



Antifouling activity of microorganisms associated with the marine organisms

Anjana Suresh*; Grasian Immanuel

Department of Microbiology, Centre for Marine Science and Technology (CMST), Rajakkamangalam, Manonmaniam Sundaranar University, Tirunelveli, Tamil Nadu, India

*Corresponding author E-mail: anjanasuresh422@gmail.com



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Abstract



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Biofouling is an ongoing problem in the marine industries that requires significant financial resources for control and new cleaning procedures. There is a feasible and immediate need to produce ecologically compatible low-toxic and harmless antifouling compounds for the maritime companies and underwater equipment; since the usage of Tributyltin (TBT) based marine coatings was banned globally in 2008. In recent years; the marine natural products have emerged as one of the most potential forms of antifouling agents. Although the natural antifoulants made from marine species; especially sponges and corals, have gained importance because of their performance in field tests; however, the gathering of larger quantities of marine animals is not a feasible choice. Several recent researches revealed that the marine microorganisms associated with sponges; corals, ascidians, seaweeds, and sea grasses, serve as the primary sources of antifouling substances and exhibit antimicrobial; antibacterial, and antifouling activity. During the screening of antifouling compounds; these marine microorganisms displayed antifouling ability against the macro and micro-foulers. This review aimed to focus on the improvements in the antifouling abilities of the natural products derived from marine organism-associated microorganisms.

Keywords: Biofouling, Antifouling, TBT, Natural antifoulants, Marine microorganisms

1. Introduction

The binding of barnacles; macroalgae, and microbial slimes results in marine biofouling ([Maureen and James, 2002](#)), which affects the marine networks everywhere. Biofouling causes the hulls of ships to become rougher, which raises the hydrodynamic drag as the ship travels through the ocean. Costs connected with biofouling include

increased fuel use; hull cleaning, paint removal and repainting, and related environmental compliance measures. The barnacles; macroalgae, and bacterial slimes adhere to the various surfaces in the ocean, which cause biofouling. Antifouling paints that contain tributyltin (TBT) were frequently used on the industrial vessels to reduce biofouling ([Yebara et al.,](#)

2004). TBT use; however, led to several environmental issues, because it is more toxic to the marine species that aren't its intended targets. On January 1, 2003; TBT was banned for marine use by the International Maritime Organization and the Marine Environment Protection Committee, due to the environmental concerns about its use (Arai *et al.*, 2009). While the fact that copper paints are employed as an alternative to antifoulants that contain TBT; however, copper is more hazardous to the marine habitat. As antifouling biocides; numerous other substances, including irgarol-1051-diuron; dichlorofluid, chlorothalonil, zine, pyridine, and zineb, are also frequently used (Nwuzor *et al.*, 2021). Despite using copper paints as an alternative to TBT-containing antifoulants; however they are more hazardous to the marine habitat than TBT (Yebra *et al.*, 2004). Antifouling paints that use hazardous biocides to prevent biofouling are recommended to be replaced with natural alternative substances. In a previous study; Qian *et al.*, (2009) conducted a detailed investigation on the antifouling capabilities of natural compounds obtained from marine organisms and their synthesized counterparts. However, compared with the "antifoulants" obtained from macroorganisms; knowledge about the marine microorganisms provided relatively little information (Fusetani, 2004). Understanding how prior marine biofilms later influence the micro- and macro fouling; as well as why some microbes are "more effective" at doing so than others, is necessary for creating an efficient "ecofriendly defence" against fouling. Chemical substances produced by the microorganisms may encourage or inhibit the development and settlement of other fouling organisms. The heterotrophic marine microorganisms; cyanobacteria, and fungi have produced a number of antimicrobials; antialgal, and anti-larval compounds (Dobretsov *et al.*, 2013). Some of these substances exhibit a variety of bioactivities. Microorganisms can destroy biofilms; by inhibiting the bacterial communication and producing enzymes that break down the bacterial signals and polymers. The secondary metabolites created by the microorganisms that are affiliated with the marine

organisms may encourage (inductively) or hinder (non-inductively) the colonisation of marine organisms by their larvae. Investigation of the antifouling compounds proposed the use of these microorganisms as possible sources that prevent larval settlement. Furthermore, it's believed that bacteria on the surfaces of aquatic invertebrates possess greater antibacterial and antifouling properties than those that are present in the planktonic forms (Briand, 2009). The high antifouling (AF) potential of the epibiotic microorganisms linked to the coastal invertebrates and algae can be used to combat the biofouling issues in industry. The objective of this study was to discuss the antifouling properties of metabolites produced by microorganisms linked to marine organisms.

