Seaweed-Associated Bacteria

Seaweeds are broadly distributed and represent an important source of secondary metabolites (e.g., halogenated compounds, polyphenols) eliciting various pharmacological activities and playing a relevant ecological role in the anti-epibiosis. Importantly, host (as known as basibiont such as algae)–microbe (as known as epibiont such as bacteria) interaction (as known as halobiont) is a driving force for coevolution in the marine environment.

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1. Introduction

The ocean is the mother of life and it harbors a vast variety of marine organisms which are diverse in their physiology and adaptations [1]. Algae (macro- and micro-) constitute anything from 30,000 to more than 1 million different species, with a great diversity of forms and sizes [2]. Despite uncertainties regarding what organisms should be included as algae and what a species is in the context of the various algal phyla and classes, an attempt is being made to arrive at a more accurate estimate of algal species [2]. Algae are best defined as "oxygenic photosynthesizers other than embryophyte land plants" [3]. Indeed, they are evolutionary quite diverse and do not represent a single taxonomic entity as compared to vascular plants which can be assigned into a single Phylum called Tracheophyta [3]. Indeed, depending on the systematics and molecular phylogeny, they roughly belong to four kingdoms: Kingdom Plantae (e.g., chlorophytes and rhodophytes—green and red algae, respectively), the Kingdom Protozoa (ex-Protista) (e.g., Euglenozoa, ex-Euglenophytes), the Kingdom Chromista (e.g., phaeophytes aka brown algae—including dinoflagellates and diatoms), and the Kingdom Eubacteria (cyanophytes, as known as blue-green algae) [3][4]. Actually, according to the International Code of Botanical Nomenclature (ICBN) (https://www.iapt-taxon.org/nomen/main.php), the algae have been classified into 11 divisions, i.e., Cyanophycophyta (blue-green algae), Chlorophycophyta (green algae), Charophyta (stoneworts), Euglenophycophyta (Euglenoids), Xanthophycophyta (yellow-green algae), Chrysophycophyta (golden algae), Bacillariophycophyta (diatoms), Phaeophycophyta (brown algae) currently included in Ochrophyta (brown and golden-brown algae), Pyrrophycophyta, Cryptophycophyta, Rhodophycophyta (red algae) [2]. It is worth noting that the euglenoids (class of Euglenophyceae) secondarily acquired a green algal chloroplast by symbiogenesis, and recently became well classified as algae and not anymore as protozoan flagellate Euglenoidina as it was the case in the 20th century [3]. Nevertheless, concerns arise because of the decline of taxonomists worldwide that has a tremendous repercussion on the improvement and completion of necessary systematic studies [2].

Seaweeds (macroalgae), mainly located on the coastline, represent a considerable part of the ocean biomass (estimate of 25,000–30,000 species) [2]. They have always been used as food and feed by the coastal populations due to their high nutritional composition [5][6]. In ancient times, traditional methodologies have been used to cultivate seaweeds; however, in the past 50 years, the development of cultivation methodologies (e.g., sea-based cultures, cultures in sea water ponds) tremendously increased their production [7].

Based on the chemical composition (e.g., pigments), seaweeds are classified into green algae, brown algae, and red algae. Thereby, brown seaweeds contains pigments of fucoxanthin and chlorophyll a and c; red seaweeds contain pigments of phycoerythrin, allophycocyanin, xanthophylls, and chlorophyll a, while green seaweeds contain pigments of xanthophylls and chlorophyll a and b [5][8].

Seaweeds also contain an excellent source of bioactive compounds including complex polysaccharides (structural and storage polysaccharides), sulfated polysaccharides [9][10], as well as polyphenols, minerals, carotenoids, amino acids (glycine, arginine, alanine, and glutamic acid) [11], proteins/peptides (phycobiliproteins, glycoprotein, phycolectins, and mycosporine) [11], water-soluble fibers [12], fat-soluble vitamins (i.e., A, D, E, and K), macro-minerals (Na, K, Ca, and Mg) in addition to trace elements (e.g., Fe, Zn, Mn, and Cu) [5][13]. However, they contain a small amount (1–5%) of lipids, mainly polyunsaturated fatty acids (PUFAs); brown and red algae containing more eicosapentaenoic acid (EPA) and

