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Marine biomolecules: a promising approach in therapy and biotechnology

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ABSTRACT: The marine environment is characterized by a wide diversity of microorganisms among which marine bacteria. To insure their survival in hostile conditions where they face high competition with pathogenic microorganisms, they produce various kinds of bioactive molecules within biofilms with unique structural and functional features. As example: marine peptides which provide a broad spectrum of antimicrobial, antitumoral, antiviral and anti-inflammatory activities, in addition to marine exopolysaccharides showing antifouling and antifungal activities, immunomodulatory properties, emulsion stabilization capacity with other various potentials. Some biofilms have shown a beneficial role for aquaculture, among which enhancement of growth performance and improvement of water quality, while others are threatening not only aquaculture and maritime fields, but also medicine and food industry. Thus, marine bioactive compounds are promising preventing agents for the establishment and growth of fouling microorganisms, which may be useful in different fields in order to decrease economic losses and avoid foodborne illnesses.

Keywords: Marine biomolecules; Biofilms; Health issues; Aquaculture.

1. INTRODUCTION

The marine environment hosts an immense biological, chemical and ecological diversity [1]. It is characterized by hostile environmental conditions in terms of variation of salinity, temperature and pressure [2] which have favored production of a great variety of novel bioactive molecules with unique structural and functional features. These polymeric substances are of renewed interest to many sectors of industrial human activities including food industries, pharmaceuticals and drug delivery due to their diverse biological and chemical properties such as antitumor, immunostimulatory, anti-inflammatory, antibacterial, antifouling and antioxidant activities [3].

Many naturally bioactive compounds are secreted on biological or non-biological surfaces submerged in the marine environment as living tissues, aquatic equipments and water distribution systems which may be covered with densely colonized sessile communities known as biofilms, enclosing microbial cells [2, 4]. The main advantage of biofilm formation is the protection of microorganisms from attack by bacterial and viral pathogens which extend their survival periods in extreme marine environments [5]. Additionally, it has been used as an ecofriendly strategy whereby substrate based aquaculture using biofilms has contributed to improvement of water quality resulting in

enhanced growth of marine organisms of interest (fishes, shellfishes, and aquatic plants). Nevertheless, these sessile biological assemblies may turn virulent and cause health diseases since they may develop on seafood. They also lead to significant economic losses in the maritime field due to biofouling and materials biocorrosion [6].

In this review, we give a general overview on the main classes of bioactive molecules produced by marine bacteria and their diverse biological activities which provide promising applications in various fields. We also describe their living modes which may have advantages and inconveniences for many aquatic organisms and eventually to human health as well as to the whole marine ecosystem.

2. MARINE DIVERSITY

Oceans are colonized by microbial species that are essential for marine ecosystems and have pivotal roles in global biogeochemical cycles. The marine environment is characterized by a taxonomic richness where bacteria are very abundant. A recent metagenomics study has reported the partition of bacterial genera communities to geographic locations. Cyanobacteria, Alphaproteobacteria and Flavobacteria dominate the photic zone samples while the aphotic zone is colonized mainly by Alphaproteobacteria, Deferribacteres, Deltaproteobacteria and Gammaproteobacteria [7].

A significant part of the world ocean is characterized by harsh conditions in terms of low nutrients, low concentrations of biodegradable organic carbon, variation of temperature, pressure and salinity. Thus, microorganisms are classified into halotolerant: which do not require salt for growth but tolerate it, then can grow in moderately salty environments, and halophilic: for which the presence of salt is essential for their survival and growth, then they only thrive in highly saline environments [8].

In parallel, microorganisms are adapted to osmotic stress. They have an endogenous balance of pressure and resistance to osmotic stress apart from any external osmoprotection. Therefore, they carry the genetic information and the enzymatic machinery necessary for osmotolerance which allow them to maintain an internal osmotic pressure higher than the surrounding environment [9].

