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Marine peptides act as novel chemotherapeutic agent

Abstract

The marine environment represents a largely unexplored source of new microbes (bacteria, fungi, microalgae-cyanobacteria) that are potent producers of bioactive peptides. Here, we have discussed some novel peptides isolated from marine species exhibiting antibacterial, antifungal, antiviral, antiprotozoal activities. Therefore, marine peptides have attracted a great deal of attention due to their potential effects in promoting health and reducing disease. We have also discussed the extraction and commercial exploitation of peptides to become a possible future drug. Advancements in isolated techniques have allowed us easy access of less explored environment. Here, we summarize the future aim and scope of commercial application and production of microbial peptides from marine sources.

Keywords: microalgae, cyanobacteria antiviral, antiprotozoal, antitumour

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Introduction

Emergence of drug-resistant pathogens and infectious diseases caused by bacteria, fungi and viruses increases the demand of developing novel and effective antibiotics. For the discovery of new antibiotics terrestrial environment was centralized for more than 50 years, and marine sources have remained unexplored for production of new anti-infectious metabolites. Now-these-days research has been focused on ocean as it occupies almost 70% of earth's surface and it provides a unique source of chemical compounds with potential bioactivities.[1] In the last few decades, marine sources have played a major role for exploring and developing new drugs.[2] But still many bioactive metabolites have to be explored, because of the difficulties in cultivation of deep water habitats. The marine habitat represents a new source of microbes including bacteria, fungi, microalgae-cyanobacteria) that can be effective producers of bioactive metabolites.[3]

Many marine species (like; bacteria, fungus, algae, fish and crab) secrets peptides so extensive research has been conducted on them. Bioactive marine peptides are effective due to their structural properties like amino acid composition and sequences with varying degrees of action. Marine peptides are currently used as antibiotics against infectious diseases such as human immunodeficiency virus (HIV) and conditions of multiple bacterial infections, antitumour, anticancer, antimicrotubule, antiproliferative and in cytotoxic activities.[4–7] Therefore, marine peptides have attracted a great deal of attention due to their potential effects in promoting health and reducing disease. In this mini-review, we discuss the marine peptides isolation and extraction from varying sources, also their activity against bacterial, fungal, protozoan and viral infections with current status of peptides at commercial level.

Marine microorganisms are major sources of microbial peptides

Marine microbial species survive in a stressful habitat, under cold, lightless, and high-pressure conditions. These factors involved in development of unique metabolisms, and result in the production of novel metabolites that differ from terrestrial organisms. Thus, marine microbes offer a magnificent source for the discovery of new compounds with different activities, including antimicrobial, anti-protozoan, anti-tuberculosis, and antiviral properties.[8,9]

Peptides from marine bacteria: A large volume of unknown marine microbes are present in environment and to be a very good source of novel molecules crack many unsolved queries. Bacteria are the best source for production of microbial peptides. They are able to produce many bioactive molecules in the marine, principally to keep away their predators and protecting themselves. Furthermore, marine bacteria produces novel microbial peptides that showing antitumour, anticoagulant and cardio protective properties.[10] According to literatures some of the unique properties of bacterial peptides, like their ability to grow and functionally active at extremely elevated salt concentrations, make them good potential targets for development of new and novel molecules against various diseases.

Peptides from marine fungi: All forms of life are present in the oceanic environment especially, fungi play a key role to isolate and produce marine peptides. There are two types of marine fungi obligate and facultative.[11] Obligate fungi are grown completely in a marine or estuarine habitat whereas facultative fungi are grown and sporulate in terrestrial or freshwater.[12] Marine fungi have proven to be a rich and promising source of novel therapeutics agents. Near about 272 microbial peptides have been isolated from marine fungi and the number is still increasing.[13] In addition, most of these microbial peptides are analogues of those discovered previously from terrestrial fungi.[14]

Peptides from marine sponges: Marine sponges (phylum Porifera) are one of the richest sources of pharmacologically-active chemicals. They are sessile marine feeders that have developed efficient defense mechanisms against foreign attackers such as viruses, bacteria, or eukaryotic organisms. It has been suggested that many of the bioactive metabolites isolated from sponges and their associated microorganisms are produced by functional enzyme clusters.[15,16] The huge number of different secondary metabolites discovered in marine sponges and the complexity of the compounds and their biosynthetic pathways can be regarded as their importance for survival. As infectious microbes evolve and develop resistance to existing pharmaceuticals, marine sponges provide novel leads against bacterial, fungal and viral diseases.