arachidonic acid (AA) than green algae [13]. It is important to mention that the chemical composition of seaweeds varies depending on the environmental factors such as salinity, geographical habitat, seasonal variation, and ambient conditions such as water temperature, nutrient concentration, light intensity, and ocean acidification [14][15][16][17]. As a consequence, some of the bioactive compounds produced by algae have attracted much interest in the food [5], pharmaceutical [18][19], biomedical [10], biotechnological [20], agricultural [1], aquacultural [21], and energy [22][23] industries. For instance, red algae (Rhodophyta) are rich at least in one type of the water-soluble sulfated polysaccharide carrageenan, which is known to exert antitumor and antiviral activities besides their wide uses in the food industry as thickeners, stabilizers, and emulsifiers [11][24]. Additionally, another sulfated polysaccharide extracted from brown seaweeds (Phylum Ochrophyta, Class Phaeophyceae), namely fucoidan, was found to elicit antiviral, anticancer, and anticoagulant activities [25]. Polysaccharides and peptides extracted from different seaweeds exerted prebiotic effects, regulating the intestinal epithelial cell, macrophage, and lymphocyte proliferation/differentiation processes as well as the immune response [25]. Seaweeds are a valuable source of vitamins (e.g., B_{12}, C, E) and pigments (carotenoids) which exert antioxidant activities (vitamins A, C, and β-carotene), decrease blood pressure (vitamin C), reduce the effects of aging and anemia (vitamin B_{12}), prevent from cardiovascular diseases (β-carotene), support the vision (vitamin A) [1][3][5][12][13]. In the last three decades, interest has grown in seaweed-derived phytochemicals as nutraceuticals, functional foods, and therapeutics to protect against superoxidation and inflammatory diseases (e.g., diabetes, cancers, cardiovascular diseases) [3][11][12][25].

Seaweeds are widely distributed along the coastal areas worldwide and form rich marine meadows and forests [26]. The temporal variation and distributional pattern of algal assemblage can be used as bioindicators that herald the reflection of self-adaption for the ecosystem to the possible changes in coastal environments [27][28]. Changes in hydrodynamic forces have a major effect on the algal diversity, abundance, distribution of macroalgae, algae–microbiota interactions, and epiphytic fauna (e.g., grazers) [29]. Seaweeds are structuring species in coastal zones, changing light, stabilizing the sediment, and modifying the hydrodynamic ecosystem [30][31]. Moreover, the submerged macroalgal beds enhance the biodiversity, supporting complex food webs by providing habitats, food, reproductive refugia to diverse organisms (e.g., mammals, seabirds, fish, invertebrates) [32]. Several studies addressed the effects of spatial and temporal variations that induce physical disturbance in macroalgae species [33][34][35].

Interestingly, the halobiont concept, which came into the limelight 10 years ago, suggests a mapping of all interactions and activities within and between a host and all its associated organisms/epiphytic species (e.g., bacteria, fungi, archaea, viruses, diatoms, and other unicellular organisms) which together form a discrete functional ecological unit [36][37]. Marine ecosystems are based on multiple interactions among organisms which may be competitive, mutualistic, parasitic, or symbiotic [38][39]. Macroalgal surfaces are coated by an organic layer, due to adsorption of organic and inorganic molecules, allowing them to harbor a rich diversity of associated microorganisms such as bacteria, fungi, diatoms, other unicellular organisms, spores, and larvae of marine invertebrates [40]. Due to the importance and pervasiveness of marine algae, there has been a strong scientific interest in elucidating halobionts in a dynamic spatial-temporal and functional context, not only for an ecological purpose but also for an industrial interest (e.g., targeted and controlled production of bioactive compounds). Many attempts are made to elucidate the precise roles of intercellular chemical signaling pathways that regulate the dynamic interactions between algae and associated epiphytic or endophytic microbiota. Since the last decade, emerging methods to better understand algal–microbial ecology using high-throughput screening (HTS) and robust metagenomic analyses are enabling (i) faster identification of algal species, microcosms [41][42][43], (ii) the build of well-supported phylogenies improving our understanding of how horizontal transfer has influenced the evolution of the algal genomes [44].

