AgriCos e-Newsletter
ISSN: 2582-7049
AgriCos e-Newsletter
Open Access Multidisciplinary Monthly Online Magazine
Volume: 04 Issue: 04 April 2023 Article No: 08

Bioactive Peptides Derived from Marine Resources and their Antibacterial, Antiviral, and Anticancer Activities

Ulaganathan Arisekar
Assistant Professor, Department of Fish Quality Assurance and Management, Fisheries College and Research Institute, TNFU, Thoothukudi, Tamil Nadu

SUMMARY

Bioactive substances with the potential for use in industry and nutraceuticals can be found in abundance in marine bioresources. New mechanisms of action have been discovered as a result of several clinical trials testing new chemotherapeutic drugs originating from marine sources. It is well known that a variety of cyclic peptides and their analogs produced from marine sources have biological characteristics such as anticancer, antitumor, antibacterial, antifungal, antiparasitic, anti-inflammation, anti-proliferative, anti-hypertensive, cytotoxic, and antibiotic activities. These substances, such as cyclic oligopeptides, cyclic lipopeptides, cyclic glycopeptides, and cyclic depsipeptides, exhibit various activities and modes of action depending on their structural constitution. Dolastatins, soblidotin, didemnin B, aplidine, salinosporamide A, kahalalide F, and bryostatin 1 are now undergoing clinical studies and have recently reported improvements in the use of the aforesaid cyclic peptides. These cyclic peptides are potential new medications that have been found and synthesized from marine sources.

INTRODUCTION

The multiple positive benefits of bioactive peptides produced from marine sources have recently received attention. Additionally, a number of studies have found that marine peptides have a range of anti-infective properties, including antimicrobial, antifungal, antimalarial, antiprotozoal, anti-tuberculosis, and antiviral properties(Lee et al., 2017;Kang et al., 2015). Numerous structurally varied and bioactive secondary metabolites have been discovered during the last few decades from the research of marine plants, animals, and microorganisms. Many infectious disorders brought on by bacteria, fungi, and viruses, however, have few effective therapies at this time. Therefore, it is important to continue finding new antimicrobial peptides and to consider all potential alternatives.There is an abundant supply of bioactive natural compounds in the marine environment, many of which have different structural or chemical properties from those found on terrestrial. Bioactive substances are abundant in marine creatures. Recent discoveries of novel metabolites from marine species have tremendous biological effects. These findings might result in the creation of novel pharmacological drugs derived from marine metabolites(Lee et al., 2017). Cyclic peptides are one of the understudied types of bioactive peptides with a marine origin that shows significant promise in the pharmaceutical industry(Kang et al., 2015).

The identification of prospective medicinal agents can be significantly assisted by the oceans, which make up more than 70% of the earth's surface. There have been several substances discovered in marine creatures during the past few decades that have promising pharmaceutical properties(Kang et al., 2015). Therefore, it is believed that marine species might be a source of important and innovative physiologically active compounds for the formulation of therapeutics. Marine peptides in particular have drawn a lot of interest because of the possibility that they might improve health and prevent illness(Lee et al., 2017).Marine peptides are particular protein fragments that not only serve as sources of nitrogen and amino acids but also have a wide range of possible pharmacological uses. These peptides are derived from marine bacteria and fungi, fish, mollusks, crustaceans, crabs, algae, and fish. Based on their structural characteristics, amino acid content, and patterns, bioactive marine peptides have been demonstrated to exhibit a range of bioactivities, including anti-tumor, antiviral, anticoagulant, antioxidant, immunoinflammatory effects, and other therapeutic capabilities(Kang et al., 2015).