Peptides from marine algae: Algae are very simple chlorophyll-containing organisms composed of one cell or grouped together in colonies or as organisms with many cells, sometimes collaborating together as simple tissues.[17] Algae are heterogeneous group of plants with a long fossil history. Blue-green algae (cyanobacteria) contain chlorophyll a and related compounds. These algae are ancient photosynthetic prokaryotic organisms that producing biologically active metabolites with diverse chemical structures such as nitrogenous compounds and cyclic polyethers.[18] Recently, several marine cyanobacterial have been the focused due to their effective biological activities and unique structures.

Peptides from marine invertebrate: Apart from microbes some invertebrates are also produces peptides and these peptides have some unique properties especially peptides from fishes are using as novel chemotherapeutics agents against microbes. Fish peptides are showing broad-spectrum antimicrobial activity against both fish and human pathogens. These peptides encoding genes are highly responsive to microbes and innate immunostimulatory molecules. Recent research has reported some unique properties of fish peptides, including their ability to act even at very high salt concentrations, make them good potential targets for development as therapeutic antimicrobials.[5] Some marine peptides from these different sources with their antagonist activity are discussed in Table 1.

Table 1 Marine peptides from diverse sources with anti-infective activities[19]

Source	Name of Peptide	Activity	Pharmacologic Activity
Bacterium: *Brevibacillus laterosporus*	Tauramamide (3)	Antibacterial	*Enterococcus* sp. inhibition
Bacterium: *Streptomyces* sp.	Anthracimycin (35)	Antibacterial	*B. anthracis*, *Enterococcus facecalis*, *Streptococcus pneumonia*, *S. aureus*, MSSA, MRSA, vanco-mycin-resistant *S. aureus* inhibition
Bacterium: *Rapidithrix* sp.	Ariakemicins A (25), B (26)	Antibacterial	*Brevibacterium* sp., *S. aureus*, *B. subtilis*
Bacterium: *Bacillus silvestris*	Bacillistatins 1 (7), 2 (8)	Antibacterial	*Streptococcus. pneumonia* inhibition
Bacterium: *Nocardiopsis* sp	Nacardiopsis thiopeptide TP-1161 (9)	Antibacterial	Vancomycin-resistant *Enterococcus faecium* inhibition
Bacterium: *Phaeobacter* sp	Indigoidine (15)	Antibacterial	*Vibrio fischeri* inhibition
Bacterium: *Photobacterium* sp.	Unnarmicins A (16), C (17)	Antibacterial	*Pseudovibrio* sp. inhibition
Bacterium: *Photobacterium* sp.	Ngercheumi-cins A–D (18–21)	Antibacterial	Gram negative strain inhibition
Bacterium: *Photobacterium* sp.	Solonamidine A (22), B (23)	Antibacterial	*S. aureus*, Methicillin-resistant *S. aureus* (MRSA)
Bacterium: *Pseudomonas* sp.	Cyclo-peptides (24)	Antibacterial	*S. aureus*, *M. luteus*, *B. subtilis*, *E. coli*, *V. anguillarum*
Fungus: *Leucostoma persoonii*	Cytosporones B (33), E (34)	Antibacterial	*S. aureus* USA100, MRSA, MSSA inhibition
Fish: *Oreochromis mossambicus*	Hepcidin (4)	Antibacterial	*Listeria monocytogenes*, *S. aureus*, and *Enterococcus faecium* inhibition
Jellyfish: *Aurelia aurita*	Aurelin (1)	Antibacterial	*Escheichia coli* inhibition
Bacterium: *Chondromyces Pediculatus*	Pedein A (39)	Antifungal	*Rhizopus glutinis*, *Saccharomyces cerevisae*, *C. albicans* inhibition
Sponge: *Latrunculia* sp.	Callipeltine J(37), K (38)	Antifungal	*C. albicans*
Sponge: *Theonella* sp.	Theuellamide F (40), G (41)	Antifungal	*C. albicans* inhibition
Bacterium: *Lyngbya majuscula*	Dragomabin (54)	Antimalarial	*Plasmodium falciparum* W2 strain inhibition
Bacterium: *Oscillatoria* sp.	Venturamid A (55), B (56)	Antimalarial	*Plasmodium falciparum* W2
Bacterun: *Microcystis aeruginosa*	Aerucyamide A–D (57–60)	Antimalarial	*Plasmodium falciparum* K1
Bacterium: *Schizothrix* sp.	Gallinamide A (61	Antimalarial	*Plasmodium falciparum* W2
Bacterium: *Lyngbya majuscula*	Lagunamide A (62), B (63)	Antimalarial	Plasmodium falciparum NF54 strain inhibition
Bacterium: *Oscillatoria nigro-viridis*	Viridamide A (65), B (66)	Antiprotozoal	*Leishmania mexicana*, *Trypanosoma cruzi* inhibition
Bacterium: *Lyngbya majuscula*	Almiramides B (67), C (68)	Antiprotozoal	*Leishmania donovani* inhibition
Bacterium: *Streptomyces* sp.	Valinomycin (69)	Antiprotozoal	*Leishmania major* & *Trypanosoma brucei* inhibition
Fungus: *A. fumigatus*, *Nectria inventa*	Diketopiperazines (70–81)	Antiprotozoal	*Trypanosoma brucei*
Fungus: *Trichoderma* sp.	Trichoderin A (82), A1 (83), B (84)	Antitubercu-losis	*Mycobacterium tuberculosis*
Fungus: *Aspergillus terreus*	Asperterrestide A (98)	Antiviral	Anti-HIN1, Anti-H3N2
Sponge: *Siliquariaspongiamirabilis*	Celebesides A (94), C (95)	Antiviral	Anti-HIV-1
Sponge: *Theonella swinhoei*	Theopapu-amide A (96), D (97)	Antiviral	Anti-HIV-1
Sponge:*Siliquariaspongia mirabilis*	Mirabamides A (85), C (86), D (87), E–H (88–91)	Antiviral	Anti-HIV-1
Sponge: *Homophymia* sp.	Homophymine A–E (99–103), A1–E1 (104–108)	Antiviral	Anti-HIV-1
Sponge: *Theonella* sp.	Koshikmaide B (109), F–H (110–112)	Antiviral	Anti-HIV-1