Hence, bacterial adaptations represent a driving force leading to new secondary metabolic products that function as a defense strategy against natural predators in order to insure their survival [5]. In this regard, the most reported genera from which novel metabolites have been isolated are phylogenetically diverse, including among them *Pseudomonas*, *Alteromonas*, *Vibrio*, *Bacillus, Streptomyces*. For example the widespread genus *Pseudomonas*, is a group of gram negative and easily cultivable gamma-proteobacteria that includes numerous marine species of great importance due to their production of various useful compounds such as antibiotics, enzymes, antitoxins, antitumorals and antivirals [2].

Moreover, widespread marine actinomycetes are known by their production of a great variety of bioactive compounds as was reported with *Pseudonocardia* sp. HS7, *Nocardiopsis* sp. strain HYJ128, *Marinispora* strain CNQ-140, *Streptomyces* sp. CNQ343 and many other species [10] as shown in Table 1.

On the other hand, *Vibrio* is an example of bacterial genus which belongs to microbial pathogens of clinical importance for humans and many marine animals. It contains different species many of which of marine and other aquatic environments, but *V. alginolyticus*, *V. vulnificus*, *V. parahaemolyticus*, *V. cholerae*, *V. fluvialis* and *V. mimicus* are the most dangerous reported species to humans and other animals. They have been associated with infections in case of wounds or after exposure to polluted water, or after eating contaminated food [11]. Thus many researchers have discovered natural compounds isolated from sponge bacterial symbionts inhibiting virulent *Vibrio* species such as docosane acting against *V. harveyi*, *V. parahaemolyticus* and *V. vulnificus* [5].

In addition, marine fungi are sources of structurally unique products. Many of marine fungal metabolites have been classified as potential therapeutic agents owned to their antimicrobial, anticancer, antiviral and antimarine fungal-inflammatory activities [10, 12] as shown in Table 1.

Table 1. Potential therapeutic bioactive molecules produced by marine bacteria and fungi.

Marine microorganisms	Source	Biomolecules	Activity	References
Bacteria	*Pseudoalteromonas piscicida*	3,4- dibromopyrrole-2,5-dione	Antibacterial	[10]
	Pseudomonas sp.	Pyolipic acid and phenazine-1-carboxylic acid	Antifouling	[10]
	Vibrio sp. WMBA	Aqabamycins A–D	Antibacterial	[10]
	Bacillus subtilis strain 109GGC020	Gageotetrins A–C	Antimicrobial	[10]
	Bacillus amyloliquefaciens SCSIO 00856	Macrolactin V	Antibacterial	[10]
	Bacillus sp. 09ID194	Macrolactins X–Z	Antibacterial	[10]
	Bacillus licheniformis ATCC 14580	BL00275	Antibiofilm	[10]
	Lyngbya majuscula	Dolastatin	Antilarval settlement	[10]
	Streptomyces caelestis	Citreamicin θ A-B-C	Antibacterial	[10]
	Streptomyces roseogilvus	Griseoviridin	Antibacterial	[10]
	Streptomyces fradiae strain PTZ0025	Fradimycins A-B	Antibacterial	[10]
	Kocuria palustris	Kocurin	Antibacterial	[10]
	Pseudonocardia sp.	Diazaanthraquinone	Antibacterial	[10]
	Streptosporangium strain DSZM 4594	Iodinin	Antibacterial	[10]
	Streptomyces sp. SCSIO 10355	Strepsesquitriol	Anti-inflammatory	[12]
	Streptomyces strain M491	T-Muurolol sesquiterpenes	Cytotoxic	[12]
	Micromonospora sp. strain WMMC-218	Micromonohalimane B	Antibacterial	[12]
	Verrucosispora gifhornensis YM28-088	Gifhornenolones	Cytotoxic	[12]
	Actinomycetes isolate CNH-099	Neomarinones	Cytotoxic	[12]
	Erythrobacter sp. strain SNB-035	Erythrazole	Cytotoxic	[12]
Fungi	*Penicillium* sp. SCS-KFD09	Chrodrimanins	Antiviral	[12]
	Alternaria alternate strain (k21-1)	Sesteralterin	Antialgal/ Antibacterial	[12]
	Strain 95-1005C *Chondrostereum* sp. SF002	Hirsutanol A	Antitumoral	[12]
	Aspergillus sp. CNL-523	Cryptosphaerolide	Cytotoxic	[12]
	Curvularia sp. strain M12	Curvularin and (S)-dehydrocurvularin	Antifungal	[10]
	Penicillium thomii KMM 4667	Thomimarine E	Anti-inflammatory	[12]
	Penicillium sp.	Ligerin	Antiproliferative	[12]
	Xylariaceae sp.	Eremophilane-type sesquiterpenoids	Cytotoxic	[12]
	Eupenicillium sp.	Curvularin and (S)-dehydrocurvularin	Antiviral	[10]
	Paraphaeosphaeria strain N-119	Curvularin and αβ-dehydrocurvularin	Antifungal/ Anti-inflammatory	[10]
	Phomopsis sp. hzla01-1	Modiolides A and B	Antibacterial/ Antifungal	[10]
	Penicillium cf. montanense	Phomolide A and B	Antibacterial/ Antifungal	[10]