Antibacterial, antiviral, and anticancer activity of peptides and their mechanisms

The marine sponge Discodermiakiiensis provided discodermin A, which was later expanded to include B-D variations. These tetradecapeptides prevent the growth of starfish embryos. Additionally, the methanolic extract of these species demonstrated notable antifungal and antibacterial action. Additional research on

discodermin A revealed that it is linked to the permeabilization of plasma membranes, most likely as a result of having six consecutive hydrophobic amino acids at the N-terminal in contrast to other known peptides with the same action. Furthermore, discodermins F through H are cytotoxic to vascular smooth muscle cells and have antimicrobial, antifungal, and antibacterial activities. Vancomycin was subjected to an antibacterial experiment by Kumar et al. (2014), and they discovered that this intracellular metabolite had a stronger antimicrobial impact on the development of gram-positive bacteria(Lee et al., 2017).

S. aureus, S. typhi, P. aeruginosa, and *T. rubrum* were all susceptible to vancomycin, and the inhibition zones for each had diameters of 25, 21, 18, 11, and 15, respectively. Vancomycin also demonstrated antifungal action against *T. rubrum* and *A. niger*, with inhibition zones of 14 mm in diameter (12 mm inhibition zone)(Zhang et al., 2012). Currently, infections caused by gram-positive bacteria are treated with vancomycin, a glycopeptide antibiotic. It is also a great choice for treating bacteria that are resistant to a variety of antibiotic compounds. Vancomycin's N-19 terminus binds to the D-alanine-D-alanine residues of the UDP-N-acetylmuramyl pentapeptide at the Cterminus, which is the peptidoglycan precursor found at the outside of the cytoplasmic membrane in bacteria. This binding serves as the scaffold for the antibiotic's activity. Vancomycin primarily prevents peptidoglycan precursors from being attached to the peptidoglycan chain by inhibiting the transglycosylase enzyme. This glycosylation process prevents the formation of cell walls.

Sun et al. (2011) investigated the in vitro antibacterial effects of fijimycins A-C against three MRSA strains of *Staphylococcus aureus*. According to the findings, etamycin A, fijimycin A, and fijimycin C all showed potent antibacterial activity against all tested MRSA strains at concentrations of 4-32 g/mL, however,fijimycin B only moderately reduced the growth. This suggests that the fijimycin group's -phenylsarcosine molecule may be crucial to the antibacterial action. An investigation comparing the antibacterial activity of the stereoisomers fijimycin A and etamycin A revealed that the replacement of D- for L—phenylsarcosine had no impact on enhanced anti-MRSA activities

Certain cyclic peptides produced by marine creatures also have antiviral properties. The cyclic peptides papuamides A and B obtained from sponges of the genus Theonella inhibited infection of human T-lymphoblastoid cells with an EC50 of around 4 ng/ml. Numerous anti-HIV medications now on the market target HIV reverse transcriptase or protease and have negative side effects such as toxicity and treatment resistance. Until the medication wears off or the virus undergoes rapid mutation, the virus may remain dormant in memory T cells. It is crucial to note that papuamide A prevents viral entrance in order to function. Papuamide A exerts direct control over the virus without affecting important envelope glycoproteins like CD4 or HIV gp120(Kang et al., 2015).

Papuamide A prevents the spread of viruses during an early stage of the viral life cycle. The viral membrane's phosphatidylserine is the target of papauamide B, which prevents the entrance of viruses. Papuamides C and D are less effective than A and B for preventing HIV entrance. *Theonellaswinhoei* and *Theonella mirabilis*, both from Papua New Guinea, generate papuamides A through C. Separate research found that the marine sponge *Melophlussppapuamide* C-F from butanol extract was lethal to brine shrimp, with LD50 values ranging from 92 to 106 g/mL.Microspinosamide, an additional cyclic depsipeptide from the sponge Sidonopsmicrospinosa, reduced the cytopathic effects of HIV-1 infection in an XTT-based in vitro experiment.