2. Antifouling activity of the marine microorganisms

A large percentage of the antifouling substances discovered in marine creatures originates from the tropical or subtropical sea invertebrates and/or from the mangrove's leaves (Hadfield and Paul, 2001). Because the bioactive compounds are produced by the marine organisms in very small quantities and in a complex mixture; their extraction and purification require enormous amounts of labor and effort. For the extraction; an enormous number of the aquatic organisms and/or algae should be gathered, which will pose a challenge for the biodiversity preservation. Nevertheless, if the microorganism is assumed to be the source of the bioactive chemical; product availability will be obtained by cultivating the bacteria or discovering the genes that express the antifouling metabolite (Qian *et al.*, 2007). A previous study conducted by Tujula, (2006) proved 16S rRNA gene clone library; denaturing gradient gel electrophoresis (DGGE), and catalyzed reporter deposition–fluorescence in situ hybridization (CARD-FISH) analysis methods, which depend on microbial cultures, have led to superior extraction of the cultivable bacteria from the marine algal surfaces. Through the fermentation process; we can easily acquire a large number of metabolites from the microbes for bioassays. Higgs *et al.*, (2001) established an efficient

method to determine when the secondary metabolites do exist in the microbial extracts. In order to overcome the difficulties and limitations associated with cultivating the marine microorganisms; metagenomic approaches have been developed to avoid the culture-dependent bottleneck that [Zhang et al., \(2005\)](#) observed. Only upon adding a growth medium; the microorganisms will be successfully cultivated.

Additionally, based on the conditions of growth; several bacterial strains of the same species may produce various bioactive molecules, which may expand the potential number of beneficial compounds. The invention of natural product-based antifouling coatings needs the examination of a compound's antifouling capabilities under both *in vitro* and *in vivo* field tests, because certain microorganisms that display antifouling activities *in vitro* assays are unable to do so in the field trials ([Qian et al., 2009](#)). The diatoms; limpets, barnacle larvae, and biofilm-forming microorganisms; can all be used in the laboratory experiments to evaluate the antifouling potential of the bioactive compounds originating from the marine microorganisms. Furthermore; the natural compounds from the marine microorganisms exhibit inhibitory actions against a variety of biofilm-forming bacteria. The microbial strains associated with the marine organism's exhibit antibiofilm activities through several primary mechanisms, including antibiotic; antimicrobial, and anti-adhesion properties. The creation of extracellular polymers (EPS), which are necessary for the development of biofilms, is also influenced by these characteristics ([Flemming et al., 2000](#)). Theoretically; the natural chemicals produced by the microorganisms linked to marine organisms can work similarly (anti-settlement) against the larval forms and macroalgal spores.

A biofilm is unable to form because the signals involved in biofilm growth are being enzymatically degraded. The turnover of the bacterial N-acyl homoserine lactone (AHL) is one of the most thoroughly studied examples of how enzymes can manipulate bacterial signalling and biofilm development ([Kim et al., 2014](#)). The Gram-negative

bacteria; Firmicutes, and true fungi (i.e., Ascomycetes and Basidiomycetes), are among the taxonomically varied groups of microorganisms that degrade AHL ([Teplitski et al., 2011](#)). A previous study reported by [Huang et al., \(2003\)](#) found that AHLs can be fully degraded by some bacteria; when several different enzymes work together. Enzymes that break down AHL include acylases; oxidoreductases, and lactone hydrolases (lactonases). Marine microorganisms may destroy the biofilms by producing lytic enzymes that can break down the matrix of the biofilm. For example, α -amylase from a coastal isolate of *Bacillus subtilis* has suppressed *Vibrio cholera* biofilms by 20-80 % ([Kalpana et al., 2012](#)). Because glucose; galactose, N-acetyl glucosamine, and mannose are the key components of the pathogen biofilm matrix; treatment of human pathogen biofilms with α -amylase do not significantly impairs the pathogens' potential to build a biofilm, including the *Vibrio* spp. ([Arunkumar et al., 2020](#)). When Dispersin B (a-b-N-acetyl-hexosaminidase) has been applied to biofilms containing poly-1, 6-N-acetyl-D-glucosamine; the pre-formed biofilms have been effectively detached ([Chen and Lee, 2018](#)). AHLs and the other small chemicals; in addition to quorum sensing (QS) inspiration, are believed to initiate the regulatory cascades that contribute to the development of biofilm or dispersion ([Swetha et al., 2021](#)). Previous studies revealed that suppressing or altering the QS regulation was effective since the middle of the 1990s; when the first bacterial AHL mimics were discovered in the red alga *Delisea pulchra*, which had extremely few to no bacterial biofilms ([Manefield et al., 1999](#)). In the semi-synthetic structures called biosensors; a reporter gene has been introduced downstream from the promoter responsive to AHLs. The reporter genes are often employed in tests for QS inhibitory effects in both the natural and the manufactured compounds ([Dobretsov et al., 2010](#)).

3. Antifouling activity of the microbial strains from the marine macroorganisms

In general, the aquatic invertebrates and plants' attached microorganisms have more physiological functions than their free-living counterparts.

