Marine microorganisms as an untapped source of bioactive compounds

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Abstract

The search for novel biologically active molecules has extended to the screening of organisms associated with less explored environments. In this sense, Oceans, which cover nearly the 67% of the globe, are interesting ecosystems characterized by a high biodiversity that is worth being explored. As such, marine microorganisms are highly interesting as promising sources of new bioactive compounds of potential value to humans. Some of these microorganisms are able to survive in extreme marine environments and, as a result, they produce complex molecules with unique biological interesting properties for a wide variety of industrial and biotechnological applications. Thus, different marine microorganisms (fungi, myxomycetes, bacteria, and microalgae) producing compounds with antioxidant, antibacterial, apoptotic, antitumoral and antiviral activities have been already isolated. This review compiles and discusses the discovery of bioactive molecules from marine microorganisms reported from 2018 onwards. Moreover, it highlights the huge potential of marine microorganisms for obtaining highly valuable bioactive compounds.

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1. Introduction

Most bioactive compounds are derived from terrestrial microorganisms and, although the terrestrial environment is a bountiful source of bioactive producers, the discovery of novel metabolites is diminishing (Jensen and Fenical, 2000). Hence, new sources of bioactive substances need to be explored. In this sense, the enormous biodiversity present in marine ecosystems offers a promising resource to find new compounds with numerous worthwhile biological activities. According to the Global Biodiversity Assessment by the United Nations Environment Programme, there are 178,000 marine species belonging to 34 phyla (Mitra and Zaman, 2016). Thus, ocean's biodiversity represents 50% of the whole globe's biodiversity, making marine microorganisms a promising sustainable source of novel biologically active compounds (Jimeno et al., 2004; Vignesh et al., 2011).

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Peer review under responsibility of King Saud University.
Oceans contain many different specific habitats characterized by a wide range of temperatures, hydrostatic pressures and levels of salinity. To survive in such unique ecosystems, marine microorganisms have developed different adaptation mechanisms, including the production of specific biomolecules. Consequently, marine microorganisms would seem to hold a considerable potential of producing bioactive compounds not found in terrestrial environments (Xie et al., 2018). In particular, extreme marine habitats are unique ecological niches in which extremophile microorganisms develop specific biochemical pathways and characteristics.

Although the first cephalosporin C antibiotic was obtained from a marine fungus in 1949, the discovery rate of biologically active metabolites from marine microorganisms remained very slow until the 1980s. Thus, since 1985, more than 15,000 new metabolites have been identified from marine organisms, many of which have displayed interesting bioactivities (Blunt et al., 2009; Al-Dhabi et al., 2019). Thus, marine microorganisms are able to produce active biomolecules with diverse pharmacological activities (e.g. anticancer, anti-inflammatory, anti-diabetic and antibiotic) (Rateb and Ebel, 2011). In addition, marine microorganisms are renewable and more easily cultured than marine macroorganisms (Blunt et al., 2015). Also, their use would avoid excessive exploitation of marine resources and adverse collection practices (Romano et al., 2017).

Excellent reviews on natural marine products that covered the available literature published in 2016 (Blunt et al., 2018) and 2017 (Carroll et al., 2019) have been published. In addition, another review by (Barzkar et al., 2019) highlighted the pharmaceutical potential of natural compounds isolated from marine microalgae. Also, Corinaldesi et al. (2017) outlined different bioactive compounds with cosmeceutical and cosmetic applications isolated from marine bacteria and marine fungi. Consequently, the present review compiles the most recent published research on the isolation of different novel biologically active metabolites from marine microorganisms.

2. Marine microorganisms

The main species of bacteria found in seawater belong to the genera Pseudomonas sp., Vibrio sp., Achromobacter sp., Flavobacterium sp. and Micrococcus sp. (Baharum et al., 2010). However, the genus Streptomyces has been the main provider of new molecules so far (Blunt et al., 2018). Marine bacteria are supposed to possess physiological, biochemical and molecular properties that are different from their terrestrial equivalents and, accordingly, they may produce different compounds (Siddharth and Vittal, 2018). As such, marine bacteria are likely the most promising microorganisms for the detection of novel molecules with antibacterial properties, especially since the majority of natural antibiotic drugs come from one group of terrestrial bacteria, the actinomycetes (Butler et al., 2013).