Furthermore, quorum sensing (QS) is a system of chemical signaling which gains increasing attention from marine ecologists [45]. QS occurs within microbial populations in a density-dependent manner, causes downstream changes in the gene regulation, and modulates many biological functions like virulence factor expression, biofilm formation, bioluminescence, sporulation, and bacterial conjugation [24][46][47]. According to the literature, epiphytic bacterial communities are pivotal in the normal morphological development of the algal host, and their antifouling capacities by QS would protect chemically undefended macroalgae (those unable to deliver defense strategies themselves) from detrimental and secondary colonization by macroscopic epibiota [48][49][50].

2. Seaweed-Associated Microorganisms Interactions: An Overview

The Earth's microbial diversity is mainly concentrated in the ocean which undeniably represents a great reservoir of bioactive substances [51]. Marine microorganisms (e.g., bacteria, fungi, other unicellular organisms, diatoms, spores, and larvae of marine invertebrates) play crucial roles in every marine ecological process, hence the growing interest in studying their populations and functions [52].

Intriguingly, the surface of seaweeds provides a suitable substratum for the settlement of microorganisms particularly because it secretes various organic substances that function as nutrients for the formation of microbial biofilms [53]. The colonization of microorganisms on the seaweed surface is extraordinarily complex and dynamic, because the abundant and diverse epiphytic microbiota (e.g., Proteobacteria, Firmicutes) play a crucial role in morphogenesis and growth of seaweeds in direct and/or indirect ways [38][39][54].

The host-associated microbiota is found to be tissue-specific [52][55]. Other biotic factors involved in the algal halobionts include interactions among bacterial taxa (i.e., both internal and from the surrounding water), consequences of biological interactions with organisms from other trophic levels (i.e., grazing, cross-feeding) and also the loss of certain functions by bacteria [56].

Marine macroalgae are typically the home to aerobic and photoautotrophic epibionts (i.e., epiphytic organisms, those living at the surface of seaweeds) or endobionts (i.e., endophytic organisms, those living within the seaweeds). Thereby, epiphytic bacteria are found at densities varying from 10^2 to 10^7 cells·cm^{-2} depending on the macroalgal species, season, and thallus section [38][57]. In recent years, researchers have paid more attention on characterizing microbiomes (epibionts and endobionts) of various algal species in order to explain the host–microbe interactions and also to understand the function of microbial communities [58]. Nevertheless, it is worth noting that most of the experimental studies have focused on epibacterial communities and little attention has been focused on the diversity of fungi, endophytic and other epiphytic organisms [1][2][3]. This is most likely due to the higher representation of the bacterial community on algae, which halobiont is one of the easiest to study. For instance, nitrogen-fixing Cyanobacteria were recently observed to be among the dominant active members of the microbial community associated with the red seaweed *Laurencia dendroidea* (J.Agardh) [59].

According to several studies, the type of algae–bacteria interactions could be classified either as (i) nutrient exchange, (ii) signal transduction, or (iii) gene transfer [59]. Thereby, the participation of epiphytic bacterial communities include [47][52][55][60] (i) production of bioactive compounds, which protect the host (algae) from harmful entities present in the pelagic realm by determining the presence of other bacterial strains; (ii) provision of other effective molecules (e.g., vitamins among other nutrients), which are responsible for morphology, development, and growth of seaweeds; (iii) consumption of organic matter and nitrogen (NO_3^-) source; (iv) defense through QS (by Gram negative bacteria)/antifouling chemicals.

Further, algae–bacteria interactions cover the whole range of symbiotic relationships, which are mainly identified as mutualism, commensalism, and parasitism [61][62]. It is important to mention that environmental factors (e.g., Azote (N):Phosphorus (P) ratio, light intensity, temperature, pH, salinity) may shift an interaction from one type to another [62].