Marine microorganisms	Source	Biomolecules	Activity	References
	Cladosporium spp.	Xestodecalactones A–C Dendrodolides A, C, M	Antifungal/ Antibacterial	[10]
	Streptomyces sp. strain 12A35	Lobophorins H and I	Antibacterial	[10]
	Penicillium sp.	β-resorcylicacid lactones	Antifungal	[10]
	Aspergillus sp.	Didehydrosydonic acid	Cytotoxic	[12]
	Aspergillus sp.	Disydonols	Cytotoxic	[12]
	Periconia byssoides Pers.	Peribysins	Cell-adhesion inhibitors	[12]
	Aspergillus versicolor	Insulicolide A	Cytotoxic	[12]
	Penicillium sp.	Breviones	Antiviral/ Cytotoxic	[12]

Table 2. Potential therapeutic bioactive molecules produced by seaweeds and sponges.

Marine organisms	Source	Biomolecules	Activity	References
Seaweeds	*Callophycus serratus*	5- and 16-membered bromophycolides J-Q	Antibacterial	[16]
	Neurymenia fraxinifolia	Neurymenolides A and B	Antibacterial	[16]
	Ecklonia kurome	8′-bieckol, eckol, dieckol, phloroglucinol & phlorofucofuroeckol-A	Bactericidal	[16]
	Ecklonia cava	Dieckol	Fungicidal	[16]
	Ecklonia cava	Eckol	Antimicrobial	[16]
	Ishige foliacea	Octaphlorethol A	Anti-inflammatory	[16]
	Eisenia arborea	Phlorofucofuroeckol B	Anti-inflammatory	[16]
	Vidalia obtusaloba	Vidalols A and B	Anti-inflammatory	[16]
	Porphyra dentate	Catechol & rutin	Anti-inflammatory/ Antioxidant	[16]
	Eisenia bicyclis	Fucosterol	Antidepressant	[16]
	Sargassum fusiforme	Saringosterol3,6,17-trihydroxy	Antidepressant	[17]
	Turbinaria conoides	Stigmasta-4,7,24(28)-triene	Antifungal	[17]
	Sargassum horneri	β-sitosterol	Antidepressant	[17]
	Ecklonia stolonifera	24-hydroperoxy24-vinylcholesterol	Anti-cholinesterase	[17]
	Ecklonia bicyclis	Phloroglucinol, eckol, phlorofucofuroeckol A & dioxinodehydroeckol	Anti-inflammatory	[17]
Sponges	*Phycopsis* sp.	Dichloromethane	Antibacterial	[18]
	Agelas dispar	Methanol bromopyrrole alkaloids	Antibacterial	[18]
	Latrunculia sp. and *Negombata* sp.	Discorhabdin R	Antibacterial	[18]
	Petrosia sp.	Methanol soluble extract	Cytotoxicity	[18]
	Cymbastela sp.	Aglestatin A	Cytotoxicity	[18]
	Pachastrella sp. and *Jaspis* sp.	Pectenotoxin II and Psammaplin A	Antitumoral	[18]
	Cymbastela sp.	Methylicosadienoicacids	Larvicidal	[18]
	Hyrtios sp.	Puupehenone	Antiviral/Antifungal	[18]
	Fasciospongia covernosa	Cacospongionolide B	Antimicrobial	[18]
	Polyfibrospongia sp.	Hennoxazoles A-D	Antiviral	[19]
	Polyfibrospongia sp.	Miyakolide	Antitumoral	[19]
	Axinella sp./ *Halichondrida*	Axinellamines B–D	Antibacterial	[19]