Microorganisms and marine organisms frequently interact for a variety of reasons. For instance; these microorganisms can create secondary metabolites to increase their chances of surviving in the hostile environments that are present on the host's body's surface ([Kaltenpoth and Engl, 2014](#)). It is thought that microorganisms generate a variety of metabolites with insecticidal and repellent properties as well as pharmacodynamics activities ([Amelia-Yap et al., 2022](#)). The primary use of these metabolites is for screening the potential drugs and the other industrially useful compounds. The metabolite that the host macroorganism is thought to generate for the defence purposes actually comes from the microorganisms. Numerous studies have been conducted to pinpoint the bacteria connected to sponges, and this theory is supported by the discovery of several novel metabolites. Microbial associations with the higher animals result in the production of novel and biologically active secondary metabolites; these associated microorganisms are viable sources of the various secondary metabolites ([Schulz et al., 2022](#)).

[Kon-ya et al., \(1995\)](#) discovered that the culture of *Alteromonas* sp., which was connected to the sea sponge *Halichondria okadai*, successfully prevented the cyprids from settling. Moreover, this study added that ubiquinone-8 was a potent cyprid settling inhibitor recorded by the bioassay-guided separation. According to [Olguin-Urbe et al., \(1997\)](#), 6-bromoindole-3-carbaldehyde was also recovered from an *Acinetobacter* sp.; such bacterium was isolated from the surface of *Stomozoa murrayi* obtained from the Caribbean coral reefs. This substance has mild antibacterial activity and inhibits settlement of the barnacle larvae *in vitro*; however it has no fish-feeding inhibitory activity or antialgal property. The marine *Pseudoalteromonas* bacteria have been found associated with the living surfaces and it is thought that these bacteria create bioactive compounds that prevent the growth of bacteria; fungi, and the invertebrate larvae, as well as the algal spores. According to [Holmström et al., \(2002\)](#), *Pseudoalteromonas tunicata*; *Pseudoalteromonas*

citrea, and *Pseudoalteromonas rubra* have all exhibited auto-inhibitory activity. *Ulva lactuca* and *Polysiphonia* sp.; two common fouling algae, in addition to the larvae of two common crustaceans; *Hydroides elegans* and *Balanus amphitrite*, may not be able to colonise the surfaces, due to the production of inhibitory compounds by *Pseudoalteromonas* spp. associated with these surfaces.

According to the previous research reported by [Egan et al., \(2001a\)](#); two strains of the genus *Pseudoalteromonas* that were isolated from *Ulva lactuca*; a common marine alga, were discovered to possess antifouling activity. They prevented the invertebrate colonization and the development of marine algal spores. All the *in vitro* antifouling assays demonstrated excellent activity of the paints containing an extract of *Pseudomonas* sp. strain NUDMB50-11. Moreover, this strain exhibited effectiveness towards a test panel of fouling bacteria. It prevents *Ulva lactuca* algal spores; *Balanus amphitrite*, and the barnacle larvae from colonising a particular area. The quantity of barnacles that has settled is also significantly reduced as a result of this paint treatment. According to [Harder et al., \(2004\)](#), the waterborne polar macromolecules have been shown to function as algal antifoulants in the seaweed *Ulva reticulata*. The results revealed that at least two different waterborne macromolecules are probably responsible for the premise of antifouling in *U. reticulata*, and that extremely water-soluble macromolecules may be important for a marine system's chemical ecology. This discovery exhibits a different principle from the other well-known examples of the algal antifoulants, which only contain very tiny and non-polar algal metabolites. Furthermore; prior study conducted by [Harder et al., \(2014\)](#) has demonstrated that the alga itself and an epibiotic *Vibrio* sp. that is attached to a thallus; both have created the watery macromolecular compounds, which impede the attachment of the polychaete *Hydroides elegans* larvae. Several studies reported by [Huggett, \(2006\)](#), [Rao et al., \(2007\)](#), [Rao et al., \(2010\)](#) have demonstrated that *Pseudoalteromonas tunicata*