Mutualism is a biologic interaction in which two or more partners of different species benefit each other [62][63]. A typical example of mutualism is that a bacterial species supplies vitamin B_{12} (cobalamin) to an algal partner in exchange for fixed carbon (C) [64]. Thereby, the freshwater green microalga *Lobomonas rostrata* is auxotrophs for the vitamin B_{12} which is supplied for its growth promotion by the Gram-negative bacterium *Mesorhizobium loti* (formerly known as *Rhizobium loti*) [65][66][67].

Commensalism can be defined as an intraspecific relationship in which the commensal obtains great benefits (e.g., food, shelter, or locomotion) from the host without causing adverse effects [62][68]. For instance, the microalga *Chlamydomonas reinhardtii* (Phylum Chlorophyta) uses vitamin B_{12} delivered by heterotrophic bacteria, although the bacteria do not make use of the organic carbon released by the alga [67].

Parasitism is an interaction in which one species (i.e., commonly, the parasites) benefits at the expense of the other (i.e., usually, the alive algae) and exerts negative effects on it [62]. It has been estimated that some algae (about 10% of known red algae) are parasitic [69]. Interestingly, many bacteria are known to "negatively" affect algae growth rates, which in fact is encouraging for scientists who strive to control algae blooms [39][58][61][70]. This effect occurs either by competition for nutrients, altruism, or through algal cytolysis which is mediated by the action of bacterial glucosidases, chitinases, cellulases, and other enzymes (pectinases), allowing the bacteria to use the intracellular algal compounds as nutrients [62][71]. Such parasites have also wide-ranging applications in industrial biotechnology (e.g., pharmaceutical, food, alcoholic beverages, paper, and/or textile industries) [72][73].

In terms of algal–bacteria interactions, it is worthwhile to mention that the presence of carbon-rich constituents of macroalgal cell walls (e.g., agar, carrageenan, alginate, fucoidan, laminarin, cellulose, and pectin), are likely to be important for bacterial colonization [3][74][75]. Indeed, parasitic bacteria are likely to supply cell-wall degrading enzymes as a mechanism to mobilize polymers for nutritional purposes [60]. It has been proposed that macroalgal-polysaccharide-degrading bacteria increase in numbers on weakened or dead macroalgae, thereby contributing to recycling of the algal biomass [76]. Several algal polysaccharide-degrading bacteria displaying hydrolytic activities, such as Flavobacteria and γ-

Proteobacteria (Gram-negative bacteria), have recently been isolated from the microflora of the brown seaweed *Ascophyllum nodosum* (Linnaeus) [59]. The functional screening of plurigenomic libraries from these bacteria resulted in a range of novel hydrolytic enzymes [60]. Bacteria with polymer-degrading traits may thus represent opportunistic pathogens or saprophytes, rather than commensal or mutualistic macroalgal symbionts [77]. Further, some epiphyte microorganisms harbor a partial cellulosome, such as the marine psychrophilic bacterium *Pseudoalteromonas tunicate* (D2), which lacks the enzymes required to hydrolyze macroalgal cell wall polymers, although they still contain the structures involved in polymer binding [60]. *P. tunicata* also maintains the capability to utilize monomers derived from the degradation of typical macroalgal polymers, such as cellulose and xylan (a group of hemicelluloses), thereby benefiting from other microorganisms once its host is compromised [38]. It is also interesting to note that *P. tunicate* produced biologically active compounds such as the antibacterial protein alpP, known to be effective against a great number of Gram-negative and Gram-positive bacteria from a range of environments, thereby conferring a competitive advantage to *P. tunicate* during the biofilm growth on algal surfaces [78].

Although studies on seaweeds–microbionts interactions are attracting growing interest there is still a paucity of reports about seaweeds and other microorganisms, such as fungi [4][5][79]. Briefly, it was reported that the algal–fungal interactions commence with spore attachment and hyphal invasion, resulting in colonization of either parasitic, mutualistic, endosymbiotic, or saprophytic fungi [6]. These algal-inhabiting fungi are called algicolous, and those associated with the thallus surface are termed as fungal epiphytes or epibiotic fungi. Due to their ecological significance, algicolous fungi gain a particular interest in recent research. However, details on the distribution and occurrence of algicolous fungi are incomplete [7]. Thus, it will be an asset to explore the structure and dynamics of these fungal assemblages to understand the ecology of fungal–algal interactions among the numerous other seaweed-associated microorganisms that exist in the marine ecosystem.

