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Review Article

Marine bioactive peptides with anticancer potential, a narrative review

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Abstract: In this paper, we explore marine bioactive peptides with anticancer potential sourced from various marine organisms, including tunicates, sea sponges, and mollusks. Peptides like Stylisin and Papuamides have been isolated, identified, and modified to enhance their activity, with many advancing to clinical trials due to their diverse biological activities, promising prospects in medicine. Enzymatic hydrolysis is a favored method for extracting peptides from marine proteins, particularly from sponges known for their rich bioactive compounds. Compounds such as Jaspamide and Homophymins exhibit potent cytotoxic activity against cancer cells, underscoring their therapeutic potential. Additionally, peptides from ascidians and mollusks, such as Aplidine and Kahalalide F, demonstrate significant anticancer properties. This study also explores peptides influencing apoptosis, microtubule dynamics, and angiogenesis, providing insights into potential mechanisms for cancer treatment. While peptides like Neovastat and mycothiazole target known pathways, others such as patellamides act through unknown mechanisms, highlighting the intricate interactions of marine peptides with cancer cells. Overall, marine-derived peptides show promise as valuable candidates for developing novel anticancer therapies.

Keywords: Marine bioactive peptides, anticancer potential, enzymatic hydrolysis, cytotoxic activity, apoptosis, angiogenesis inhibition

Introduction

Seventy percent of the Earth's surface is covered by seas, which host a biodiversity significantly richer than that found on land, encompassing about 75% of all living organisms. The marine environment is widely recognized as a fertile reservoir of natural products with extensive therapeutic applications. Investigating the regulatory roles of various endogenous peptides in organisms involves studying the molecular mechanisms through which bioactive peptides derived from natural sources act on specific target cells. Efforts to harness peptides for drug development have shown promising advancements in treatment strategies. Recently, marine peptides have emerged as a burgeoning frontier in pharmaceutical research [1].

Marine bioactive peptides are short sequences of amino acids derived from marine organisms, which exhibit a range of biological activities beneficial for health. These peptides have been found to possess various bioactive properties, including antioxidant, antimicrobial, anti-inflammatory, antihypertensive, and anticancer effects [2]. They function by interacting with cellular receptors, enzymes, and ion channels to modulate physiological processes. The main sources of marine bioactive peptides include fish, shellfish, algae, and marine microorganisms. These peptides are typically obtained through enzymatic hydrolysis of marine proteins, fermentation processes, or direct extraction from marine organisms [3]. The unique marine environment contributes to the distinctive structures and potent activities of these peptides, making them valuable for pharmaceutical, nutraceutical, and functional food applications [4].

Peptides derived from marine organisms induce cell death through various mechanisms,

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including apoptosis, modulation of tubulin-microtubule balance (anti-microtubule activity), vascular inhibition, anti-proliferative effects, and cytotoxicity. These findings have significantly expanded our understanding of the novel capabilities of marine peptides in combating toxicity. Recognition of many other properties has led to the discovery of new chemical structures and the primary mechanisms of activity of these peptides in pharmaceuticals [2]. These developments position marine peptides as promising candidates for discovering new compounds in biomedical research. In the developing world, cancer has emerged as a leading cause of death. Certain DNA mutations disrupt planned regulatory processes and contribute to cancer development. Carcinogenesis involves the transformation of normal cells into cancerous cells, characterized by progressive genetic and molecular changes that drive uncontrolled cell division. Consequently, malignant tumors form and have the potential to metastasize to distant sites [5].

In recent years, there has been a growing emphasis on bioactive peptides sourced from marine food sources, obtained either through natural means or enzymatic processes. These peptides not only provide nutritional benefits but also demonstrate significant physiological effects on bodily functions and growth. Marine organisms such as sponges, bacteria, dinoflagellates, and seaweeds harbor a wide array of chemical components, including phenols, alkaloids, terpenoids, polyesters, and other secondary metabolites. The diversity of these compounds contributes to the bioactivity observed in marine-derived peptides [6].