and *Phaeobacter* sp. produce a variety of extracellular inhibitory substances in associations with the alga *Ulva australis*, which are effective toward common fouling microorganisms, such as the marine fungi; marine bacteria (i.e., *Pseudoalteromonas gracilis*, *Alteromonas* sp., and *Cellulophaga fucicola*), invertebrate larvae (*Bugula neritina*), algal spores (*Polysiphonia* sp.), and the gametes of *Ulva australis*. According to [Lo Giudice and Rizzo, \(2022\)](#), the *Gammaproteobacteria* and *Alphaproteobacteria* have the ability to provide their host bivalves with bioactive metabolites that either serve as chemical defences against the opportunistic microorganisms and/ or provide essential functions. However; the Firmicutes, *Actinobacteria*, and *Cytophaga-Flavobacterium-Bacteroides* (CFB) group have less defence against the opportunistic microorganisms. According to [Thenmozhi et al., \(2009\)](#); the coral-associated bacteria (CAB) have antibiofilm activity and QS inhibitory properties that prevent the growth of streptococcal biofilms, due to the development of biofilms in *Streptococcus pyogenes* that depend critically on the quorum sensing (QS). By using CAM; the biofilm development has reduced by up to 80 %. [Ma et al., \(2010\)](#) revealed that the *Pseudoalteromonas* bacteria generate an extracellular component that severely inhibits *Ulva pertusa* spore germination. The study also showed that these inhibitory metabolites are heat-sensitive and possess a molecular weight of 3-10 kDa. The activity of this inhibitory component has not substantially affected by pronase or carboxypeptidase Y; indicating that this component is not a protein or a peptide. According to the previous study reported by [Sulistiyan et al., \(2010\)](#); *Mycobacterium tuberculosis* H37Rv and other resistant strains, such as *M. tuberculosis* strain HE that is resistant to isoniazid and etambutol, and *M. tuberculosis* strain SR, are both affected by the antibacterial activities induced by the marine bacteria, which produce secondary metabolites and are found in the soft coral *Sinularia* sp. [Marhaeni et al., \(2011\)](#) investigated the potential function of the bacterial symbionts; mainly *Thalassia hemprichii*; *Enhalus acoroides*, *Bacillus* spp., and *Virgibacillus*; associated with the sea grasses, which have shown

antifouling potential against several marine biofilm-forming bacteria; identified from the nearby sea grass colonies.

Another surface-associated marine epiphytic bacterium; *Pseudovibrio* sp. D323, produces secondary metabolites that have antagonistic properties ([Nappi et al., 2019](#)); where the bacterium's tropodithietic acid (TDA) is thought to be the source of this antimicrobial potential. Numerous marine bacteria from various taxonomic groups have been successfully inhibited by TDA. Still; the TDA-producers exhibit resistance, and it is anticipated that they will possess resistance mechanisms that prevent auto-inhibition. Several pathogenic and non-pathogenic bacterial strains, including *Pseudomonas fluorescens* and *Escherichia coli* PHL628, are inhibited from forming biofilms by a polysaccharide from a *B. licheniformis* strain, which is linked to the marine organism *Spongia officinalis*; without causing bactericidal effects ([Sayem et al., 2011](#)). Given that this compound's structure is detached to any of the QS molecules that are currently known; its mode of action is probably distinct from that of QS. It was reported that the filamentous bacterium *Leucothrix mucor* contains several potent antifouling steroids. The biofouling diatom *Navicula annexa*; the soft fouling macroalga *Ulva pertusa*, the *P. aeruginosa* KNP-3 bacterium, and *Alteromonas* sp. KNS-8, are all resistant to the antifouling effects of these steroids ([Cho, 2013](#)). The *Ulva pertusa* and the fouling diatom *Navicula annexa* are both resistant to fouling by *Streptomyces praecox*, which has been identified from the seaweed *Undaria pinnatifida*. The biofilm-forming bacteria are inhibited by the bacterial strains that emerged from the surface of the sponge *Sigmadocia* sp. ([Satheesh et al., 2012](#)). These bacterial strains' extracts have a significant impact on the capacity of the biofilm-forming bacteria to adhere and produce extracellular polymeric substances. Furthermore; a strong microalgal settlement inhibitory action has been detected in these strains extracts. It was determined that one of these strains was *B. cereus*. When isolated from *Undaria pinnatifida*; the epibiotic

bacterium *Streptomyces violaceoruber* exhibited antifouling properties (Hong and Cho, 2013). As furanone derivatives; 3-octa-1'; 3'-dienyl-4-methylfuran-2(5H)-one, and 3-octa-1'-enyl-4-methylfuran-2(5H)-one, have been discovered as soon as these compounds are isolated from the bacteria. The zoospores of *Ulva pertusa*; the diatom *Navicula annexa*, and the mussel *Mytilus edulis*, are few instances of the fouling microorganisms that these compounds have demonstrated anti-fouling actions against them (Cho et al., 2012). The bacterium *Bacillus* spp. linked with sponges collected from the ocean at San Juan Island; may have chemical defences against the diatom biofouling, and its metabolites may be a source of the naturally occurring antifouling compounds Jin et al., (2014). Furthermore; these metabolites have no negative impact on the *Amphora* sp. development. The antifouling (AF) activity is present in several bacterial spp., including *Bacillus* sp.; *Micrococcus* sp., *Paracoccus* sp., *Pseudobacter* sp., *Pseudovibrio* sp., *Psychrobacter* sp., *Staphylococcus* sp., and *Terribacillus* sp., which are associated with the sponge *Aplysina gerardogreeni* (Aguila-Ramírez et al., 2014). This study has shown how the AF bioactivity has fluctuated throughout time; reaching its highest points in February and June and its lowest points in October. The *Bacillus* bacteria predominated and displayed AF activity throughout the whole year. The results demonstrated that the marine bacteria connected to sponges; particularly those belonging to the *Bacillus* taxa; are prospective AF agents. As a rich source of the bioactive metabolites; *B. subtilis* is linked to three species of the *Sargassum* spp. brown algae (i.e., *Sargassum polycystum*; *S. duplicatum*, and *S. echinocarphum*) (Susilowati et al., 2015). This bacterium exhibited antibacterial activity against two pathogenic microorganisms; mainly *Staphylococcus aureus* and *Staphylococcus epidermidis*. According to the study reported by Viju et al., (2019), the antagonistic marine bacterium *B. subtilis* MUT: M15, which has been isolated from the surface of *Sepia* sp.; has antibacterial and antifouling properties in both of its intracellular and extracellular extracts. This study demonstrated that the biofilm-forming *Alteromonas*