In summary, this variety of exchanges between biotic communities in aquatic ecosystems, has an impact that can range from beneficial to detrimental effects on the algal growth and the environment (e.g., cycling of NO_3^-. The control of halobionts may serve as an incredible useful tool to control (i) the production of a given algal species, thereby avoiding harmful algal blooms, (ii) feed animals (e.g., pelagic fishes), and/or (iii) harvest algal biomass at a low cost for industrial considerations [62][80].

3. The Multifaceted Roles of Seaweed-Associated Bacteria: Friends or Foes?

3.1. Bacteria Supply Key Nutrients and Are Required for Normal Morphological Development of Seaweeds

Epiphytic heterotrophic bacteria supply key substances, such as carbon dioxide (CO_2) and fixed NO_3^-, required for macroalgal photoautotrophy, growth, and survival [59][81].

Epiphytic bacteria may also assist in or complement the macroalgal host's primary production since autotrophic cyanobacteria are often abundant on benthic macroalgal species [58].

In addition, epiphytic bacteria have a positive impact on the morphological development of several macroalgal species. Indeed, certain green macroalgae do not develop normal morphology in the absence of native bacterial communities. Specifically, the axenically grown green seaweed *Ulva australis* (Areschoug), formally known as *Ulva pertusa* (Kjellman) and commonly named sea lettuce, developed an abnormal 'pincushion'-like morphology, which could be restored to the typical foliose thallus upon reinoculation with bacterial strains isolated from the alga [38][39]. Similar effects have been reported for other species of green seaweeds, including, *Ulva linza* (Linnaeus), formally known as *Enteromorpha linza*, *Ulva compressa* (Linnaeus), formally known as *Enteromorpha compressa*, *Ulva fasciata* (S.F.Gray), and *Gayralia oxysperma* (Kützing) K.L. Vinogradova ex Scagel and al., formally known as *Monostroma oxyspermum* (Kützing) [7][39][82].

In addition to epiphytic bacteria, endophytic bacteria such as endophytic actinobacteria play helpful roles for seaweeds. Actinobacteria are widely found in sediments or in association with macroalgae among other marine organisms, such as fish, sponges, corals, and tunicates [73][83]. Such endophytic microorganisms live in the inner tissues of plants and algae without causing negative damages to the host [58]. During this symbiotic association, endophytes produce secondary metabolites that improve the fitness of the host and its resistance against environmental stressors, obtaining in return nutrients and shelter from their host [20].

3.2. Microorganism-Mediated Biofouling: Ecological Significance for Seaweeds and Their

Antibiofouling

Biofouling is the undesirable accumulation of microorganisms, plants, algae, and animals on wetted surfaces. The bacterial-mediated biofouling represents the "Achilles heel" due to bacteria's ability to multiply over time, forming a very dangerous pervasive biofilm, including on seaweeds' surface [84][85]. These bacterial biofilms display a complex 3D structure made of a consortium of bacterial species which are encased in an extracellular polymeric substance matrix comprising biomacromolecules (e.g., polysaccharides) and humic substances [86][87].

Studies of the epiphytic microbial communities present on macroalgae (10^2–10^7 cells·cm^{-2}) [38][45][57][88] have accentuated the spatial distribution of bacteria, with specific parts of the thallus hosting specific bacterial populations. In some cases, the bacterial populations even change with the season or the age of the host [88][89]. Further, these bacterial biofilms facilitate the attachment and growth of a range of other fouling organisms, namely diatoms, invertebrate larvae, and algal spores [88][90].