The marine environment boasts higher biological diversity compared to terrestrial ecosystems, prompting increased research into the medicinal potential of marine products. Over evolutionary time, marine organisms have developed sophisticated physiological and biochemical systems to thrive in challenging conditions such as darkness, cold temperatures, and high pressures. Notably, marine invertebrates and bacteria are prolific producers of secondary metabolites known for their diverse beneficial effects, including anti-inflammatory, anti-cancer, and antibiotic properties [7]. These characteristics underscore the potential of marine-derived compounds, including bioactive peptides, as valuable resources for developing new therapeutic agents in medicine and biotechnology.

Numerous bioactive peptides and depsipeptides showing potential anticancer properties have been extracted from diverse marine organisms such as tunicates, sponges, molluscs, and others. Some of these compounds are currently progressing through various phases of clinical trials, while others like Aplidine have already reached commercial availability. The use of marine-derived compounds in medicine represents a promising frontier and remains a focal point of extensive research and development [8].

Bioactive peptides sourced from marine organisms exhibit a broad spectrum of activities, including regulation of the immune system, antimicrobial effects, antioxidant properties, anticoagulant activity, hypocholesterolemic effects, and antihypertensive properties. This article provides a comprehensive review of recent studies focusing on marine peptides and explores the latest prospects for developing new compounds. The primary objective is to discover more drugs with therapeutic applications, particularly in the realm of cancer treatment. The potential for marine peptides to serve as valuable pharmaceutical agents is a subject of considerable interest and holds substantial promise for future medical advancements.

Sources of bioactive marine peptides

Various peptides with significant biological activities have been successfully extracted from a range of marine organisms, particularly tunicates, sea sponges, and molluscs. Recent studies have identified diverse groups of bioactive peptides from these sources, such as Stylisin from the Stylissa caribia sponge and Papuamides from the Melophelus sponge found in the Solomon Islands. These compounds have been isolated, characterized, and subject to modifications aimed at enhancing their activity, including the development of analogs with improved properties [8]. Among the investigated bioactive peptides and depsipeptides, several have progressed to various stages of clinical trials. Many of these compounds exhibit multiple biological activities, making them promising candidates for enhanc-

ing health and treating a variety of diseases. The exploration of marine-derived bioactive peptides presents exciting potential for developing novel therapeutic agents with diverse applications in medicine [2].

In recent years, there has been considerable interest in exploring the structural characteristics, composition, and sequence-related properties of bioactive peptides derived from marine organisms. Three primary methods are typically used to produce marine bioactive peptides: solvent extraction, enzymatic hydrolysis, and microbial fermentation of marine proteins. Enzymatic hydrolysis, in particular, is highly favored in the food and pharmaceutical industries due to its ability to generate peptides without residual organic solvents or toxic chemicals [9]. The ocean hosts a vast diversity of sponges, with approximately 100,000 species found worldwide. Among these, 11 genera have been identified as rich sources of biologically active compounds. Notably, genera such as Petrosia, Discodermia, and Haliclena are known for yielding effective anti-cancer and anti-inflammatory compounds. Extensive research has focused on bioactive peptides derived from sponges, particularly cyclo depsipeptides, which are secondary metabolites featuring uncommon amino acids and non-amino acid components. These compounds exhibit a wide range of biological activities. However, their isolation in sufficient quantities for drug testing remains a significant challenge. Nevertheless, ongoing research efforts are dedicated to overcoming these challenges and unlocking the full potential of marine-derived bioactive peptides for pharmaceutical applications [10].