Several myxomycetes were recovered from freshwater environments (Shearer and Crane, 1986; Lindley et al., 2007; Winsett and Stephenson, 2013), where they appear to be relatively common. Dykovà et al. (2007) reported that they identified a possible myxomycete living as an endocommensal of a sea urchin in the Adriatic Sea. Studies of myxomycetes in aquatic freshwater habitats are few in number and we are not aware of any study that has been directed towards surveying myxomycetes in marine habitats. It seems likely that any species of myxomycetes isolated from marine habitats would include unusual taxa, possibly including those new to scientists.

Numerous novel secondary metabolites were isolated from myxomycetes (Dembitsky et al., 2005; Huynh et al., 2017; Nguyen et al., 2017). However, the comprehension of their biological properties is still rather limited. Biologically active molecules from myxomycetes were highly researched from the 1950’s to the 1970’s and then they were stopped until the beginning of the twenty-first century (Tran and Adamatzky, 2017). Overall, nearly all bioactive compounds isolated from myxomycetes exhibited the highest inhibition effects on Gram positive bacteria (e.g. Bacillus subtilis) followed by fungi (e.g. Candida albicans) and low or no inhibition effects on Gram negative bacteria (Sawada et al., 2000). Nonetheless, their effect on other microbial cells has not been investigated yet.

Marine fungi constitute the main degraders of lignocellulosic and aromatic materials in marine habitats (Ameen et al., 2016; 2015a; 2015b; 2014; Hyde et al., 1998). According to their capability to grow in marine habitats, they are classified as obligate or facultative marine fungi (Borse et al., 2012). The former grow rapidly and sporulate only in a marine or estuarine environment, whereas the latter usually come from the terrestrial environment and are adapted to the marine one. Marine fungi are linked to algae, corals and detritus of marine macrophytes. About 1500 species of marine fungi, from which 530 correspond to obligate marine fungi, are established. Occasionally, it is hard to distinguish the obligate or facultative character of the marine fungi and hence, the more extensive term “marine-derived fungi” is utilized (Bugni and Ireland, 2004). Most marine fungi belong to the phylum Ascomycota (Jones et al., 2015), whereas the phylum Basidiomycota is under-represented (Jones and Pang, 2012; Jones et al., 2015; Raghukumar, 2017). Very recently, an online database devoted to marine fungi has been developed (Jones et al., 2019).

The severe physical and chemical conditions existing in the marine environment are responsible for the development of particular metabolic routes in marine fungi not found in their terrestrial counterparts (LiBerra and Lindequist, 1995; Abdel-Lateff, 2008). During the past few decades, a large array of novel natural metabolites with a diverse range of pharmacological activities was obtained from marine fungi (Rateb and Ebel, 2011). However, few drugs from marine fungi are at present commercially available (Kiuru et al., 2014).

Marine microalgae are tiny unicellular plants which form what is known as phytoplankton. They play a crucial role in oceans as primary producers of biomass and organic compounds, thanks to their photosynthetic process (Camacho et al., 2007; Sieg et al., 2011; Kiuru et al., 2014). In addition, marine microalgae produce about 50% of atmospheric oxygen (Singh et al., 2011). Marine microalgae can be classified into three groups: blue-green algae (Cyanobacteria), diatoms (Bacillariophyta) and dinoflagellates (Dinophyceae). It is thought that there are about 50,000 species of microalgae, however few of them have been characterized (Lee et al., 2013). The considerable biochemical differences found among marine microalgae make them an untapped source for the biosynthesis of a huge diversity of bioactive molecules (Abida et al., 2013; Coelho et al., 2019). Microalgae can be applied for biomass production, primary metabolite production (e.g. carotenoids, proteins and lipids), as biosorbent for heavy metals (Al-Homaidan et al., 2018) and secondary metabolite production (generally compounds with pharmaceutical applications) (Barra et al., 2014) (Fig. 1) (Khan et al., 2018). In Fig. 2, the cultivation of microalgae in the laboratory is illustrated (Malibari et al., 2018).