Marine organisms	Source	Biomolecules	Activity	References
	Cribrochalina sp.	Cribrostatin 6	Antibacterial	[19]
	Aaaptos aaptos	Isoaaptamine	Antibacterial	[19]
	Arenosclera brasiliensis	Arenosclerins A–C	Antibacterial	[19]
	Arenosclera brasiliensis	Haliclona cyclamine E	Antibacterial	[19]
	Caminus sphaeroconia	Caminosides A–D	Antibacterial	[19]
	Jaspis sp.	Jaspamide	Antiviral	[19]
	Hymeniacidon sp.	Monamphilectine A	Antimalarial	[19]

Moreover, the marine environment contains diverse marine multicellular macroscopic organisms including seaweeds and invertebrates which represent other potential resources of natural products.

Seaweeds (also called macroalgae) are an heterogeneous group of macroscopic, multicellular, marine macroalgal species; they can be divided into three main phyla: red (Rhodophyceae), brown (Phaeophyceae), and green (Chlorophyceae) macroalgae. They comprise a highly significant element of the marine ecosystem contributing a major feeding ground for marine lives as well as potentially therapeutic resources for human. Numerous secondary bioactive metabolites including carotenoids, polyphenolics, polysaccharides, and sterols have been isolated from seaweed and applied in different industrial usages due to their health promoting therapeutic qualities combatting various human ailments, comprising antihypertensive, antioxidant, antithrombotic and immunomodulatory properties [13].

On the other hand, invertebrates comprise a wide range of animal species belonging to various phyla with different morphological structures and physiology, including Mollusca, Arthropoda, Porifera and Echinodermata, from which secondary metabolites mainly alkaloids, terpenoids and steroids, have shown biological activities and are commercially applied [14].

Additionally, marine invertebrates have been reported to actively interact with their associated bacterial symbionts resulting in the discovery of new compounds as biosurfactants and exopolysaccharides, with application in pharmaceutical and medical fields for their antifungal, antiprotozoal, antiviral and antifouling functions [15]. The exploration of the different phyla is related to the discovery of a greater amount of natural substances with functional biodiversity as shown in Table 2.

3. MARINE BIOMOLECULES WITH RELEVANT CHEMICAL AND THERAPEUTIC PROPERTIES

3.1. Chitin and chitosan

Chitin and chitosan are natural glucosamine biopolymers mostly found in the structural backbone exoskeleton of marine invertebrates. Chitin is a neutral crystalline substance with a structure of n-acetyl-glucosamine monomerswidely derived from shrimps, crabs and squid which revealed an important role in maintaining cutaneous homeostasis and neutralizing free radicals activity [20]. Its deacetylated derivative called chitosan is found in lobster, crab, shrimp and also in mollusks exoskeletons. It is recognized by its multiple applications in cosmeceutical formulations for skin care, as moisturizer because of its water absorbing properties. Its oligomers revealed an important role in stimulating fibroblast production, providing wound healing benefits, and exhibiting antioxidant and metalloproteinase inhibiting effects. It has also antimicrobial activity against bacteria, yeasts and fungi. In the form of nanoparticles, chitosan helps to protect from aggressive environmental factors such as light and oxidation [20].

Additionally, marine bacterial chitinases are exoenzymes that play an important role in the nutrient cycling and waste management in the oceans. They convert chitin to biologically useful carbon and nitrogen forms for marine organisms and biodegrade exoskeletal chitinous wastes generated from the production and processing of shellfish to reduce environmental pitfalls [21].