sp. is significantly inhibited in its growth and adhesion by both of these intracellular and extracellular extracts. According to Wang et al., (2015), *Pseudovibrio denitrificans* produces eight naturally occurring substances that are classified as di(1H-indol-3-yl) methane (DIM) family members, and they have antifouling activity against the barnacle *Balanus amphitrite* and the bryozoan *Bugula neritina* larval development, including both the attachment and metamorphosis. The green alga *Ulva australis* zoospores and the marine biofilm-forming *Pseudoalteromonas* sp. strain S91 are resistant to the antifouling substances present in the biofilms of *Pseudoalteromonas piscicida*; *P. Tunicate*, and *Ulvae* spp.; obtained from the Danish coastal waters (Bernbom et al., 2011). The Gram-positive and Gram-negative bacteria including *Vibrio parahaemolyticus*; *B. cereus*, *Streptococcus uberis*, and *Pseudomonas* sp. can be killed away by the marine bacterium *P. aeruginosa* (Rawi et al., 2023). The inhibitory activity of *P. aeruginosa* is attributed to its biofilm formation. This suggests that this isolated bacterium may be used to avoid the formation of microfoulers instead of the toxic antifoulants. Priya et al., (2013) revealed that the bacterial red pigment prodigiosin, which is derived from *Serratia marcescens* CMST 07; has antifouling properties. When applied against the marine fouling microorganisms such as *Alteromonas* sp. and *Gallionella* sp.; prodigiosin has demonstrated a potent antifouling impact. Against *Alteromonas* sp.; the pigment's minimum bactericidal concentration (MBC) and minimum inhibitory concentration (MIC) are approximately 6.75 and 12.5 µg/ ml, respectively. Prodigiosin's LD₅₀ against the brine shrimp *Artemia parthenogenetica* (KKT1) is approximately 50 µg/ ml. It is more probable that the bacterial pigments can be employed as sources of the antifouling substances; since prodigiosin significantly diminishes the adhesion of cyanobacteria to the glass surfaces. This lowers the fouling in the marine environments.

Marine cyanobacteria; sometimes known as blue-green algae, are single-celled microorganisms that produce compounds to aid in biofilm formation and

resource competition with the other microbial species. Consequently, it is known that secondary metabolites having AF characteristics are widely distributed in the marine cyanobacteria ([Burja et al., 2001](#)). Chemical investigation has shown that the majority of these compounds are lipopeptides; polyketides, amides, alkaloids, indoles, and fatty acids, which are produced by 15 different cyanobacterial genera ([Dahms et al., 2006](#)). *Lyngbya majuscula*; a marine cyanobacterium, represents a significant source of the bioactive chemicals; mainly the antibacterials ([Nagle et al., 1996](#)). In another study, [Garima et al., \(2009\)](#) extracts from the cyanobacterium *L. majuscula* reduced the growth of *Enterococcus faecalis*; *Staphylococcus epidermis*, *B. subtilis*, and *B. cereus*. The new brominated indole alkaloid 6-bromo-3hydroxy-methyl-indole-2-one, which is effective against several bacterial spp., including *B. cereus*; *Arthrospira laxissima*, *Nostoc carneum*, *Chroococcus minutus*, and *Synechococcus*, has been created by the marine cyanobacterium *Anabaena constricta* ([Volk et al., 2009](#)). Norharmane (9H-pyrido(3,4-b) indole) and 4,4'-dihydroxybiphenyl; are two novel metabolites derived from the marine cyanobacteria *Nodularia harveyana* and *Nostoc insulare*, have suppressed the development of *E. coli*; *P. aeruginosa*, *Staphylococcus aureus*, and *B. subtilis* ([Volk and Furkert, 2006](#)). On the contrary, the antibacterial effects of *Synechocystis* spp. and *Synechococcus* spp. do not affect the Gram-negative bacteria ([Martins et al., 2008](#)). Furthermore, the antibacterial properties of the cyanobacteria isolated from the benthic mats in the Antarctic seas have been established ([Biondi et al., 2008](#)). *Staphylococcus aureus*; the filamentous fungus *Aspergillus fumigatus*, and the yeast *Cryptococcus neoformans*, have all been suppressed by 17 of the tested 48 cyanobacterial strains. The growth conditions of the cyanobacterium *Geitlerine-mastrain* Flo1 have been discovered to affect its antimicrobial potential. Several depsipeptide derivatives (lyngbyabellins), including lyngbyabellins G; O, P, H, A, 27-deoxylyngbyabellin A, and homohydroxydolabellin, have all demonstrated antifouling activity against *Amphibalanus amphitrite* barnacle larvae, and have