3. Bioactive compounds from marine microorganisms

In Table 1 a list of the different biologically active molecules from marine microorganisms reported recently are presented.
bacteria from marine soil samples, which were identified as and bacter melonis (Shin et al. (2018). a promising approach to find new bioactive microbial metabolites indicated that co-cultivation of marine microorganisms could be obtained from the shore of a muddy wetland, showing antiproliferative features to be used as a viscous antioxidant in various industries. Nevertheless, more research is required to identify the antioxidant compounds produced and their possible industrial utilisation.

3.1. Bioactive compounds from marine bacteria

Galaviz-Silva et al. (2018) reported acute antimicrobial activity against the food borne poisoning strains Staphylococcus aureus and Vibrio parahaemolyticus by the bacteria Bacillus aerius, B. oryzicola, B. safensis, B. boroniphilus, B. altitudinis and Virgibacillus senegalensis isolated from marine habitats in Mexico. It would seem that these marine bacteria could serve as a potential alternative against other clinically important bacteria for the elaboration of new antimicrobials.

A new discovered metabolite named dentigerumycin E by co-cultivation of the marine strains Streptomyces sp. and Bacillus sp., obtained from the shore of a muddy wetland, showing antiproliferative and antimetastatic activities against human carcinoma. This indicated that co-cultivation of marine microorganisms could be a promising approach to find new bioactive microbial metabolites (Shin et al. 2018).

Shivale et al. (2018) isolated two novel antioxidant-producing bacteria from marine soil samples, which were identified as Janibacter melonis and Pseudomonas stutzeri. Nevertheless, more research is required to identify the antioxidant compounds produced and their possible industrial utilisation.

A marine actinobacterium Streptomyces sp.S2A, was identified and isolated from sea sediment samples. This organism produced an extract that exhibited antimicrobial activity against pathogen bacteria and fungi, inhibitory activity against α-glucosidase and α-amylase enzymes and antioxidant and cytotoxic activities against different cell lines. They identified the principal constituent of the extract (80%) as pyrrolo[1–a] pyrazine-1,4-dione, hexahydro-3-(2-methylpropyl), corresponding to a peptide derived from diketopiperazine (Siddharth and Vittal 2018).

Wang et al. (2018a) isolated and purified an exopolysaccharide from the marine bacterium Aerococcus uriaeaequi that exhibited antioxidant activities which, according to its safety assessment on mice, was safe for both topical and oral application. Therefore, it could have potential applications in medicine.

Zhang et al. (2018) identified five bagremycin analogues, including two new ones, from a marine actinobacterium, isolated from a marine mud sample and identified as Streptomyces sp. ZZ745. The two novel bagremycins exhibited antibacterial activity against E. coli.

Al-Dhabi et al. (2019) demonstrated significant antimicrobial activity of extracts from the Saudi Arabian marine-derived actinomycete Streptomyces sp. Al-Dabhi-90 against drug resistant pathogens such as S. aureus, Klebsiella pneumoniae, E. coli, Pseudomonas aeruginosa, Proteus mirabilis and Enterococcus faecium. Furthermore, they found that the main components of the Streptomyces extracts were 3–methylpyridazine, n-hexadecanoic acid, indazol-4-one, octadecanoic acid and 3a-methyl-6–((4-methylphenyl) sul. Therefore, Streptomyces sp. Al-Dhabi-90 is a promising source for the production of new antibiotics to fight against multidrug resistant clinical pathogens.

A marine actinomycete isolated from the mollusc Drupa granulata that showed antagonistic activity against prochloraz-resistant strains of Penicillium digitatum, which cause green mould in post-harvested citrus. The isolated actinomycete was identified as Streptomyces chumphonensis (Hu et al. 2019).

Kim et al. (2019) isolated four 2-alkyl-4-hydroxyquinoline compounds from semi-solid rice cultures of the marine-derived actinobacterium Streptomyces sp. MBT13. Among them, one compound highly inhibited the hyphal growth of Candida albicans.