Therefore, bacterial biofouling is recently gaining much interest due to its severe economic (e.g., annual loss estimated to USD 6.5 million), and environmental adverse (e.g., release of CO_2 and sulphur dioxide (SO_2)) effects) [85]. Indeed, bacterial biofouling can physically damage the host organism (e.g., through production of toxins, digestive enzymes, and waste products by the microbial communities) and cause biological competition leading to environmental modifications [91]. Bacteria use specific appendages to bind to the host (e.g., macroalgal) surface [20][45]. Attached epiphytes bacterial populations must then compete with each other for nutrients and space through antifouling mechanisms (e.g., production of antagonist chemical metabolites/antibiotics) [92][93]. Thereby, the transcriptome analysis of microbiome associated with the red alga *L. dendroidea* revealed an overexpression of extracellular polysaccharides [59][93]. Thus, the balance between the bacterial biofouling and antifouling, through the production of bioactive substances from microbial (e.g., bacterial) strains that produce bioactive substances within the host (e.g., macroalgal) surface, largely contribute to the ecosystem's dynamism [60]. Interestingly, biofouling can lead to the production of biologically active compounds/chemicals by either the epiphytic microorganisms and/or the host organism when it can control the biofouling. Thereby, infochemicals (e.g., phenolics) produced on the algal surface can act as a chemical defense against pathogens and other microorganisms that compete for nutrients (e.g., mucilage) [37]. For instance, actinobacteria isolated from macroalgae can produce bioactive compounds, including antibiotics, antitumor, and anti-inflammatory compounds. In this regard, our team has made a recent breakthrough discovery by isolating an original antibiotic, effective against MRSA clinical strains, originated from a new epibiotic actinobacterium that we named *Kocuria marina* CMG S2 which was using the brown seaweed *Pelvetia canaliculata* (Linnaeus) as a basibiontic organism (i.e., providing substrate for other organisms) [73]. Additionally, the marine bacterium *P. tunicata*, frequently found associated with the green seaweed *U. australis*, produce a diverse range of biologically active compounds against common fouling organisms [88][94]. Indeed, as earlier evoked, *P. tunicata* produce the antibacterial protein alpP, which in the context of biofilm growth provided a competitive advantage to *P. tunicata* when tested in laboratory [78][88]. Since *U. australis* has no known physical or chemical defense systems against fouling organisms, it has been consequently suggested that the host may manipulate the bacterial community on its surface, which in turn protects the host by interfering with the development of a mature biofouling community [88]. Thereby, within the bacterial community related to *U. australis*, abundant multidrug-efflux pumps and nonribosomal peptide synthetases were found to be frequently involved in the production of bioactive substances, further supporting the role of chemically mediated antagonism and counteractive defense processes in such marine environments [55][95].

Besides, some other algae, such as tropical marine brown macroalgae members of the Fucales (e.g., *Turbinaria ornata* (Turner) and *Sargassum pacificum* (Bory), formally known as *Sargassum angarevense* (Grunow)), were able to directly produce bioactive compounds (e.g., fatty acids, lipopeptides, glucids, pigments, amides, alkaloids, lactones, steroids, terpenoids, pyrroles, halogenated metabolites) which are generally assumed to function as chemical defenses against herbivores/grazers, bacteria, other undesirable epiphytic associations, and even as inducible screens against UV radiation [49][96][97][98]. Thus, these secondary antibiofouling metabolites represent a robust selective factor for epiphytic bacterial colonizers, influencing the bacterial biofilm formation and its community composition [38][45][99][100][101].

Major microorganismal antifouling (i.e., antimicrobial colonization, inhibition of biofilm formation) compounds (e.g., brominated, polyphenolic) produced by macroalgae are summarized in Table 1.

Table 1. Antifouling compounds produced by some macroalgae from a different phylum.