antiplasmodial effect against *Plasmodium falciparum* ([Fathoni et al., 2020](#)). The marine cyanobacterium *Okeania* sp., which is found in the Red Sea; produces several new metabolites called lyngbyabellins O and P, in addition to three known lyngbyabellins F, G, and dolastatin 16; where all these substances have strong antifouling potential against *Amphibalanus amphitrite* larvae ([Petitbois, 2018](#)). In order to confirm that acetylcholinesterase (AChE) predominates in tissues of the important biofouling species; several researches have been performed in order to search for the presence of different cholinesterases (ChEs) types ([Almeida et al., 2015](#)). The previous study reported by [Pereira et al., \(2020\)](#) demonstrates that AChE inhibitors derived from the cyanobacteria prevent biofouling. This approach used mostly pure AChE activity to develop an *in vitro* AF test. As possible sources of the AF and AChE inhibitors; 18 cyanobacterial strains have been examined. The results showed effectiveness in the selection of the potential ecologically acceptable AF treatments, and allowed for a better knowledge of the biochemical mechanism of action of the diverse substances on AF. In addition, this research emphasizes the cyanobacteria's potential to act as sources of AF agents for the invertebrate macrofouling species. The major fouling organisms like mussels cause significant technological and financial issues. Three substances are found in the marine bacterium *Vibrio alginolyticus* linked to the sea anemone *Haliplanella* sp., which have been recorded to have antifouling activity towards mussels ([Wang et al., 2017](#)). The three bacterial small molecules include indole; 3-formylindole, and cyclo (Pro-Leu); with an EC₅₀ value of 24.45 µg/ ml for indole, which dramatically reduced the green mussel *Perna viridis* ability to produce byssal threads. According to these investigations; these three compounds may be useful for managing the mussels in an environmentally benign way and/ or for creating new antifouling additives that are effective against a variety of biofoulers. Although more researches are needed to establish the antifouling process; the compounds produced by microorganisms related to the marine macroorganisms are expected to have an analogous

modes of operation (*i.e.*, anti-settlement) against the larval stages and the macroalgal spores.

4. Fungal strains with anti-biofouling and antimicrobial activity

Nowadays; the marine-derived fungi are believed to be potential sources of new chemically and physiologically active substances ([Bhatnagar and Kim, 2010](#)). *A. versicolor* makes two altered cytotoxic tripeptides; *Aspergillus* sp. creates a brand-new pentacyclic oxindole alkaloid, *A. tamari* creates four prenylated indole alkaloids, and *Aspergillus* sp. creates four sesquiterpenoids with a distinct nitro benzoyl ester ([Chen et al., 2013](#), [Song et al., 2014](#); [Sun et al., 2022](#)). The fungus *Aspergillus* sp., which is isolated from a gorgonian *Dichotella gemmacea* by [Wei et al., \(2010\)](#); produced three phenolic bisabolane-type sesquiterpenoids and two known fungal metabolites. These phenolic bisabolane-type sesquiterpenoids are biologically potent metabolites with antibacterial activities. In their experiment; [Yang et al., \(2007\)](#) discovered that the sponge-associated fungus *Letendreaa helminthicola* produced antifouling substances, such as cyclohexane (D-Pro-D-Phe) and 3-methyl-N-(2-phenylethyl) butanamide. [Kwong et al., \(2006\)](#) highlighted that the fungus *Ampelomyces* sp. produced 3-chloro-2, 5-dihydroxybenzyl alcohol, which prevented growth of the marine bacterial species, and the establishment of *Hydroides elegans* and *Balanus amphitrite* larvae. In the deep-sea-derived fungus *A. versicolor* SCSIO 41502; [Huang et al., \(2017\)](#) identified three new anthraquinones, including aspergilols G-I (1-3); one new diphenyl ether, 4-carbglyceryl-3,3'-dihydroxy-5,5'-dimethyldiphenyl ether (4), and one new benzaldehyde derivative, 2,4-dihydroxy-6-(4-methoxy-2-oxopentyl)-3-methylbenzaldehyde; along with 23 known phenolic compounds. The amount of the phenolic hydroxyl groups that can freely rotate can greatly alter the antioxidant activity of these phenolic compounds.