Marine bioactive peptides employ several pathways to combat cancer cells, leveraging their diverse biological activities to inhibit tumor growth and promote cancer cell apoptosis. One primary mechanism involves inducing apoptosis through the mitochondrial pathway, where peptides trigger the release of cytochrome c, leading to the activation of caspases that orchestrate cell death [11]. Additionally, some peptides can enhance the expression of pro-apoptotic proteins like Bax and downregulate anti-apoptotic proteins such as Bcl-2, further tipping the balance towards cell death in cancerous cells. These apoptotic pathways are crucial as they selectively target and eliminate cancer cells while sparing normal cells, reducing potential side effects [12].

Another significant pathway involves the inhibition of angiogenesis, the process by which new blood vessels form to supply nutrients to tumors. Marine bioactive peptides can interfere with angiogenic factors like vascular endothelial growth factor (VEGF), thus starving the tumor of essential nutrients and oxygen needed for its growth. Additionally, these peptides may disrupt cell signaling pathways such as the PI3K/Akt and MAPK pathways, which are often overactive in cancer cells, leading to unchecked proliferation and survival. By modulating these pathways, marine peptides help suppress tumor growth and enhance the efficacy of existing cancer therapies [13].

Previous studies have substantiated the anticancer potential of marine bioactive peptides, demonstrating their effectiveness in various in vitro and in vivo models. For instance, research has shown that peptides derived from marine sponges, sea cucumbers, and fish can significantly inhibit cancer cell proliferation and induce apoptosis [14]. Ongoing research aims to further elucidate the molecular mechanisms underlying these effects and to optimize the extraction and utilization of these peptides. These efforts are critical for developing new, more effective anticancer therapies that leverage the unique properties of marine-derived compounds.

Jaspamide is a cyclic depsipeptide obtained from Jaspis and Hemiastrella sponges. It features a large 15-carbon ring comprising 3 amino acids. Extensive research has confirmed that Jaspamide is a bioactive compound capable of inducing apoptosis in human promyelocytic leukemia cells HL-60. Additionally, nine novel cyclic depsipeptides, namely Homophyminics B-E and A1-E1, have been isolated from the sponge Hamophymia [15]. These newly discovered compounds exhibit potent cytotoxic activity, with IC50 values in the nanomolar range. This remarkable activity has been observed against various types of human cancers. Furthermore, among these cyclic depsipeptides, Homophymins A1-E1, characterized by a 4-amino acid-6-carbamoyl-2,3-dihydroxyhexanoic acid core, demonstrate higher potency compared to the corresponding compounds A-E, which have the same core but in a carbox-

ylic form. These findings underscore the importance of the structural configuration in determining the cytotoxic efficacy of these compounds. Such research not only enhances our understanding of the potential therapeutic value of marine-derived cyclic depsipeptides but also opens new avenues for the development of novel and effective anti-cancer treatments.

Geodiamolide H is a compound extracted from the sponge Geodia Corticostylifera, exhibiting antiproliferative activity against breast cancer cells. Its mechanism of action involves inducing changes in the cytoskeleton actin of the cells. Discodermins tetradecapeptides, obtained from the sponge Discodermia sp., represent another group of cytotoxic peptides. Tests on these peptides, specifically Discodermin A-H, were performed against A549 human lung cell line and p388 mouse leukemia cells [16]. All of them exhibited cytotoxic properties, demonstrating their potential as anticancer agents. Arenastatin A is a cyclic depsipeptide isolated from Dysida arenaria, showing strong cytotoxic properties against KB cells, which are human cervical carcinoma cells. Papoamides A-D are bioactive peptides isolated from Theonella genus sponges. Among them, papoamides A and B have been proven to inhibit the infection of human T lymphocyte cells by HIV in vitro, indicating their potential for antiviral therapy. Phakellastatin is a bioactive compound isolated from the sponge Phakellia carteri. It has been found to inhibit the growth of leukemia cells [16]. A related compound, phaclastatin 13, was derived from the sponge Phakellia fusca and has exhibited cytotoxic properties against human liver tumor BEL-7404 cells [17]. The discovery and research of these marine-derived bioactive peptides offer promising avenues for the development of novel and effective treatments for various diseases, particularly cancer and viral infections. Further exploration of these compounds may lead to the development of valuable pharmaceutical agents in the future.