3.2. Carotenoids

Carotenoids, or tetraterpenoids, are important yellow, red, and orange coloured pigments isolated from photosynthetic bacteria, algae and plants that have relevant antioxidant roles. Physiologically, oxidative stress is implicated in pathological degenerative processes and aging, atherosclerosis, cancer, malaria, neurodegenerative diseases and arthritis. Thus, carotenoids have proven their ability to prevent, delay, or neutralize the effects of oxidative stress and suppression and/or scavenging of free radicals. Beta carotene and lycopene have been reported to remediate ultraviolet oxidative damage to the skin and retina [22]. In addition, lutein and zeaxanthin have shown a protecting role against age-related macular degeneration through antioxidant and light protective mechanisms [23]. Zeaxanthin, has also shown to have various beneficial effects for human health due to its ability to quench free radicals, exert antioxidant effects, as well as decrease inflammation [24]. Astaxanthin, another carotenoid has gained a growing interest as a multi-target pharmacological agent against neurological diseases such as Alzheimer's disease, Parkinson's disease, neuropathic pain, aging, depression, and autism. It has shown a neuroprotective effects due to its anti-inflammatory, antioxidative, and anti-apoptotic properties to tackle neurodegeneration [25, 26]. Moreover, several biological properties are provided by fucoxanthin, a marine natural compound produced by brown algae and diatoms, reported to provide anti-obesity, anti-diabetic, anticancer, antioxidant and antimicrobial activities [27].

3.3. Polysaccharides

Polysaccharides are the high molecular weight carbohydrate molecules, mostly polymers of glucose, linked through glycosidic bonds. They have known a grown interest in various industries which demand applications of natural polymers for their diverse biological activities. For example, a sulfated O-polysaccharide isolated from the marine bacterium *Poseidonocella sedimentorum* KMM 9023T has shown high anticancer activity. It inhibits colony formation of human colorectal adenocarcinoma HT-29, human breast adenocarcinoma MCF-7 and human malignant melanoma SK-MEL-5 cells [28]. Anticancer therapeutic properties have also been shown for other carbohydrate types, as is the case of the sulfated lipopolysaccharide isolated from the marine bacterium *Cobetia litoralis* KMM 3880 3880T. It inhibits colony formation of human melanoma SK-MEL-28 and colorectal carcinoma HTC-116 cells [29].

Additionally, these natural polymers are used in cosmetics in order to prevent aging, inflammation, and skin degradation as they are formulated with ingredients including vitamins, minerals and antioxidants [30]. They are also commercialized as emulsifiers, gelling agents, viscosifiers, stabilizers, and texture enhancers provided by fucoidans isolated from brown algae, carrageenans from red algae, and alginate and agar from brown and red algae [31].

3.4. Peptides

Recently, many biologically active compounds of peptidic nature have proven their ability to impair biofilms development. They may represent a biofilm preventing strategy for investigation in aquaculture, maritime fields and food industries in order to reduce economical losses worldwide [32].

For example, a peptide molecule produced by *Pseudoalteromonas* sp. strain 3J6 called alterocin

impaired the ability of initial attachment of *Paracoccus* sp. strain 4M6, *Vibrio* sp. D01 and *Vibrio tapetis* to form biofilms. It has also impaired biofilm development by three human pathogenic strains: *Pseudomonas aeruginosa*, *Salmonella enterica* and *Escherichia coli* [33].

In the same way, another *Pseudoalteromonas* strain, *Pseudoalteromonas* sp. strain 41, has impaired biofilm development ofmany marine bacterial strains including *Pseudoalteromonas* sp. strain 3J6, *Paracoccus* sp. strain 4M6, *Alteromonas* sp. 1J3, *Algibacter* sp. 1M6, *Micrococcus* sp. 5J6 and *Colwellia* sp. 4J3 [34].

In addition, many microbes associated with marine living surfaces have been reported to secrete peptides with antifouling activity which inhibits the adhesion of biofilm bacteria and microalgae and showed inhibitory activities against larval forms of barnacle, polychaete, ascidian and spores of macroalgae [35].