Isolation of marine peptides from microbes

To isolate the peptides from sea water sample at different depth is collected from ocean. A variety of pre-treatment methods including enrichment, physical, and chemical techniques (e.g., dry heat, exposure to 1%–1.5% phenol, sucrose-gradient centrifugation, and filtration through cellulose membrane filters) are employed to favor the isolation of specific genera and improve the recovery of marine peptides.[20] These pre-treatment's eliminate or strongly reduce the risk of contamination, thereby facilitating the isolation of marine peptides.

Extraction of marine peptides for commercial applications

Bioactive peptides or protein hydrolysates from marine species can be extracted and isolated by various methods in industrial-scale production. The organic solvent extraction method was used traditionally, but due to its time-consumption and costlier, some improved extraction techniques like pressurized solvent, supercritical fluid, pulsed electric field-assisted, microwave-assisted, ultrasound-assisted and enzyme-assisted are preferred.[21]

After the extraction procedure, the proteins are hydrolyzed into bioactive peptides. Enzymatic hydrolysis is preferred in the nutraceutical and pharmaceutical industries in order to avoid harsh chemical and physical treatment and preserve the functionality and nutritive values.[22] A novel ultra filtration membrane bioreactor technology has recently emerged. Nowadays, marine peptide are obtained by multistep recycling membrane reactor combined with an ultra filtration membrane system to fractionate marine hydrolysates according to different molecular weight ranges.[23] Some of marine peptides obtained from these sources are in clinical trials which have been elaborated in Table 2.

Table 2 Marine peptides in clinical trials[24]

Source	Compound	Applications	Status
ω-conotoxin toxin from *Conus magus*	Ziconotide	Analgesics	FDA approved
Dolabella auricularia	Brentuximab vedotin	Cancer treatment	FDA approved
Dolabella auricularia	Glembatumumab vedotin	Cancer treatment	Phase I/II clinical study
pentapeptide from hydrolysate of dried bonito	Katsuobushi	Antihypertensive	Sold as nutraceuticals
oligopeptide extract from *Chlorella vulgaris*	Dermochlorella®	Skin toner and firmer	Sold as skin care product
Aplidium albicans	Plitidepsin	Cancer treatment	Phase I/II clinical study
Hemiasterella minor	HTI-286	Cancer treatment	Preclinical study
Elysia rufescens	Kahalalide F	Cancer treatment	Phase I clinical study
Elysia rufescens	Elisidepsin	Cancer treatment	Phase I clinical study
Hydrolysate of fish collagen and gelatin	Fish gelatin	Supplements and bone health	Sold as nutraceuticals
Hydrolysate of fish protein	Stabilium Protizen/Procalm	Anxiolytic	Sold as nutraceuticals
Hydrolysate of fish protein	Seacure	Intestinal health	Sold as nutraceuticals
Hydrolysate of fish protein	Nutripeptin®/ Hydro MN Peptide®	Postprandial blood glucose control	Sold as nutraceuticals

Conclusion

The discovery of bio regulatory roles with elucidation of the marine peptides mechanisms would promote the peptides to be used as potential drugs for treatment of diseases. With the advancement of marine peptides to the current preclinical and clinical stages, their contribution in the future shows some potential. New technologies and close collaborations between institutional and industrial investigators will be crucial to ensure the future success of marine peptides as novel therapeutics that can make a vital contribution to the treatment or prevention of various diseases.