Tunicates and ascidians

Bioactive peptides with unique structures have been discovered in ascidians, some of which inhabit the ocean floor. These organisms produce a complex anti-tumor compound that surpasses the potency of existing anti-cancer agents. One notable example is didemnin, initially isolated from the Caribbean tunicate Tridemnum solidum and subsequently found in other species within the same genus [17]. Among these compounds, Didemin B stands out for its profound anti-tumor activity and ability to inhibit the proliferation of human prostate cancer cells by blocking the synthesis of DNA, RNA, and proteins. The compelling results from preclinical studies, including dose-dependent effects and tolerance to toxicity, prompted phase I clinical trials, marking Didemnin B as the first marine natural product to undergo such evaluations. However, phase II trials revealed that Didemnin B, when administered at recommended doses, was ineffective against cancer. Attempts to escalate treatment regimens to enhance efficacy resulted in heightened toxicity levels. Despite these challenges encountered in phase II trials, the initial clinical assessment represents a significant milestone in marine natural product research aimed at developing potential anti-cancer therapies.

Aplidine is a cyclic depsipeptide isolated from the tunicate Aplidium albicans, known for its significant anticancer activity against various human cancer cells, including those associated with breast, lung, and skin cancers [18]. Aplidine achieves its effects through multiple pathways, such as cell cycle arrest, inhibition of protein synthesis, and induction of apoptosis in cancer cells. What distinguishes aplidine is its unique cytotoxic mechanism, which involves inhibiting ornithine decarboxylase, a critical enzyme involved in tumor formation and growth. Additionally, aplidine suppresses the expression of genes encoding endothelial vascular growth factors and exhibits anti-inflammatory properties. In phase I clinical trials, aplidine has demonstrated promising antitumor activity, prompting its investigation in phase II trials for the treatment of solid tumors. Tamandarin A and B, also cyclic depsipeptides derived from sea ascidians of the Didemnidae family, have similarly been extensively studied for their effects against various human cancer cells [17]. Mollamide, a cyclic depsipeptide extracted from the ascidian Didemnum molle, displays potent cytotoxic effects against a broad spectrum of cancer cells, including murine leukemia P388, human lung cancer A549, and colon cancer HT29. Another notable com-

Table 1. Peptides with anti-cancer potential extracted from marine organisms

Biological activity	Marine organism	Marine source	Name of the peptide
Anti-tumor-anti-leukemia	Aplidium albicans	Ascidian	Aplidine
Anti-microtubule	Dysidea arenaria	Sponge	Arenastatin A
Antitumor	Dolabella auricularia	Tunic	Aurilide
Antitumor	Tridemnum sp.	Tunic	Didemnin
Anticancer	Dolabella auricularia	Molluscs	Dolastatin
Anti-proliferation	Geodia sp.	Sponge	Geodiamolide H
Antitumor	Homophymia sp.	Sponge	Homophymines.
Anti-proliferation	Jaspis sp., Hemiastrrella sp.	Sponge	Jaspamide
Anti-microtubule	Elysia rufescens, Spisula polynyma	Molluscs	Kahalalide F
Antitumor	Pleurobranchus forskalii	Molluscs	Keenamide A
Anti-proliferation	Didemnum molle	Ascidian	Mollamide
Anti-proliferation	Phakellia carteri	Sponge	Phakellistatins
Antitumor	Didemnum sp.	Ascidian	Tamandarins A and B
Antitumor	Lissoclinum sp.	Ascidian	Trunkamide A

pound, Trankamid A, a cyclic peptide featuring a thiazoline ring similar to Mollamide, is sourced from the genus Lissoclinum. Trankamid A has demonstrated antitumor activity in both laboratory settings and clinical trials. **Tables 1** and **2** provide an overview of peptides derived from marine sources that exhibit potential anticancer properties and detail their respective mechanisms of action. The ongoing research into these marine-derived compounds holds tremendous promise for developing effective cancer treatments.