The antioxidant properties of the methanolic extract from the marine Gram-negative bacterium Novosphingobium sp. PPIY, was reported and obtained from a contaminated zone in the seaport of Pozzuoli (Naples, Italy) (Petruk et al. 2019).

Sran et al. (2019) isolated a marine actinobacterium from Rasthakouda Beach (Tamil Nadu, India), identified as Microbacterium aurantiacum FSW25 according to polyphasic taxonomy. The cultivation of this bacterium produced a large amount of an exopolysaccharide with interesting rheological and antioxidant features to be used as a viscous antioxidant in various industries.

Fig. 1. Microalgae convert atmospheric CO2 to a variety of valuable bioproducts by using light (after Khan et al., 2018).

Fig. 2. Marine microalgae cultured in the laboratory (Reprinted from Journal of Cleaner Production 198. Malibari, R., Sayegh, F., Elazzazy, A.M., Baeshen, M.N., Dourou, M., Aggelis F, G., Reuse of shrimp farm wastewater as growth medium for marine microalgae isolated from Red Sea-Jeddah, 160–169, Copyright (2018), with permission from Elsevier Ltd., UK).
| Microorganism | Compound | Activity | Reference |
|---------------|----------|----------|-----------|
| **Bacteria** | Bacillus aerius, Bacillus oryzicola, Bacillus safensis, Bacillus boroniphilus, Bacillus altitudinis and Virgibacillus senegalensis | Not identified | Antimicrobial | Galaviz-Silva et al. (2018) |
| Streptomyces sp and Bacillus sp | Dentigerumycin | Antitumoral | Shin et al. (2018) |
| Janibacter melonis Pseudomonas stutzeri | Not identified | Antioxidant | Shivale et al. (2018) |
| Streptomyces sp.52A | Pyrrol[1-a]pyrazine-1,4-dione,hexahydro-3-(2-methylpropyl) | Antimicrobial, enzyme inhibitory, antioxidant and cytotoxic | Siddharth and Vittal (2018) |
| Aerococcus uraeaequi HZ | Exopolysaccharides | Antioxidant | Wang et al. (2018a) |
| Streptomyces sp. ZZ745 | Bagremycins | Antimicrobial | Zhang et al. (2018) |
| Streptomyces sp. Al Dhabi-90 | 3-methylpyridazine, n-hexadecanoic acid, indazol-4-one, octadecanoic acid and 3a-methyl-6-[(4-methylphenyl) sul | Antibacterial | Al-Dhabi et al. (2019) |
| Streptomycus chumphonensis | Not identified | Antimicrobial | Hu et al. (2019) |
| Streptomycys. | 2-Alkyl-4-hydroxyquinolines | Antifungal | Song et al. (2018) |
| Novosphingobium sp. PP1Y | Not determined | Antioxidant | Liu et al. (2018a) |
| Microbacterium aurantiacum FSW-25 | Exopolysaccharide | Antioxidant | Sran et al. (2019) |
| Penicillium sp. ZZ380 | Abyssomicin | Antiviral | Zhang et al. (2020) |
| **Fungi** | Simplicillium lamellicola, Leptosphaerulina sp., Penicillium citrinum, Penicillium chrysogenum, Aspergillus sydowii Hansfordia sinuosae | Not identified | Antibacterial | Agrawal et al. (2018) |
| Penicillium sp. ZZ901 | Polysaccharide | Antimicrobial | Li et al. (2018a) |
| Fusarium sp. 152 | Equisetin | Antigloma and antibacterial | Li et al. (2018b) |
| Diaporthe sp. SCSIO 41,011 | Polyketides | Anti-MRSA | Luo et al. (2018a) |
| Trichoderma sp. SCSIO41004 | 5-acetyl-2-methoxy-1,4,6-trihydroxy-anthraquinone | Antiviral | Luo et al. (2018b) |
| Penicillium sp. ZZ380 | Pyrrospirone alkaloids | Antigloma | Song et al. (2018) |
| Aspergillus niger ARK-MKBU | L-asparaginase | Anticancer | Vala et al. (2018) |
| Chaetomium sp. NA-501-R1 | Chaephilone, chaetovirides | Antimicrobial, Anti-tumoral | Wang et al. (2018b) |
| Aspergillus alabamensis EN-547 | 4-epi-seco-shornephine A carboxylic | Antimicrobial | Yang et al. (2018) |
| Truncatella angustata | Isoprenylated cyclohexanols | Antiviral | Zhao et al. (2018a) |
| Fusarium equiseti | (11S)-1,3,6-trihydroxy-7-[(1-hydroxyethyl)-anthracene-9,10-dione | Cytotoxic | Zhao et al. (2018b) |
| Alternaria sp. | 7-acetyl-1,3,6-trihydroxyanthracene-9,10-dione | Antifungal | Zhao et al. (2018b) |
| Curvularia sp. IFB-Z10 | Alterperylenol | Antibacterial | An et al. (2019) |
| Penicillium chrysogenum | Tyrosol | Anti-quorum sensing | Chang et al. (2019) |
| Penicillium sp. | 2-[(5-methyl-1,4-dioxan-2-yl)methoxy]ethanol | Antimicrobial | Le et al. (2019) |
| Penicillium sp. IMB17-046 | 2-[(2R-Hydroxypropanoyl)amino]benzamide, 4-hydroxybenzaldehyde | Antimicrobial | Li et al. (2019) |
| Penicillium sp. IMB17-046 | 3b-Hydroxyergosta-8,14,24(28)-triene-7-one | Anti-α-glucosidase | (continued on next page) |
Table 1 (continued)