Discobahamins A and B isolated from Theonella sp. exhibited limited antifungal efficacy against Candida albicans yeast growth. These cyclic peptides share structural similarities with keramamides B–D and orbiculamide A,Hymenamides A and B shown antifungal activity against Cryptococcus neoformans and Candida albicans, respectively. Zhang et al. (2012) used the CLSI broth microdilution technique and amphotericin B as a positive control to examine the antifungal activity of microsclerodermins J, K, A, and B against *C. albicans, A. fumigatus,* and *C. neoformans*. Compared to microsclerodermins A and B, microsclerodermins J and K are less effective.

The four substances are effective antifungal agents in immunocompromised hosts. In another study, microsclerodermin A had an inhibitory impact on nuclear factor kappa B and promoted apoptosis in pancreatic cancer cells by lowering chronic inflammation mediated by NF kB. When tested against Candida glabrata, lobocyclamides B and C demonstrated poor antifungal efficacy with a 6 mm zone of inhibition and 8 mm zone of inhibition, respectively. Interestingly, a combination of lobocyclamides A and B (1:1) showed notable synergism and had greater action (MIC 10–30 g/mL) than the individual compounds [30]. It is assumed that the macrocyclic structure of the methyl ester from halicylindramide B is essential for its cytotoxic and antifungal effects because it demonstrated little cytotoxicity and only minimal antifungal activity. Halicylindramide D exhibited antifungal action against *Mortierellaramanniana* and cytotoxic activity targeting P388 murine

leukemia cells, according to subsequent research on the halicylindramides D and E isolated from *Halichondriacylindrata*(Kang et al., 2015)**.**

Marine peptides under in clinical trials

There are various instances of recent developments in the use of the aforementioned technologies to find and create innovative marine-derived pharmaceuticals. Vancomycin is one antibiotic, for instance, that is used to treat a variety of bacterial illnesses. There are now clinical studies for other cyclic peptides. On tumor cell lines, dolastatins had strong apoptotic and growth-inhibiting effects. Phase I and II clinical trials using dolastatins were unsuccessful due to their insufficient ability to treat prostate cancer. Dolastatin 10, a cyclic peptide from the dolastatin family, provided a better starting place for future clinical research and synthetic therapeutic production. By inhibiting the microtubules, dolastatins 10 and 23 stop cells from progressing through the metaphase. They also trigger apoptosis by phosphorylating Bcl-2, which is a known death receptor(Kang et al., 2015).

Under the direction of the NCI, didemnin B was examined in preclinical and clinical studies (phase I and phase II) against a range of human malignancies, such as renal cell carcinoma, epithelial ovarian cancer, breast cancer, small cell lung cancer, myeloma, and lymphoma. The eukaryotic translation elongation factor (eEF1A), which is involved in protein synthesis, is the chemical target of didemnin B. It is the first known chemical substance that was directly derived from a marine source and has entered clinical studies. Trials were unsuccessful due to significant side effects, and clinical research was discontinued in order to create a didemnin B counterpart with more potent anticancer efficacy(Kang et al., 2015).

Phase II investigations are now being conducted, and aploidine (plitidepsin) is well tolerated in clinical trials with little toxicity. Aplidine's mode of action includes early oxidative stress induction, cell cycle arrest, and antiangiogenic activity. Aplidine was evaluated in phase II clinical study for the treatment of advanced renal cell carcinoma, advanced small cell lung cancer, and advanced medullary thyroid carcinoma. The findings demonstrated that aplidine's anticancer impact in those experiments was quite limited. Aplidine and dexamethasone are being tested in phase III clinical study for multiple myeloma that has relapsed or become resistant to treatment(Kang et al., 2015).

Salinosporamide A went into phase I clinical trials for multiple myeloma three years after it was discovered. Intense academic and industry research has been attracted to salinosporamide A due to its proteasome inhibitory function, which contains substantial biological activity and a very intriguing structure(Zhang et al., 2012). Salinosporamide A has undergone more than 10 syntheses in recent years to clarify its structure-activity connections and oncological origins. Salinosporamide A is a successful example of contemporary drug discovery since it was produced and biosynthesized using all available research methods in pharmacology, medicinal chemistry, and natural product chemistry(Lee et al., 2017).