Molluscs

Molluscs encompass a diverse group of species that hold significant pharmacological potential. Among them, the sea hare produces bioactive metabolites with applications in cancer treatment. One prominent peptide from this source consists of 25 amino acids and features 3 disulfide bonds. Notably, it exhibits remarkable analgesic activity, surpassing the effectiveness of morphine by a thousandfold. Cone snails belonging to the genus Conus represent another valuable source of active peptides known as Conotoxins. These peptides are characterized by short amino acid chains and are rich in disulfide bonds. Several studies indicate that Conotoxins may harbor potential for cancer treatment. Additionally, dolastatin, a family of cytotoxic peptides isolated from the mollusc Dollabella auricularia, has demonstrated highly promising anti-proliferative activity. This compound holds significant potential as an effective cancer treatment [19]. Keenamide A, a cytotoxic cyclic hexapeptide isolated from the mollusk Pleurobranchus forskahii, demonstrates potent antitumor effects, although its specific mechanism of action remains unidentified. This compound exhibits significant activity against various tumor cell lines, including A549, MEL20, P388, and HT29. Another notable group of peptides derived from mollusks is the Kahalalids, isolated from the mollusk Elysia rufescens. Kahalalide F, a peptide within this family, contains dihydro-amino-butyric acid and displays remarkable antitumor activity, particularly against prostate cancer tumors. Research has revealed that Kahalalide F disrupts lysosomal function and induces cell death by intracellular acidification. This mechanism targets cells with high lysosomal activity, such as prostate cancer cells, making Kahalalide F a promising candidate for treatment. Currently, Kahalalide F is undergoing phase clinical trials for prostate, lung, and skin cancers. The diverse range of peptides obtained from mollusks underscores their potential as valuable sources for developing novel and effective cancer treatments. Ongoing research and clinical trials hold promising prospects for leveraging the therapeutic properties of these marine-derived peptides in combatting various types of cancer [19].

Analysis and hydrolysis of marine proteins

In recent years, significant research efforts have focused on isolating bioactive peptides

Table 2. Introduction of peptides obtained from marine sources with anti-cancer potential and their mode of action