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Conflicts of interest

No conflict of interest declared.

References

1. Abad MJ, Bedoya LM, Bermejo P. *Marine compounds and their antimicrobial activities*. Science against microbial pathogens: communicating current research and technological advances A. Mendez-Vilas (Ed.); 2011. 1293–1306 p.
2. Xiong ZQ, Wang JF, Hao YY, et al. Recent Advances in the Discovery and Development of Marine Microbial Nat Products. *Mar Drugs*. 2013;11(3):700–717.
3. Aneiros A, Garateix A. Bioactive peptides from marine sources: Pharmacological properties and isolation procedures. *J Chromatogr B Analyt Technol Biomed Life Sci*. 2004;803(1):41–53.
4. Mayer AM, Rodriguez AD, Berlinck RG, et al. Marine pharmacology in 2009–2013: Marine compounds with antibacterial, antidiabetic, antifungal, anti -inflammatory, antiprotozoal, antituberculosis and antiviral activities; affecting the immune and nervous systems, and other miscellaneous mechanisms of action. *Mar Drugs*. 2013;11:2510–2573.
5. Masso SJA, Diamond G. Antimicrobial Peptides from Fish. *Pharmaceuticals*. 2014;7(3):265–310.

6. Kim SK, Wijesekara I. Development and biological activities of marine-derived bioactive peptides: A review. *Journal of Functional Foods*. 2010;2(1):1–9.
7. Ngo DH, Vo TS, Ngo DN, et al. Biological activities and potential health benefits of bioactive peptides derived from marine organisms. *Int J Biol Macromol*. 2012;51(4):378–383.
8. Lu X, Gao X, Liu X, et al. Marine microbes-derived anti-bacterial agents. *Mini Rev Med Chem*. 2010;10(11):1077–1090.
9. Rahman H, Austin B, Mitchell WJ, et al. Novel anti-infective compounds from marine bacteria. *Mar Drugs*. 2010;8(3):498–518.
10. Austin B. A review novel on pharmaceutical compounds from marine bacteria. *J Appl Bacteriol*. 1989;67:461–470.
11. Holler U. *Isolation, biological activity and secondary metabolite investigations of marine derived fungi and selected host sponges*. PhD Thesis, Universitat Carolo, USA: Wilhelmina; 1999. 163 p.
12. Kohlmeyer J. Bremerhaven: Veroff Inst Meeresforsch. 1974;Suppl 5:263–286.
13. Bugni TS, Ireland CM. Marine derived fungi: a chemically and biologically diverse group of microorganisms. *Nat Prod Rep*. 2004;21(1):143–163.
14. Davidson BS. New dimensions in natural products research: cultured marine microorganisms. *Curr Opin Biotechnol*. 1995;6(3):284–291.
15. Laport MS, Santos DC, Muricy G. Marine sponges: Potential sources of new antimicrobial drugs. *Curr Pharm Biotechnol*. 2009;10(1):86–105.
16. Sagar S, Kaur M, Minneman KP. Antiviral lead compounds from marine sponges. *Mar Drugs*. 2010;8(10):2619–2638.
17. Cardozo KHM, Guaratini T, Barros MP, et al. Metabolites from algae with economical impact. *Comp Biochem Physiol C*. 2007;146(1-2):60–78.
18. Tan LT. Bioactive natural products from marine cyanobacteria for drug discovery. *Phytochemistry*. 2007;68(7):954–979.
19. Kang HK, Chang HS, Yoonkyung P. Marine Peptides and Their Anti-Infective Activities. *Mar Drugs*. 2015;13(1):618–654.
20. Esin E, Hames KAU. Isolation strategies of marine-derived actinomycetes from sponge and sediment samples. *J Microbiol Methods*. 2012;88(3):342–347.
21. Grosso C, Valentao P, Ferreres F, et al. Alternative and efficient extraction methods for marine-derived compounds. *Mar Drugs*. 2015;13(5):3182–3230.
22. Clemente A. Enzymatic protein hydrolysates in human nutrition. *Trends Food Sci Technol*. 2000;11(7):254–262.
23. Zhao Y, Li B, Dong S, et al. Novel ACE inhibitory peptide isolated from *Acaudina molpadioidea* hydrolysate. *Peptides*. 2009;30(6):1028–1033.
24. Randy CF, Tzi BN, Jack HW. Marine Peptides: Bioactivities and Applications. *Mar Drugs*. 2015;13(7):4006–4043.