| Microorganism | Compound | Activity | Reference |
|---------------|----------|----------|-----------|
| Penicillium sclerotiorin | Azaphilone derivative | Anti-inflammatory | Liu et al. (2019) |
| Penicillium citrinum HDN-152–088 | Isochromophiline IX Scleroketide C Dicitrones | Antioxidant Antimicrobial | Wang et al. (2019) Baе et al. (2020) |
| Aspergillus sp. | Asperphenin A | Antitumoral | Ma et al. (2020) |
| Penicillium minioluteum ZZ1657 | N-acetyl-L-valine conjugated drimaranene sesquiterpenoids Drimane sesquiterpenoids | Antimicrobial | Xu et al. (2020) |
| Aspergillus sp. LS116 | Aspergilisteroid A | Antibacterial | de Vera et al. (2018) |
| Microalgae | Not identified | Apoptotic | Fimbres-Olivaria et al. (2018) |
| Prorocentrum hoffmannianum, Prorocentrum arenarium, Prorocentrum reticulatum, Alexandrium tamarenseis Gambierdiscus australies | Not identified | Antibacterial | Martinez et al. (2019) |

* MRSA: anti meticillin-resistant Saphylococcus aureus.

Zhang et al. (2020) identified a new abyssomicin and six known abyssomicin and proximin analogs from extracts of the cultures of a marine bacterium isolated from sea sediments and identified as Verrucosisspora sp. MS100137. The new compound and two of the known ones exhibited considerable antiviral effects against the IAV.

3.2. Bioactive compounds from marine fungi

Agrawal et al. (2018) isolated new marine fungal species identified as Simplicillium lamellicola, Leptosphaerulina sp., Penicillium citrinum, Penicillium chrysogenum and Aspergillus sydowii with high antimicrobial activity against the acne-inducing bacteria Cutibacterium acnes and Staphylococcus epidermidis with minimum inhibition concentrations (MIC) ranging from 0.8 to 1.0 mg/mL. Hence, the extracts of these fungi could represent an interesting option for obtaining antibiotics for acne vulgaris cure. Nevertheless, the specific bioactive molecules conferring the antimicrobial activity were not determined.

Li et al. (2018a) demonstrated the antitumoral effect on cervical cancer (HeLa cells) and breast cancer (MCF-7) human cells of a polysaccharide, containing mainly mannose, produced by cultivation of the marine fungus Hansfordia sinuosae.