Mechanism	Peptide class/type	Marine resources	Name of the peptide
Caspase 3 activation and reduction of Bcl2 protein expression	Depsi cyclic peptide	Sea sponge Jaspis, johnstoni	Jaspamide (Jasplakinolide)
Caspase 8 activation	Lipopeptide	Lyngbya majuscula/Schizothrix sp.	Somocystinamide A (ScA)
Caspase-dependent apoptosis	Tetrapyrrole protein complex	Agmenellum quadruplicatum, Mastigocladus laminosus, Spirulina platensis cyanobacteria	C-phycocyanin (C-PC)
Activation of p38 MAPK, JNK phosphorylation	Depsi cyclic peptide	Aplidium albicans tunicate	Aplidine (dehydrodidemnin B, DDB, Aplidin)
Apoptosis, but the pathway is unclear	Depsi cyclic peptide	Tridemnum solidum tunicate	Didemnin B
Apoptosis, but the pathway is unclear	Depsi cyclic peptide	Sea mushrooms	Sansalvamide A
Apoptosis, but the pathway is unclear	Depsi cyclic peptide	Sea ascidian Lissoclinum bistratum	Cycloxazoline
Apoptosis, but the pathway is unclear	Linear tripeptide	Ascidian Diplosoma virens	Virenamides A-C
Inhibition of tubulin polymerization	Linear peptide	Dolabella auricularia marine molluscs Didemnum sea ascidian	Dolastatin 10
Inhibition of tubulin polymerization	Bicyclic peptide	Polysyncranton and cuculiferum lithostrotum	Vitilevuamide
Inhibition of tubulin polymerization	Cyclic peptide	Sea ascidian Diazona angulata	Diazonamide
Inhibition of tubulin polymerization	Cyclic peptide	Scleroderma nodosum sponge	Scleritodermin A
Inhibition of tubulin polymerization	Tripeptide	Sea sponge Auletta sp. and Siphonochalina sp.	Hemiasterlin
Inhibition of tubulin polymerization	Depsi cyclic peptide	Cyanobacterium Lyngbya majuscula	DMMC
Inhibition of VEGF and HIF 2alpha pathways	Less than KD 500	Shark cartilage Squalus acanthias	Neovastat (AE-941)
Vascular inhibition	Polypeptide	Shark cartilage Prionace glauca	PG155
Unknown	The presence of amide at the end of the c terminal	Ascidian Styela clava	Styelin D
Unknown	Cyclic peptide	Lissoclinum patella ascidian	Lissoclinamides
Unknown	Cyclic peptide	Sponge Geodia sp.	Geodiamolides A-G
Unknown	Cyclic peptide	Sponge Theonella sp.	Orbiculamide A
Unknown	Lactone peptide	Sponge Theonella sp.	Koshikamide B
Unknown	Linear peptide	Clathria (Thalysias) Abietina sponge	Microcionamides A, B
Unknown	Cyclic hexapeptide	Pleurobranchus forskohlii mollusks	Keenamide A
Unknown	Depsi cyclic peptide	Scopulariopsis brevicaulis mushrooms	Scopularides A and B
Unknown	Depsi cyclic peptide	Cyanobacterium Symploca sp.	Symplocamide A
Unknown	Cyclic peptide	Cyanobacteria Lyngbya majuscula and Lyngbya sordida	Apratoxin D
Unknown	Linear peptide	Cyanobacteria Geitlerinema sp.	Mitsoamide

Table 3. Bioactive peptides obtained from the enzymatic hydrolysis of marine proteins with anticancer potential

Biological activity	Amino acid sequence	Enzyme	Source
Antioxidants	Unknown	Trypsin and Flavourzyme	Alaska pollack collagen (Theragra chalcogramma)
Antioxidants	GNRGFACRHA	Pepsin, trypsin and alpha chymotrypsin	Croaker muscle (Otolithes ruber)
Antioxidant, anti-proliferation	Unknown	Trypsin	Flyingfish (Exocoetus volitans)
Antioxidants	NHRYDR	Pepsin, trypsin and alpha chymotrypsin	Horse mackerel muscle (Magalapsis cordyla)
Antioxidants	Unknown	Trypsin and Flavourzyme	Jellyfish umbrella collagen (Rhopilema esculentum)
Antioxidant, antiproliferative and cytotoxic	Unknown	Alcalase and Esperase	Jumbo flying squid, skin gelatin (Dosidicus gigas)
Antitumor	Unknown	Protease	Oyster (Crassostrea gigas)
Anti-proliferation	LPHVLTPEAGATPTAEGGVYMVT	Papain and protease	Tuna dark muscle byproduct (Thunnus tonggol)
Antioxidants	Unknown	Alkalase	Tuna skin gelatin (Thunnus spp)