3.5. Antibiotics

Marine microorganisms represent a significant source for the development of antibiotics. Most of them are synthesized by bacteria, in particular, actinomycetes which produce diverse products with clinical or pharmaceutical applications due to their broad spectrum of biological properties. For example, marthiapeptide A isolated from *M. Thermotolerans* SCSIO 00652, desotamide B isolated from *Streptomyces scopuliridi* SCSIO ZJ46, marfomycins A, B, and E isolated from *Streptomyces drozdowiczii* SCSIO 10141 and vitroprocines A-J derived from *Vibrio* sp. QWI-06 providing all of them antimicrobial activities. In addition, there are antibiotics with potent antitumor properties, they have been designated as spirotetronate polyketides, like lobophorin F isolated from *Streptomyces* SCSIO 01127, lobophorin H isolated from *Streptomyces* sp. 12A35*S* and abyssomicin C isolated from *Verrucosispora* strain AB 18-032 [36, 37].

On the other hand, marine fungi have been also considered as an excellent source of bioactive compounds since the discovery of the antibiotic cephalosporin. As example of natural compounds isolated from fungi, there are gliotoxin isolated from an *Aspergillus* sp., prenylxanthones and emerixanthones A–D isolated from *Emericella* sp. SCSIO 05240 and engyodontiumone H purified from *Engyodontium album* DFFSCS021 providing antifungal and antibacterial properties with many other antibiotics providing various biological activities [36].

4. IMPACTS OF MARINE BIOFILMS

4.1. Advantages

Bacterial biofilms are an extracellular matrix mainly composed of polysaccharides, proteins and lipids. It facilitates signals exchange and nutrient uptake between different bacterial species, and with other symbiotic microorganisms, like fungi and microalgae. This sessile form gives the bacterial community protection against a huge number of environmental stressors such as antimicrobial agents, predators, UV radiation, etc. [5, 38].

The nutritional composition of biofilms is considerably appropriate to fish dietary needs. Consequently, food availability as well as water quality improved by bacterial biofilms enhance aquaculture growth and production.

It has been reported in a research that application of biofilm during the culture of fingerlings of the fish *Catla catla* has shown lower concentrations of total ammonia in comparison with control treatment [5]. Then, the presence in biofilms of nitrifying bacterial communities belonging to *Nitrosomonas* and *Nitrosococcus* genera helps in the management of water quality by decreasing ammonium level in cultured water with a parallel increase of nitrite and nitrate concentrations [6].

Aquaculture used to need water exchange for feed addition as well as preventing accumulation of toxic substances. However, frequent water exchange is expensive and may increase the risk of introducing bacterial pathogens and toxic metabolites, but since the use of biofilm has been introduced in aquaculture ponds, it is not required to exchange water [5, 6]. The use of biofilms sequesters excess nutrients such as dissolved phosphorus, ammonia ions and nitrates that are accumulated in aquaculture ponds including bacteria of the genera *Nitrobacter*, *Nitrococcus*, *Nitrospira*, and *Nitrospin*. It does not only maintain water quality but also reduce the occurrence of pathogenic microorganisms which may suppress microbial infection and prevent diseases. For example, *Vibrio* strain C33 a marine bacterium associated with the aquaculture of bivalve *Agropecten purpuratus* has been reported to produce bioactive compounds controlling the growth of pathogenic strains forming biofilms such as *Vibrio alginolyticus*, *Vibrio anguillarum, Vibrio parahaemolyticus and Vibrio splendidus* [39].

On the other hand, there are several situations in which higher organisms encourage biofilm formation by protective biofilms. One example of this feature is the macroalga *Ulva lactuca*, it encourages colonization by the marine gram negative bacterium, *Pseudoalteromonas tunicate*. This endophytic bacterium produces antifouling compounds identified as a large extracellular protein that inhibits colonization by other undesirable bacteria [40].

Thus, biofilm can be used as a novel alternative strategy of disease control in marine fisheries and aquaculture industries in order to improve growth performance and health conditions of aquatic organisms [41, 42]. It can also serve as active biofilters to absorb and degrade excessive nutrients and remove ammonia in seawater supply systems [43].

