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Editorial: Cyanobacterial and microalgal compounds: Chemical ecology and biotechnological potentials

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Editorial on the Research Topic
Cyanobacterial and microalgal compounds: Chemical ecology and biotechnological potentials

Introduction - marine chemical ecology

Since the beginning of life on the earth, chemical relationships have ruled all aspects of nature (Cole, 2016) and ecological interactions are linked to chemical and biochemical processes (Overbeck and Chrost, 2012). Infochemical interactions are among the oldest and most widespread forms of communication both in terrestrial and aquatic ecosystems (Wyatt, 2014; Roggatz et al., 2022). Aquatic organisms respond to small concentrations of chemicals released in the environment and such molecules, called infochemicals, are involved in recognition of prey and predators, chemotaxis, allelochemical defenses, mate recognition, reproductive and settlement cues, larvae metamorphosis, sex pheromones, and more in general organism's interactions (Ferrari et al., 2010; Schwartz et al., 2016; Zupo et al., 2016; Zupo et al., 2019; Mutalipassi et al., 2019). In addition, chemical interactions led to the study of chemical defenses which should be considered not only as defenses against consumers but also as weapons against competitors (allelopathy) and as reduction of colonization (anti-fouling) (Leão et al., 2012; Mutalipassi et al., 2021; Mutalipassi et al., 2022). Chemical communications shape the structure and the functioning of marine ecosystems (Hay, 2009), providing crucial services, often essential for humans (Parachnowitsch and Manson, 2015). Seagrasses, that are considered key species for the development of rich associated communities, produce a large array of diverse bioactive compounds including phenolic compounds, steroids, terpenes, glycosides, sulfated polysaccharides, pectins, glycolipids, triglycerols, fatty acids, and volatile organic compounds (Harder et al., 2018). These compounds can deter herbivores' grazing, inhibit the proliferation of pathogens and the settlement of fouling organisms (Harder et al., 2018). In addition, several infochemicals are produced by seagrass-associated organisms with a role in the regulation of macroalgal-associated microbial communities within benthic marine environments (Saha and Weinberger, 2019; Mutalipassi et al., 2021). Thus, the molecules produced by seagrasses and their associated organisms play important roles in mediating ecological interactions among the organisms inhabiting these highly productive communities (Mutalipassi et al., 2019; Mutalipassi et al., 2020). In the complex array of interactions triggered by chemical cues, antagonistic interactions promote diversified adverse cascading effects on both benthic and planktonic species (Ribeiro et al.). However, it is accepted that anthropogenic stress can disturb and interfere with these mechanisms, reducing or destroying the ability of an organism to produce the correct information or receive and interpret the message (Atema et al., 2012). Further, chemical ecology investigations can be seen as a starting point for developing new strategies for the discovery of novel compounds for biotechnological purposes (Leào et al., 2012; Mutalipassi et al., 2021). In fact, the investigation of the roles of marine-derived chemicals produced for defensive, offensive, and communication purposes can lead to the identification of bioactive molecules with a wide array of potential applications (Gerwick and Moore, 2012; Nishida, 2014). Indeed, several investigations analyzed chemical ecology interactions of marine species in order to have inference on potential bioactive compounds that can be used in biotechnology, as in the case of terpenes, polyphenols, alkaloids, and flavonoids (Bohlmann, 2011). The production of novel compounds during peculiar physiological states, *e.g.* in symbiotic relationship or in altered and extreme marine environments, is largely underestimated from a biotechnological point of view (Mutalipassi et al., 2021). This is the case of several extreme environments where interaction among microorganisms, able to produce a large array of secondary metabolites, demonstrated healing properties for humans (Vadlja et al.). This concept can be considered as an extension of the One Strain Many Compounds theory (OSMAC), considering that some gene clusters can be "silent" and not expressed during some life stages or environmental conditions, but activated by specific infochemicals. Chemical ecology may help to unlock the chemical diversity they control, favoring the discovery of novel molecules of medical and biotechnological interest (Romano et al., 2018; Pan et al., 2019).

