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OPINION

Phycosphere associated bacteria; a prospective source of bioactive compounds

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Abstract

Co-occurrence of bacteria and algae can be traced back to billions of years ago. Their coexistence for more than 200 million years in common habitat has fostered a multitude of promising interactions among these two groups over evolutionary time scales. These associated bacteria produce various biologically active secondary metabolites and play a pivotal role in algal growth and metabolism. Consequently, specific chemical microenvironment created by algal microbiome signifies a promising source of bioactive compounds. Although these associations may be of substantial importance, only limited knowledge on the chemical ecology of algal microhabitat is available. Thus, better insight into the metabolic capabilities of phycosphere microbiome could allow targeted isolation of novel bioactive compounds with manifold beneficial effects. Moreover, further research contributing towards the chemistry behind these interactions is needed for exploring phycosphere bacteria for desired industrial and biotechnological applications.

Keywords Phycosphere bacteria · Bioactive compounds · Algal-bacterial association · Secondary metabolites

Oceans, the largest biome on earth, harbour tremendous diversity of living microorganisms (Penesyan et al. 2010; Amin et al. 2012). It was estimated that oceans contribute nearly half of the global productivity which has been carried out by ubiquitous photoautotrophs referred to as marine algae (Geng and Belas 2010; Ramanan et al. 2016). The organic carbon produced by these photosynthetic organisms is further remineralised to CO_2 by heterotrophic bacteria. Thus, bacteria play a pivotal role in converting ocean's primary productivity to dissolved organic matter (Geng and Belas 2010; Amin et al. 2012). Altogether, these ubiquitous populations drive marine biogeochemical cycles and thus ensure a balance in energy flow. Hence, these foremost functional entities together are considered structural pillars of the marine ecosystem (Natrah et al. 2014; Ramanan et al. 2016). Undoubtedly, this inter-organism association plays a crucial role in shaping aquatic ecosystem function and has gained current research interest (Ramanan et al. 2016). The term 'Phycosphere' – the aquatic analogue of the rhizosphere, was coined in 1972 by Bell and Mitchell to define a zone that extends outward from an algal colony or cell for an undefined distance, in which growth of bacteria is enhanced by extracellular products of algae. Bacterial groups such as *Gammaproteobacteria, Alphaproteobacteria, Actinobacteria, Betaproteobacteria, Bacilli* and *Bacteroidetes* were most prominently found in the phycosphere of different algal groups (Nicolas et al. 2004; Sapp et al. 2007; Amin et al. 2012; Natrah et al. 2014). Many associated bacteria secrete numerous growth promoters which can improve the physiological state of the algal host (Croft et al. 2005; de-Bashan and Bashan 2008; Guo and Tong 2014). Simultaneously, algae excrete organic carbon compounds and other products that have a stimulatory effect on bacterial associates (Natrah et al. 2014). Algal-bacterial interactions do not always have positive effects; rather, may have negative consequences. Active compounds released by many algicidal bacteria can lyse algal cells (Amin et al. 2012; Natrah et al. 2014). A summary of algal-bacterial interactions that exists in the phycosphere is depicted in Fig. 1.

It has been well proven that marine organisms, especially marine algae represent a vital source of fascinating bioactive compounds (Konig et al. 2006; Bai and Krishnakumar 2013).

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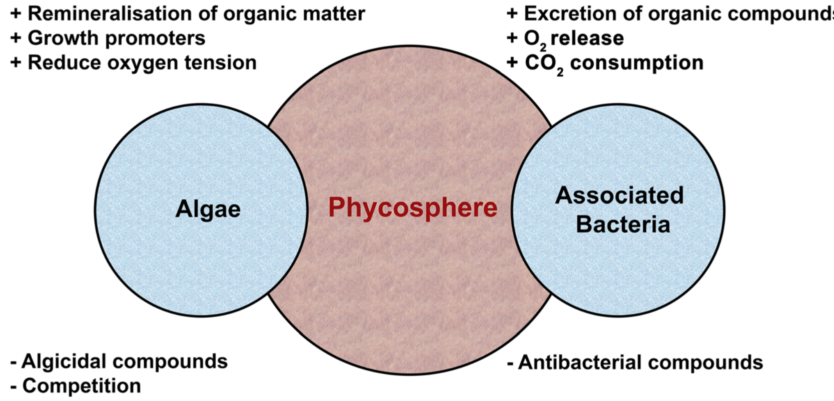

Fig. 1 A schematic summary of positive and negative interactions between algae and bacteria that exist in the phycosphere