4.2. Inconvenients

Over the past few decades, the consumption of raw food including seafood products has grown as it has a high nutritional value. It contains proteins, omega-3 fatty acids, minerals and vitamins. Consequently, the occurrence of foodborne illnesses is increasing because of these new nutritional trends making food safety a universal issue [44].

Consumers are most vulnerable to foodborne illnesses because of dangerous bacterial pathogens found as biofilms on seafood formed by *Listeria* spp., *Salmonella* spp., *Vibrio* spp. (*V. cholerae*, *V. parahaemolyticus*, *V. vulnificus*), *Clostridium* spp. (*C. perfringens*, *C. botulinum)*, *Campylobacter* spp., *Shigella* spp., etc. Other species of the genera *Mycobacterium* are also deleterious to humans health especially *Mycobacterium marinum* as well as a number of *Streptococcus*, *Aeromonas*, *Erysipelothrix*, and *Pseudomonas* species [45].

Some bacteria may produce potent natural toxins. Many of them are thermostable, and since they cannot be destroyed by food preparation methods (cooking, frying, freezing, etc.) they lead to acute illnesses such as emetic reaction, gastroenteric symptoms, and neurologic reactions [46].

When microorganisms form biofilm on food, they survive for long periods. Consequently, antibiotics and numerous chemical compounds habitually used in aquaculture to control the occurrence of these bacterial pathogens are less effective [47]. Moreover, these compounds have a negative impact not only on quality and safety of cultivated organisms (including oysters, mussels, fish and crustaceans) but also on human health, as well as on the environment [46]. Firstly, the excessive exposure may damage the nervous and immune systems and lead to cancer and impairment of reproductive development and function. Additionally, some seafood pathogens may become resistant to many drugs and the resistant determinants may be transmitted by horizontal gene transfer to bacterial human pathogens after consumption of contaminated seafood leading to dangerous outbreaks [47].

On the other hand, the marine environment is being progressively polluted by these wide varieties of drugs and chemicals. It is also affected by novel microbial communities colonization which may be developed on any submerged surface and cause biofouling and biocorrosion [48]. These ecological phenomena have major impacts on marine engineering contributing to economic losses worldwide. They can lead to reduction of heat transfer capacity of heat exchangers by 20 to 30% and decrease of underwater cameras and nephelometers effectiveness. They can also develop on ship hulls and boats which may increase their weight and consequently consumption of fuel, then increase CO_2 emissions [49].

Thus, the discovery of novel secondary metabolites from the marine environment has been necessary to overcome biofilm issues occurring in marine habitats. An example of a non-toxic glycolipid biosurfactant named BS-SLSZ2 derived from a marine bacterium *Staphylococcus lentus* is used to treat aquaculture associated infections as it inhibits *Vibrio harveyi* and *Pseudomonas aeruginosa* biofilms. *Vibrio harveyi* biofilm is also inhibited by a lipopeptide of the fengycin family produced by the actinobacterium *Nesterenkonia* sp. MSA31, while another lipopeptide produced by a newly identified bacterium, *Pontibacter korlensis* strain SBK-47 named pontifactin exhibits an anti-adhesion potential against *Vibrio cholerae*. Therefore, marine secondary metabolites are taking a high interest for use as an eco-friendly manner in aquaculture ponds as they may act as biofilm controlling agents in order to decrease the usage of antibiotics in aquaculture settings [42, 50].

5. CONCLUSION

Marine species are taxonomically diverse, which makes them of a renewed interest for the discovery of a wide range of novel natural molecules. Marine secondary metabolites are recognized by unique structural and functional features. They provide diverse biological activities such as antitumor, immunostimulatory, anti-inflammatory, antibacterial, antifouling and antioxidant activities. Consequently, it makes them possess a great potential for exploitation in different areas such as pharmaceutical, cosmetics and food industries as well as maritime and aquaculture fields. Thus, the marine environment needs to be more explored to strengthen the use of natural bioactive compounds as an adequate alternative to synthetic molecules.

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