Aspergillus sp. of the sponge *Xestospongia testudinaria* is found to have four new optically active compounds of the bisabolane-type, including

aspergiterpenoid A; (-)-sydonol, (-) sydonic acid, and (-)-5-(hydroxymethyl)-2-(2', 6', 6'-trimethyltetrahydro-2H-pyran-2-yl) phenol, which have cytotoxic; antifouling, and acetyl cholinesterase inhibitory activities ([Li et al., 2012](#)). A study reported by [Abdel-Lateff et al., \(2013\)](#) found *Drechslera* sp. as an algicolous fungus that produces three known sesquiterpenes; mainly helminthosporic acid; drechslerine A, and (+) secolongifolene-diol, which exhibit antimicrobial properties; antioxidant scavenging activity, antioxidants and antifouling activity. [Li et al., \(2013\)](#) discovered 49 secondary metabolites, including diterpenoids; steroids, and polyketides in the soft corals; gorgonians, brown algae, and fungi gathered along the Chinese coast in 2013. Furthermore, this study showed that the cyprids of the barnacle *Balanus* (*Amphibalanus*) *amphitrite* are resistant to the antifouling effects of these secondary metabolites. Additionally; this work demonstrated the significance of furanon and furan moieties for antifouling functioning. From the *Penicillium* sp. SCSGAF 0023 fungus that is connected to gorgonian coral; two new polyketides; mainly 6, 8, 5'6'-tetrahydroxy-3'-methylflavone and paecilin C, in addition to six well-known analogues, including secalononic acid D; secalononic acid B, penicillixanthone A, emodin, citreorosein, and isorhodoptilometrin, are identified ([Bao et al., 2013](#)). These compounds exhibit antibacterial efficacies against the marine bacteria and antifouling properties against the marine creature larvae, including *Balanus amphitrite* larval settlement. A mould species known as *Penicillium* sp. that is associated with gorgonian corals can generate antifouling and antibacterial substances, which may aid the host gorgonian coral in defending itself against the marine bacterial disease; biofouling species, and the other invasive creatures ([Raimundo et al., 2018](#)). Another study discovered that the marine-derived fungus *A. terreus* SCSGAF0162 contains seventeen lactones; eight termitrem derivatives, and nine butyrolactone derivatives, which are highly effective against the barnacle *Balanus amphitrite* larvae and have antiviral and antifouling activities ([He et al., 2013](#), [Nong et al.,](#)

2014). In more than 50 % of the 24 fungal strains connected to the black coral *Antipathes dichotoma* and forming the orders Eurotiales; Hypocreales, Pleosporales, and Botryosphaerales, have shown antimicrobial activity against the bacterial and fungal infections, according to the previous study conducted by Zhang *et al.*, (2012a).

Aspergillus elegans; a fungus obtained from soft coral, had been used by Zheng *et al.*, (2013) to discover the bioactive phenylalanine derivatives and the cytochalasins that exhibit antifouling properties. In *A. elegans*; eight known cytochalasin analogues; two new cytochalasins; mainly aspochalasin A1 and cytochalasin Z24, and one known phenylalanine derivative, have been also discovered. Cytochalasins 5; 6, 8, and 9 displayed significant antifouling efficacy in preventing larval colonization of the barnacle *Balanus amphitrite*, with EC₅₀ values ranging from 6.2 to 37 µM. The antifouling activity of this family of metabolites has never been reported before. The cytochalasins 8 have a wide range of targets for their antibacterial activity, including *Staphylococcus aureus*; *Staphylococcus albus*, *E. coli*, and *B. cereus*, which are among the harmful bacteria (Zheng *et al.*, 2013). The marine-derived fungal strain *Xylariaceae* sp. SCSGAF0086 contains derivatives of eighteen polyketides, including six derivatives of citrinin; two derivatives of phenol, one derivative of cyclopentenone, two derivatives of naphthol, and seven derivatives of tetralone (Nong *et al.*, 2013). These derivatives have potent antifouling potentials against the development of *Bugula neritina* larvae. The antifouling and enzyme-inhibitory capabilities of these compounds have being described for the first time in this study. The *Aspergillus* taxa of the *Moniliaceae* family are excellent sources of several bio-chemicals, such as xanthonenes; polyketides, terpenoids, and alkaloids (Abonyi *et al.*, 2018). These chemicals exhibited cytotoxic; antifungal, anti-HIV, antibacterial, and anti-HIV activities. The marine anemone-derived fungus *Cochliobolus lunatus* produced three 14-membered resorcylic acid lactones, cochliomycins D-F, 1-3, and eight known analogues;