derived from food proteins. These peptides serve as functional compounds in food that promote health and show potential as therapeutic agents for treating chronic diseases [9]. Interestingly, these peptides are typically inactive within the parent protein and require enzymatic or other forms of hydrolysis to be released and exert their beneficial effects. Most bioactive peptides are composed of amino acids, with some reported to exceed 20 amino acids in length [20]. Protein hydrolysis is a widely used method to extract peptides from protein-rich food sources, offering various biological activities such as antioxidant, blood pressure-lowering, antimicrobial, and anticancer properties. Among the hydrolysis methods, enzymatic hydrolysis is preferred due to its ability to operate under controlled pH and temperature conditions, minimizing the production of undesirable products. In contrast, alkaline hydrolysis at high pH levels can lead to racemization and degradation of specific amino acids, and acid hydrolysis may completely degrade amino acids like tryptophan, asparagine, and glutamine into their constituent parts [11]. Thus, enzymatic hydrolysis stands out for its efficiency and selectivity in producing bioactive peptides from food proteins while preserving their beneficial properties. Digestive and microbial proteases, including alkalases, trypsin, pepsin, and chymotrypsin, are widely utilized enzymes for protein hydrolysis. Research indicates that enzymatic hydrolysis can significantly enhance the antioxidant activity of peptides by increasing their ability to scavenge free radicals. The biological activity of peptides derived from protein hydrolysis depends crucially on their molecular weight and specific amino acid sequence. As a result, enzymatic hydrolysis of food proteins is recognized as an effective method for extracting potentially bioactive peptides, some of which may hold promise as anti-cancer agents [20]. Bioactive peptides with potential anti-cancer properties, such as anti-proliferative and antioxidant effects, have been discovered in hydrolyzed products of marine proteins. Marine by-products obtained through enzymatic hydrolysis, such as fish bones, shrimp by-products, and fish heads, have been identified as rich sources of these biologically active peptides. Peptides derived specifically from fish intestines and Sardinelle fish by-products have demonstrated particularly high antioxidant activity [21]. These findings underscore the importance of enzymatic hydrolysis in unlocking the therapeutic potential of marine protein by-products for various health applications, including potential treatments for cancer. Enzymatic hydrolysis of collagen and gelatin has proven effective in producing bioactive peptides, particularly from sources like Scomberoid fish skin, which demonstrate significant antioxidant activity. **Table 3** offers an overview of bioactive peptides derived from the enzymatic hydrolysis of marine proteins, highlighting their potential anti-cancer properties alongside their amino acid sequences and sources. These findings underscore the promising potential of marine-derived peptides as valuable candidates for the development

of novel and effective anti-cancer treatments [12].

Conclusion

The potential of marine peptides to contribute significantly to the discovery of anti-cancer drugs is indeed promising. Extensive research has already highlighted that peptides derived from the hydrolysis of marine proteins exhibit noteworthy antioxidant, anti-proliferative, and anti-mutagenic properties, positioning them as promising candidates for combating cancer. Ongoing clinical trials focused on marine peptides underscore their growing importance in both medicine and pharmaceuticals. To fully leverage the therapeutic benefits of marine peptides, further research is essential to elucidate their specific mechanisms of action. Such insights will not only advance our knowledge of marine peptide biology but also enhance their potential as effective therapies for cancer treatment. Continued investigation into marine peptides holds significant promise for developing new and innovative approaches to cancer therapy.

Disclosure of conflict of interest

None.

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References

[1] Nawaz T, Gu L, Fahad S, Saud S, Jiang Z, Hassan S, Harrison MT, Liu K, Khan MA, Liu H and El-Kahtany K. A comprehensive review of the therapeutic potential of cyanobacterial marine bioactives: unveiling the hidden treasures of the sea. Food Energy Secur 2023; 12: e495.

[2] Cunha SA and Pintado ME. Bioactive peptides derived from marine sources: biological and functional properties. Trends Food Sci Technol 2022; 119: 348-370.

[3] Xing L, Wang Z, Hao Y and Zhang W. Marine products as a promising resource of bioactive peptides: update of extraction strategies and their physiological regulatory effects. J Agric Food Chem 2022; 70: 3081-3095.

[4] Rauf A, Khalil AA, Khan M, Anwar S, Alamri A, Alqarni AM, Alghamdi A, Alshammari F, Rengasamy KRR and Wan C. Can be marine bioactive peptides (MBAs) lead the future of foodomics for human health? Crit Rev Food Sci Nutr 2022; 62: 7072-7116.