Upon recognition that most of the algal habitat harbor metabolically diverse bacterial counterparts, one of the most intriguing questions in marine bioprospecting is which partner organism produces which secondary metabolite (Konig et al. 2006; Penesyan et al. 2010). Moreover, many compounds, formerly ascribed to eukaryotic hosts, have later been proved to be produced by bacterial symbionts (Li and Vederas 2009). Hence, bacterial richness in algal microhabitat opens up new avenues for the discovery of novel bioactive compounds. Bacterial symbionts construct chemical microenvironments with their algal host and contribute significantly to host evolution, performance and function (Penesyan et al. 2010). Algal growth stimulatory compounds released by associated bacteria include vitamins, essential minerals, polyunsaturated fatty acids, quorum sensing signaling molecules, auxins, carbohydrates and proteins (Krug et al. 2020; Zhang et al. 2020). Several algal species are incapable of synthesizing specific vitamins required for their growth (cobalamin, thiamin) and obtain these vitamins from their bacterial counterparts (Natrah et al. 2014). For example, the microalga *Amphidinium operculatum* obtain vitamin cobalamin from its bacterial associate *Halomonas* (Croft et al. 2005). Likewise, *Ruegeria pomeroyi* associated with the diatom *Thalassiosira pseudonana* secrete vitamin B_{12} in exchange for diatom derived organic carbon (Seymour et al. 2017). In addition, bacterial groups found in association with algae are reported to produce phytohormones (indole-3-acetic acid), siderophore and antibiotics (Villarreal-Gómez et al. 2010; Natrah et al. 2014; Lian et al. 2018). Previously, we reported that *Labrenzia* sp. Mab 26 associated with microalgae, *Isochrysis galbana* is capable of synthesizing both siderophore and indole-3-acetic acid (Sandhya and Vijayan 2019). Similarly, *Marinobacter* spp., one of the most predominant bacterial groups in diverse algal habitats could produce siderophore, vibrioferrin (Amin et al. 2012; Fuentes et al. 2016; Sandhya et al. 2017). Bioactive molecules produced by associated bacteria often contribute to algal defense mechanisms to fight with pathogens and other competitive predators (Paul et al. 2011; Balakrishnan et al. 2014). It was reported that bacterial populaces that reside in algal habitat produce toxins, signaling molecule and other secondary metabolites as their inhibitory traits (Kizhakkekalam and Chakraborty 2020). These bacterial defense communities make the phycosphere a potential reservoir of new antibiotics, drug molecules and pharmaceutical agents. For instance, *Phaeobacter gallaeciensis*, the bacterial associate of *Emiliania huxleyi* could produce tropodithietic acid, a broad-spectrum antibiotic (Lian et al. 2018). The heterotrophic bacteria associated with brown algae *Sargassum* sp. and red marine macroalgae *Ceratodyction spongiosum* were reported to inhibit pathogenic methicillin resistant *Staphylococcus aureus* (Isnansetyo et al. 2001; Susilowati et al. 2015). Moreover, a study conducted by Kizhakkekalam and Chakraborty (2019) recognized macroalgae associated *Bacillus amyloliquefaciens* as a potent candidate to develop products with broad biotechnological and therapeutic applications. Additionally, the antioxidant production potential of heterotrophic bacteria associated with *I. galbana* has also been reported (Sandhya and Vijayan 2019).

Motone et al. 2020 showed that antioxidant carotenoid produced by a bacterial symbiont could mitigate light and thermal stresses in cultured *Symbiodiniaceae* algae, isolated from coral reef, *Galaxea fascicularis*. Such metabolic potential of symbiotic bacteria could open up novel approaches toward coral protection from environmental stress. Likewise, Fradinho et al. (2013) demonstrated successful production of polyhydroxyalkanoates (a green alternative to plastic) using a consortium of algae and bacteria. Finally, the phycosphere of several seaweed species harbour metabolically versatile bacterial associates capable of producing anticancer substances, polysaccharides, bacteriocines, protease, lysozymes and organic acids (Soria-Mercado et al. 2012). These metabolic or chemical based interactions clearly emphasize the significance of phycosphere bacteria as an epitome source of bioactive compounds. However, to date, biotechnological potential of phycosphere bacteria is largely unexplored. Difficulties in isolation and cultivating these bacterial symbionts represent a key bottleneck in their exploitation. One of the successful strategies to boost up culturability of bacterial symbionts is to mimic conditions of their natural habitat. Such manipulation of physical and chemical growth parameters may help to obtain maximum yield of desired metabolites (Penesyan et al. 2010). Advent of genome sequencing technologies such as metagenomics and next generation sequencing could provide better insight into the diversity of the phycosphere microbiome. Additionally, other omics methodologies including proteomics, metabolomics and transcriptomics could further elucidate the functional aspects and ecological implications of various metabolites synthesised by these bacterial communities (Zhang et al. 2020). For instance, Cooper and Smith (2015) deciphered thiamine biosynthetic pathways of the bacterium *Pseudoalteromonas* sp. TW7 in *Ostreococcus tauri* co-culture using transcriptomes analysis. Thus, functional metagenomics approaches along with suitable culturing conditions would certainly trigger additional studies and the pursuit for unique bioactive compounds. Design of a "bacterial consortium" is another promising horizon for industrial microbiology. A consortium of bacteria can carry out various complex functions that are impossible for a single bacterium (Bhatia et al. 2018). Hence, in-depth understanding of algal-bacterial interaction using advanced functional genomic tools is critical to facilitate the construction of novel consortia of phycosphere bacteria with broad spectrum applications.

Overall, a close and strong association occur between marine algae and bacteria which make the phycosphere a hotspot for the exchange of numerous chemical currencies.The interactions between algae and bacteria are primarily controlled by the chemical characteristics of these exchanged mediator molecules including growth resources and other infochemicals. Thus, unravelling algal-bacterial interactions provide new perspectives on utilizing such knowledge in search of diverse bioactive compounds. Moreover, further research focusing on the microbiological and chemical features of phycosphere will ultimately have a great impact on the biotechnological and pharmaceutical industry.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no potential conflict of interest.

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