Li et al. (2018b) obtained six novel peniciphenalineins and the already identified metabolites (+)-sclerodin, (+)-scleroderolide, (+)-sclerodion and physscion from cultured extracts of the marine-derived fungus Penicillium sp. ZZ901. They found that the known (+)-scleroderolide compound inhibited the growth of glioma cells and also presented antibacterial activity against the pathogenic bacteria S. aureus (MIC 7.0 μg/mL) and Echerichia coli (MIC 9.0 μg/mL).

Luo et al. (2018a) found a novel anti meticillin-resistant S. aureus (MRSA) compound from the deep marine fungus Fusarium sp. 152. Subsequently, that compound was identified as equisetin and showed a MIC value of 1 μg/mL against MRSA.

Luo et al. (2018b) isolated twenty-eight aromatic polyketides from the mangrove-associated fungus Disporthae sp. SCSIO 41011, four of which showed high antiviral activities against three varieties of the influenza A virus (IAV). These compounds were identified as 2 pestalotiposone, 3,8-dihydroxy-6-methyl-9- oxo-9H-xanthene-1-carboxylate and 5-chloroisorotiorin.

Pang et al. (2018) obtained three new and six known molecules from the rice cultivation extract of the sponge-derived fungus Trichoderma sp. SCSIO41004. From the isolated compounds only one (the already known compound 5-acetyl-2-methoxy-1,4,6-tri hydroxy-anthraquinone) exhibited significant antiviral activity against the human Enterovirus 71 (EV71).

Song et al. (2018) found that the fungus Penicillium sp. ZZ380, collected from a wild crab, produced new seven pyrrospyrone alkaloids, one of which exhibited high anti-glioma activity and the other three presented antimicrobial activity against MRSA and E. coli with MIC values of 2.0–5.0 μg/mL.

Vala et al. (2018) produced an L-asparaginase enzyme with anticancer activities by the marine-derived fungi Aspergillus niger. In addition, a cost-effective production at laboratory bioreactor scale (5 L) utilizing groundnut oil cake as an inexpensive substrate was achieved.

Various bacteria from marine sponges, collected from the Red Sea coast of Saudi Arabia were isolated and cultivated for the production of the anticancer enzyme L-asparaginase. Among them, a bacterium identified as Bacillus subtilis produced L-asparaginase with no glutaminase activity which is very important from a medical point of view (Ameen et al., 2020).

Wang et al. (2018b) identified four new chlorinated compounds, named chaetovirides A, B and C, and four known ones derived from azaphilone, designed as chaetoviride A, chaetoviride B, chaetoviride E and chaetoviride D, from the deep sea derived fungus Chaetomium sp. NA-S01–R1. Chaetoviride A and chaetoviride B presented antibacterial activities against Vibrio rotiferianus and Vibrio vulnificus and chaetoviride C, chaetoviride B and chaetoviride C showed anti-MRSA activities. In addition, chaetoviride A exhibited cytotoxic activity against Hep G2 cells and chaetoviride C and chaetoviride B towards HeLa cells.

Yang et al. (2018) obtained three new and four known natural derivatives from the extracts of the marine-derived fungus Aspergillus olabamensis EN-547, obtained from the marine red alga Ceramium japonicum. The new molecules were identified as 4-epi-seco-shornephine A methyl ester, 4-epi-seco-shornephine A carboxylic...
acide and 28-acetoxy-12b,15a,25-trihydroxyergosta-4,6,8(14),22-t etraen-3-one and the known compounds as shornepine A, 25-hydroxyergosta-4,6,8(14),22-tetraen-3-one, 25,28-dihydroxyy ergosta-4,6,8(14),22-tetraen-3-one and 12b,15a,25,28-tetrahydroxy ergosta-4,6,8(14),22-tetraen-3-one. The three new compounds and shornepine A presented inhibition against the human pathogens *E. coli* and *Micrococcus luteus* and the aquatic bacteria *Edwardsiella ictaluri* and *Vibrio alginolyticus* with MIC values varying from 16 to 64 μg/mL.

Zhao et al. (2018a) isolated eight novel isoprenylated cyclohexanols and fourteen known analogous compounds from solid cultures of the sponge-associated fungus *Truncatella angustata*. From the eight-novel isolated isoprenylated cyclohexanols, one of them displayed considerable levels of inhibition towards both human immunodeficiency virus 1 (HIV-1) and swine-origin influenza A virus (H1N1) virus and another one against the HIV-1 virus.