[5] Oliyaei N, Moosavi-Nasab M and Mazloomi SM. Therapeutic activity of fucoidan and carrageenan as marine algal polysaccharides against viruses. 3 Biotech 2022; 12: 154.

[6] Peighambardoust SH, Karami Z, Pateiro M and Lorenzo JM. A review on health-promoting, biological, and functional aspects of bioactive peptides in food applications. Biomolecules 2021; 11: 631.

[7] Pettit RK. Culturability and secondary metabolite diversity of extreme microbes: expanding contribution of deep sea and deep-sea vent microbes to natural product discovery. Mar Biotechnol (NY) 2011; 13: 1-11.

[8] Zeng M, Tao J, Xu S, Bai X and Zhang H. Marine organisms as a prolific source of bioactive depsipeptides. Mar Drugs 2023; 21: 120.

[9] Marciniak A, Suwal S, Naderi N, Pouliot Y and Doyen A. Enhancing enzymatic hydrolysis of food proteins and production of bioactive peptides using high hydrostatic pressure technology. Trends Food Sci Technol 2018; 80: 187-198.

[10] Fonseca S, Amaral MN, Reis CP and Custódio L. Marine natural products as innovative cosmetic ingredients. Mar Drugs 2023; 21: 170.

[11] Méresse S, Fodil M, Fleury F and Chénais B. Fucoxanthin, a marine-derived carotenoid from brown seaweeds and microalgae: a promising bioactive compound for cancer therapy. Int J Mol Sci 2020; 21: 9273.

[12] Li J, Elkhoury K, Barbieux C, Linder M, Grandemange S, Tamayol A, Francius G and Arab-Tehrany E. Effects of bioactive marine-derived liposomes on two human breast cancer cell lines. Mar Drugs 2020; 18: 211.

[13] de la Fuente B, Berrada H and Barba FJ. Marine resources and cancer therapy: from current evidence to challenges for functional foods development. Curr Opin Food Sci 2022; 44: 100805.

[14] Bharadwaj KK, Ahmad I, Pati S, Ghosh A, Sarkar T, Rabha B, Patel H, Baishya D, Edinur HA, Abdul Kari Z, Ahmad Mohd Zain MR and Wan Rosli WI. Potent bioactive compounds from seaweed waste to combat cancer through bioinformatics investigation. Front Nutr 2022; 9: 889276.

[15] Carroll AR, Copp BR, Grkovic T, Keyzers RA and Prinsep MR. Marine natural products. Nat Prod Rep 2024; 41: 162-207.

[16] Nasufović V, Küllmer F, Bößneck J, Dahse HM, Görls H, Bellstedt P, Stallforth P and Arndt HD. Total synthesis and bioactivity mapping of Geodiamolide H. Chemistry 2021; 27: 11633-11642.

[17] Magalhães F, Andrade C, Simões B, Brigham F, Valente R, Martinez P, Rino J, Sugni M and Coelho AV. Regeneration of starfish radial nerve cord restores animal mobility and unveils a new coelomocyte population. Cell Tissue Res 2023; 394: 293-308.
[18] Youssef DTA, Almagthali H, Shaala LA and Schmidt EW. Secondary metabolites of the genus Didemnum: a comprehensive review of chemical diversity and pharmacological properties. Mar Drugs 2020; 18: 307.
[19] Dong W, Ren Y and Xue H. Fabrication and application of carrier-free and carrier-based nanopesticides in pest management. Arch Insect Biochem Physiol 2024; 116: e22124.
[20] Yosri N, Khalifa SAM, Guo Z, Xu B, Zou X and El-Seedi HR. Marine organisms: pioneer natural sources of polysaccharides/proteins for green synthesis of nanoparticles and their potential applications. Int J Biol Macromol 2021; 193: 1767-1798.
[21] Hayes M. Measuring protein content in food: an overview of methods. Foods 2020; 9: 1340.