where all these substances demonstrated potent antifouling activities against settling of the *Balanus amphitrite* larvae (Liu *et al.*, 2014). The *Aspergillus* sp. fungus, which is isolated from the soft coral gorgonian produced six steroid derivatives and five butyrolactone derivatives. These compounds reduced the barnacle *Balanus amphitrite* larval settling with EC₅₀ values that ranged from 0.63 to 18.4 µg/ ml. Moreover, these compounds of butyrolactone have shown strong antibacterial activity against *Staphylococcus aureus* (Chen *et al.*, 2015). *Scopulariopsis* sp.; a fungus derived from the gorgonian corals, has six dihydroquinolin-2-one-containing alkaloids; three monoterpenoids, and three 4-phenyl-3, 4-dihydroquinolin-2(1H)-one alkaloids. This family of metabolites has antifouling activity, which is first discovered against the barnacle *Balanus amphitrite* larval settlement (Shao *et al.*, 2015). Approximately nine recognized chemicals; three new azaphilone derivatives, pinophilins, one new diphenyl ether derivative, and hydroxypenicillide, are obtained from the fungus *Penicillium pinophilum* XS-20090E18, which is produced from the gorgonians (Zhao *et al.*, 2015). These substances demonstrated cytotoxicity against the Hep-2, RD and HeLa cell lines, in addition to inhibitory effect against the barnacle *Balanus amphitrite*'s larval settlement. According to a previous research reported by Thiagarajan *et al.*, (2016); the biofouling bacteria such as *Methylococcus* sp.; *Flavobacterium* sp., *Marinococcus* sp., *Serratia* sp., and *Pseudomonas* sp., are inhibited by the antifouling compound Fumonisin B2 found in the marine fungi *Aspergillus* spp. Ha *et al.*, (2017) presented the first study on the antifouling abilities of thielavins against the barnacle cyprids. *Thielavia* sp. UST030930-004 is a marine-derived fungal strain that produces eleven unique depsides known as thielavins W to Z and thielavins Z1 to Z7, in addition to four well-known thielavins A; H, J, and K. These substances possess antifouling activities that are effective against the barnacle *Balanus amphitrite* cyprids. The fungus *P. sclerotiorum* (CHNSCLM-0013) has been isolated from the gorgonian coral *A. ocracea*; where its sclerotioramine derivatives

demonstrated strong antifouling action against the barnacle *Balanus amphitrite* larval settlement ([Wei et al., 2017](#)).

Six indole alkaloids have been discovered in the gorgonian *Subergorgia suberosa* derived fungus *Eurotium* sp. These compounds have the unique spiro-anthronopyranoid-diketopiperazine moiety and have significant antifouling properties. Moreover, the neoechinulin A and echinulin from *Eurotium* sp. have antifouling efficacy against the barnacle *Balanus amphitrite* larval settling with EC₅₀ values of 15.0 and 17.5 µg/ ml, and are not teratogenic to the zebra fish *Danio rerio* embryo ([Chen et al., 2018](#)). The previous study conducted by [Zhang et al., \(2019\)](#) presented the first one that focused on the biodiversity and antifouling capabilities of the fungi in *Cladiella krempfi* and *Sarcophyton tortuosum*; obtained from the South China Sea. In this study; the soft coral species *Phaeoshaeria* sp. and *Mucor* sp. have exceptionally powerful antifouling action against *Bugula neritina*. The *Balanus neritina* and *Balanus amphitrite* larval settlement was significantly reduced by the secondary metabolite obtained from the soft coral.

The antifouling secondary metabolites produced by the marine-derived fungus *Cladosporium* sp. F14 were studied by [Qi et al., \(2009\)](#); where nine compounds were isolated. Among them; 3-phenyl-2-propenoic acid; cyclo-(Phe-Pro), and cyclo-(Val-Pro), had different antibacterial activities toward several fouling bacteria. Moreover; 3-phenyl-2-propenoic acid and bis(2-ethylhexyl) phthalate effectively inhibited the larval settlement of *Bugula neritina* and *Balanus amphitrite* larvae; respectively, indicating that these two compounds were potential natural antifouling agents.

Conclusion

In recent years, one of the most promising sources of the antifouling agents is the marine natural products. Although the natural antifoulants made from marine species; especially the sponges and corals, have gained importance because of their performance

in the field tests; however, gathering of larger quantities of the marine animals is not a feasible choice. According to the recent researches; the primary sources of the antifouling chemicals and exhibitors of antimicrobial; antibacterial, and antifouling activity, are the marine microorganisms linked to sponges; corals, ascidians, seaweeds, and sea grasses. The current investigation clearly demonstrates the antifouling behaviors displayed by microorganisms connected to the living surfaces in the marine environment. Therefore; more laboratory studies are required to demonstrate the antifouling activity of the marine microorganisms. Because the natural antifoulants derived from marine associated microbial species; particularly the sponges and corals, have become more important as a result of their success in the field tests; thus, it is not practical to collect larger numbers of the marine animals.

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Conflict of interest

The authors declare that they have no conflict of interests.

Ethical approval

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Authors' Contribution

Conceptualization, A.S. and G.I.; Data curation, A.S.; Investigation, A.S.; Supervision, A.S.; Validation, A.S.; Roles/Writing - original draft, A.S.; Writing - review & editing, A.S.

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