetic derivative	Derived from hemiasterlin isolated from *Hemiasterella minor*	Evaluated for cancer treatment applications	Under preclinical investigation
Kahalalide-F	Natural cyclic tridecapeptide	Isolated from *Elysia rufescens*	Explored for antineoplastic activity	Phase I clinical trials
Elisidepsin	Peptide derivative	Developed from kahalalide-F of *Elysia rufescens*	Studied as an anticancer compound	In Phase I clinical trials
Fish gelatine	Natural marine hydrolysate	Produced from fish collagen and gelatine	Used as a nutritional supplement to support bone health	Commercial nutraceutical product
Gabolysat PC 60/Stabilium/ Protizen/Procalm	Natural peptide preparations	Fish protein hydrolysates	Utilized for anxiolytic and stress-relieving effects	Sold as nutraceutical formulations
Seacure	Natural peptide supplement	Hydrolyzed fish protein	Promotes gastrointestinal and intestinal health	Commercially available nutraceutical
Nutripeptin/hydro MN peptides	Natural bioactive peptides	Derived from fish protein hydrolysates	Helps regulate postprandial blood glucose levels	Sold as nutraceutical products

FDA: Food and drug administration

Anti-diabetic peptide

It is extremely important to discover novel treatment medicines to enhance glucose metabolism and prevent and suppress problems associated with Type-2 diabetes mellitus. Due to the presence of biologically active components, marine algae are widely used and abundant dietary ingredients, particularly in Asian nations. They are also well known for their positive health effects. Marine polyphenols and phlorotannins are among the physiologically active components of marine algae that have been investigated. Marine red algae such as *Bryothamnion triquetrum* [Figure 25] have been investigated as promising sources of bioactive compounds with potential antidiabetic properties. Brown algae [Figure 26] are maritime algae that have been thoroughly investigated for their possible anti-diabetic properties.[40]

The majority of studies on phlorotannins derived from brown algae have demonstrated their various anti-diabetic mechanisms, including the inhibition of α-glucosidase and α-amylase, the improvement of insulin sensitivity in Type 2 diabetic mice, the inhibition of protein tyrosine phosphatase 1B (PTP 1B) enzyme, and the protective effect against diabetes complications.[41] Selected marine peptide products available in the market and those under clinical evaluation are summarized in Table 1.

CONCLUSION

The marine environment has emerged as a prospective source of medicinal medicines, chemicals, and natural products. Approximately half of the world's biodiversity is found in marine species, which are also a vast and priceless source

of naturally occurring bioactive compounds. The potential for producing more innovative items from the water is considerable due to its vast diversity of organisms and virgin areas of marine life. In-depth research on the protein hydrolysates will help create new bioactive substances. The waters are now recognized as a possible source of novel therapeutic leads due to scientific and commercial curiosity. Researchers have developed a wide range of medications, the most significant of which are antivirals, analgesics, anti-inflammatory, and anticancer. Globally, these lead compounds are undergoing various phases of preclinical and clinical research. Numerous medications derived from marine sources show promise in treating a number of chronic and incurable illnesses, including cancer. They might pave the way for more effective and affordable chronic illness therapy. Marine peptides may find use in the pharmaceutical industry due to their wide range of bioactivities, which include antimicrobial, antiviral, antitumor, antioxidative, cardioprotective (antihypertensive, antiatherosclerotic, and anticoagulant), immunomodulatory, analgesic, anxiolytic, anti-diabetic, appetite suppressing, and neuroprotective properties. The outcomes of preclinical and clinical research are crucial for the marketing and economic exploitation of promising marine natural products with therapeutic benefits after they have been identified, extracted, and produced on a wide scale. A big and quick random screening method should be used in addition to the present screening for active natural compounds. Numerous universities and research centers are working in this subject to create new materials and educate workers. For medication research, approvals, and launches, the technology should be optimally targeted. To aid our nation in the production of novel drugs, Indian medical pharmacologists ought to think about conducting additional studies in marine pharmacology. The development of marine pharmacology as a specialty in India would enable us to make the best use of the abundant marine resources found across our stunning nation, which is endowed with a long, three-sided coastline.

AUTHORS' CONTRIBUTIONS

Mitali M. Bodhankar: data collection, data review, manuscript review, and supervision; Pranali S. Band: data compilation and original draft preparation; Shubham S. Gupta: data compilation, and original draft preparation; Snehal J. Shrivastav: data collection and manuscript review. All authors have read and agreed to the published version of the manuscript.

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