Macroalgae	Class (Secondary Metabolite(s))	References
Green algae		

Ulva rigida (C.Agardh)	Brominated furanones (3-bromo-5-(diphenylene)-2(5H)-furanone)	[102]
Ulva sp.	Tetraterpenoids (β-carotene)	[103]
Brown algae		
Dictyota menstrualis (Hoyt)	Diterpenes (dictyol D, pachydictyol A)	[104]
Sargassum spp.	Polyphenols (phlorotannins)	[105]
Bifurcaria bifurcata (R.Ross)	Acyclic linear diterpenoids (eleganediol, eleganolone, geranylgeraniols)	[106]
Fucus vesiculosus (Linnaeus)	Fucoxanthin (carotenoid/epoxycarotenol)	[107]
Lobophora variegata (J.V.Lamouroux)	Cyclic lactone (lobophorolide)	[108][109]
Canistrocarpus cervicornis (Kützing)	Diterpenes (dolastane, *seco*-dolastane)	[110]
Red algae		
Laurencia sp. (J.V.Lamouroux)	Omaezallene derivatives, sesquiterpenes (omaezol, hachijojimallene A, elatol)	[111]
Laurencia translucida (Fujii and Cordeiro-Marino)	Fatty acids (docosane; hexadecane)	[112]
Asparagopsis taxiformis (Delile) Trevisan	Sulfonate/dodecanoic acid (FA)-derived (2-dodecanoyloxyethanesulfonate)	[46]
Bonnemaisonia hamifera (Hariot)	Poly-brominated ketone (1,1,3,3-tetrabromo-2-heptanone)	[98]
Delisea pulchra (Greville)	Brominated furanones (N-acyl-homoserine lactones-like compounds)	[113]

| Callophycus serratus (Harvey ex Kützing) | Bromophycoic acids (Bromophycolides and callophycoic acids) | [114] |
| Mastocarpus stellatus (Stackhouse) | Glucids (Floridoside) | [115] |

FA: fatty acid.

3.3. Disturbance of the Macroalgal Halobiont by Bacterial Pathogens: The Crucial Role of Quorum Sensing

Macroalgae are the major habitat formers and they contribute to the primary production in temperate marine ecosystems [116]. Unfortunately, there is some evidence to suggest that microbial disease is a possible factor contributing to the (i) decline of macroalgal populations, (ii) environmental changes, such as increase of seawater temperatures which impact halobionts, (iii) reduction of innate defense strategies in macroalgal hosts, and (iv) susceptibility to colonization and infection of macroalgae by pathogens [52][113].

Suitable models are being developed to address the specific virulence mechanisms employed by seaweed pathogens [13]. The bacterial-induced bleaching of the red alga *Delisea pulchra* (Greville) caused by the bacterium *Nautella italica* R11 (formerly *Ruegeria* sp. R11), a member of the Roseobacter clade, is one of the best-studied models for disease in macroalgae [31][117]. The infection process of *N. italica* R11 in the chemically defended marine macroalga *D. pulchra* was shown to be temperature dependent [118].

There seems to be a link between QS and diseases through the regulation of certain phenotypes. Therefore, it is thought that the induction of virulence factors are liable for pathogen–host association [81]. Several reports indicated that numerous aquatic organisms like microalgae, macroalgae, invertebrates, or maybe other bacteria have the potential to disrupt QS [119]. Importantly, the disruption of bacterial communication by QS is considered as a novel and environmentally friendly approach to avoid harmful consequences for the algal health and fecundity. The mechanism of action varies from degradation of signals through enzymatic or chemical inactivation to antagonistic and agonistic activities [120]. Thereby, QS systems, such as the classical LuxR-type QS, mediate the host colonization and coordinate the expression of virulence genes in pathogenic bacteria [50]. For instance, in *N. italica* R11, it was demonstrated that the acylated-homoserine lactone (AHL) signal molecule, produced in a LuxI-dependent manner, binds a unique response regulator (LuxR)-type gene, *varR*, which modulates the expression of biofilm-associated proteins that control its colonization, persistence, and virulence on the surface of a macroalgal host [50]. Importantly, such a *varR* gene with homology to LuxR-type transcriptional regulators was present in another bleaching-associated disease pathogen, namely *Phaeobacter* sp. LSS9 [45].

Furthermore, it has also been established that macroalgae-associated bacterial isolates produce signal molecules, like N-acyl homoserine lactone (AHLs) [48], thereby facilitating the settlement of zoospores in seaweeds such as in the green macroalgae *Ulva* spp. [45]. Deeper investigations about zoospore settlement revealed that the orientation of zoospore does not change during the settlement but the mechanism underlining this phenomenon has not been clearly reported yet [45]. However, it has been assumed that AHLs influence Ca^{2+} in fluxin zoospore which preferentially induces the settlement through chemokinesis [121]. To date, there is limited knowledge about the significant role of the cross-kingdom QS signaling between associated bacterial communities and carpospore liberation from red macroalgae [45][48].

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