In phase I studies, patients with malignant melanoma, lymphoma, and ovarian cancer demonstrated antitumor activity for bryostatin 1, one of the bryostatin family's most prevalent and well-studied chemicals. The activation of protein kinase C, which causes the differentiation of many cancer cell lineages, is linked to bryostatin 1's antitumor effect. A large phase II clinical study is now evaluating bryostatin 1. However, it manifested certain adverse effects in the earliest clinical trials, including myalgia, local phlebitis, tiredness, nausea, and thrombocytopenia. In advanced solid tumours such as renal cell carcinoma, non-small-cell lung cancer, and malignant melanoma, bryostatin 1 did not exhibit any discernible objective anticancer action, while being thought to promote cell differentiation in individuals with refractory chronic lymphocytic leukemia(Lee et al., 2017).

CONCLUSION

Natural products that are pharmacologically active can be found in abundance in marine species. Over the past 50 years, there has been a significant development in our understanding of the chemistry of marine natural products. The use of marine cyclic peptides in biological research on particular targets is advantageous and encouraging. Cyclic peptides from various marine species have various chemical compositions and pharmacological characteristics. Recent therapeutics for a number of cancers and disorders have benefited tremendously from the discovery and development of marine cyclic peptides and their derivatives(Kang et al., 2015). Many of these substances are now utilized in therapeutic settings.Marine peptides have intrinsic activity and the capacity to prevent infection, despite the fact that they are largely unexplored. Marine peptides are extremely selective to their targets, have a wide range of therapeutic effects, and have a low deposition rate in

body tissues. Peptides derived from marine sources also have a lower likelihood of unintended negative side effects. Marine peptides are often harmless and non-toxic since they are made of metabolically acceptable amino acids. Marine peptides can be utilized as excipients in therapeutic formulations to alter biological activity, target delivery, or transport across cellular membranes in addition to being employed as active components. Comprehensive research on anti-infective peptides will help develop new pharmaceuticals. Marine peptides are a rich source of bioactive chemicals that may be used for pharmaceutical industry research and development.

ACKNOWLEDGMENT

A Special thanks to Fisheries College and Research Institute, Tamil Nadu Fisheries University, Thoothukudi for providing the necessary facilities to prepare this article

REFERENCES

Kang, H.K., Seo, C.H. and Park, Y., 2015. Marine peptides and their anti-infective activities. *Marine drugs*, *13*(1), 618-654.

Kumar, R.M., Priyadarisini, B.V., Srigopalram, S., Kumar, S., Arasan, T. and Nou, S., 2014. Studies on a marine Streptomyces fradiae BW2-7 producing glycopeptide antibiotic vancomycin effective against skin pathogens. *Scholars Academic Journal of Biosciences*, *2*(11), 746-761.

Lee, Y., Phat, C. and Hong, S.C., 2017. Structural diversity of marine cyclic peptides and their molecular mechanisms for anticancer, antibacterial, antifungal, and other clinical applications. *Peptides*, *95*,94-105.

Sun, P., Maloney, K.N., Nam, S.J., Haste, N.M., Raju, R., Aalbersberg, W., Jensen, P.R., Nizet, V., Hensler, M.E. and Fenical, W., 2011. Fijimycins A–C, three antibacterial etamycin-class depsipeptides from a marine-derived Streptomyces sp. *Bioorganic & medicinal chemistry*, *19*(22), 6557-6562.

Zhang, X., Jacob, M.R., Rao, R.R., Wang, Y.H., Agarwal, A.K., Newman, D.J., Khan, I.A., Clark, A.M. and Li, X.C., 2012. Antifungal cyclic peptides from the marine sponge Microsclerodermaherdmani. *Research and reports in medicinal chemistry*, *2*, 7-15.