Zhao et al. (2018b) identified two promising fungi with bioactive activities among different 141 fungal strains isolated from marine plants. These two fungi were identified as *Fusarium equiseti* and *Alternaria* sp. The former produced two compounds, identified as (11S)-1,3,6-trihydroxy-7-(1-hydroxyethyl)-anthracene-9,10-dione and (11S)-1,3,6-trihydroxy-7-(1-hydroxyethyl)-anthracene-9,10-dione with cytotoxicity against lung (A-549), cervical (HeLa) and hepatic (HepG2) cancer and 7-acetyl-1,3,6-trihydroxyanthracene-9,10-dione with cytotoxicity against human colon cancer cells. Therefore, it could have potential as a new chemotherapeutic agent (Bae et al. (2020).

Ma et al. (2020) isolated three new purpuride compounds, a new isocoumarin peniscoumarin compound and 15 known metabolites from the marine-derived fungus *Penicillium minioluteum* Z21657. Two of the purpurides, which resulted to be N-acetyl-L-valine conjugated digaramine sesquiterpenoids, exhibited antimicrobial activities against MRSA, *E. coli* and *C. albicans* (MIC values of 6–12 and 3–6 μg/mL, respectively), whereas the other purpuride, identified as a new drimane sesquiterpenoid, presented high antiproliferative activities against human glioma cells.

Xu et al. (2020) firstly isolated two cycloctribol analogs, designated as aspergillisteroid A and neocyclocitrinol B, from a marine sponge-associated *Aspergillus* fungus. Aspergillisteroid A showed considerable antibacterial activity against the aquatic pathogen *Vibrio harveyi* (MIC 16 μg/mL).

3.3. Bioactive compounds from marine microalgae

De Vera et al. (2018) studied the bioactive potential of the extracts of thirty-three marine microalgae. They found that the dinoflagellates *Prorocentrum hoffmannianum*, *P. arenarium*, *P. reticulatum*, *Alexandrium tamarense* and *Gambierdiscus australis* showed promising apoptotic activities.

Fimbres-Olivarria et al. (2018) extracted sulphated polysaccharides from the marine diatom *Navicula* sp. grown at three wavelengths (i.e. white light, red light and blue light). The recovered polysaccharides exhibited antioxidant activity, especially the ones grown under white and blue light. Consequently, these sulphated polysaccharides can have potential applications in biotechnology as antioxidants.

Lauritano et al. (2018) reported anti-tuberculosis activity in diatoms for the first time. They found that the organic extracts of the diatoms *Skeletonema costatum* and *Chaetoceros pseudocurvisetus* presented activity against tuberculosis when cultured under control (i.e., with no stress) and phosphate starvation conditions.

The production of bioactive compounds by the marine microalga *Amphidinium carterae* was investigated. They identified a new substance linked to the amphidinol family, given the name amphidinol 22, with potent cytotoxicity activity and moderate antimicrobial activity against *C. albicans* (Martinez et al. 2019).

4. Conclusions

The biodiversity of the oceans represents a potentially abundant source of new chemically diverse compounds with potential industrial applications. Thus, bioprospecting of marine ecosystems has resulted in the identification of new microorganisms able to produce bioactive compounds with interesting pharmacological activities (i.e. antibacterial, antitumoral and antiviral). In addition,
marine microorganisms are a renewable and environmentally friendly alternative for drug discovery. Results reported up to now are very encouraging. Hence, compounds obtained from marine microorganisms could be the solution in the ongoing struggle against antibiotic-resistant bacteria and many awful diseases such as the acquired immune deficiency syndrome (AIDS), cancer and even the current major global pandemic Covid-19 provoked by the virus SARS-CoV-2.

Acknowledgements

This project was funded by the National Plan for Science, Technology and Innovation (MAARIFAH), King Abdulaziz City for Science and Technology, Kingdom of Saudi Arabia, Award Number (13-BIO2290-02).

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