Chemical ecology and response to climate change

The increase of atmospheric greenhouse gas concentrations gives rise to climate changes, with a cascade of consequences for marine environments with potential additive effects by other anthropogenic stressors (Gissi et al., 2021). Recent studies demonstrated the severe impacts of predicted foreseen CO_2 concentrations on the chemical communication in aquatic organisms (Ferrari et al., 2011; De la Haye et al., 2012; Zupo et al., 2016). The study of the disruption of infochemical production in relation to climate change is considered a frontier field in the chemical-ecology (Draper and Weissburg, 2019; Mutalipassi et al., 2019; Zupo et al., 2019; Roggatz et al., 2022). Chemical-ecology interesting insights have been provided by studies focused on the seagrass meadows community (Maibam et al., 2015; Zupo et al., 2016; Zupo et al., 2019; Mutalipassi et al., 2020). Marine macrophytes depend on chemical communication to manage stable relationships with epifauna, colonizers, and pathogen populations and these relationships are disturbed by acidification (Campbell et al., 2011) with consequences on the grazing activities (Pereira et al., 2003) and on settlement (Da Gama et al., 2003). Volatile organic compounds have been demonstrated to be fundamental for invertebrate chemical communications both in planktonic (Maibam et al., 2015) and benthic (Mutalipassi et al., 2020) environments, structuring food webs (Fink, 2007) and acting as settlement signals in species belonging to the same environment, as in the case of the sea urchin *Paracentrotus lividus* (Zupo et al., 2018) or in the case of the shrimp *Hippolyte inermis* (Zupo et al., 2019). Investigations also showed that acidification can act as an interfering agent on the bouquet of odors released by *P. oceanica* meadows with consequences on the chemotactic reactions of the associated vagile community (Zupo et al., 2016; Mutalipassi et al., 2019; Mutalipassi et al., 2020; Mutalipassi et al.). These differences in the invertebrate behaviors can be linked to the differences in the abundance of the same invertebrate in areas at different pH values (Maibam et al., 2014), confirming the role of VOC infochemicals in the structuring of the epifaunal communities (Mutalipassi et al.). These relationships mediated by VOCs have been confirmed in planktonic environments, where diatoms release volatile-aldehydes teratogenic for copepods (Miralto et al., 2003; Barreiro et al., 2011; Lauritano et al., 2011). At the same time, copepods evolved mechanisms to discern, using VOCs, between beneficial algae and aldehyde-releasing diatoms (Maibam et al., 2015) but this co-evolved mechanism is not adapted to a high-CO_2 world. On one side, ocean acidification can alter the three-dimensional conformation of several infochemicals and a change in charge distribution has been demonstrated even by small difference of pH values (Roggatz et al., 2016; on the other side, electrophysiological and transcriptomic measurements have demonstrated that elevated CO_2 concentrations act on the olfactory system of several organisms (Porteus et al., 2018; Velez et al., 2019) or on the neurotransmitter functioning itself, with an alteration in brain ion gradients (Nilsson et al., 2012).

Dietary interaction

Organisms detect and interact with their favorite food items using chemical signals (Jüttner et al., 2010). In the marine environment, invertebrates follow the signals emitted by preys and exhibit chemotactic behavior indicating preference or repulsion, according to a chemical language that evolved over time (Maibam et al., 2014). These compounds are transported by currents and this further modifies the perception by invertebrates, as demonstrated by contrasting results achieved using static chambers and flumes (Mutalipassi et al.). Organisms evolved to recognize the infochemicals emitted by toxic prey present in their own environment and this helped to stabilize several aquatic communities (Maibam et al., 2014). However, toxic substances produced by organisms outside their own community are not always recognized and this also helps to stabilize the composition of typical communities, because alien species are damaged after the ingestion of toxic algae. Consequently, we can hypothesize that a common chemical language reinforces the relationships among definite benthic communities. However, infochemicals not only modulate the chemotactic reactions of consumers but often influence their physiology, indicating a potential role as "functional foods", as in the case of the protandrous shrimp *Hippolyte inermis* and of the co-evolved diatoms of the genus *Cocconeis* which influence its sex regulation, triggering apoptosis of androgenic gland in early postlarvae (Zupo and Messina, 2007; Levy et al., 2021). Small lipophilic compounds present in the diatoms are able to selectively destroy such tissues and this peculiar relationship will be worth producing interesting biotechnologies in the fields of aquaculture and medicine. Clark et al., through a multidisciplinary approach, used the chemical ecological dietary interactions between marine organisms as a tool to identify and then isolate novel ecologically relevant compounds with biotechnological potential (Clark et al.). Thus, we should state that the thermodynamic importance of foods, as a source of energy for heterotrophic organisms, is quite less important than their regulatory roles, because foods may change both the physiology and the behavior of terrestrial and marine animals. In the cases herein considered, the infochemicals produced by selected organisms represent a "signal" for a given species but, in several cases, the signals may be shared among various species and produce shifts in the spatial distributions of animal communities. In other cases, multiple interactions may rule the behavior of various species, as in the case of tri-trophic interactions (Helms et al., 2017; Castano-Duque et al., 2018), when the warning signals emitted by a given species call for the attention of potential predators of their own consumers. On the whole, dietary interactions are influenced by the sharing of a common chemical language and deeply affect the structure of animal communities and the physiology of individual species.

High-value compounds from cyanobacteria and microalgae

It has been well known that cyanobacteria and microalgae produce a broad range of high-value compounds. They are often involved in dietary interaction or chemical ecology processes and possess important biological activity (Riccio et al., 2020; Khavari et al., 2021; Xia et al., 2021) as demonstrated by the Green Microalga *Dunaliella terctiolecta* that possess an antiproliferative activity against four different human cancer cell lines: melanoma, hepatocellular liver carcinoma, and two lung adenocarcinoma cell lines (Martínez et al.). Microalgal interesting compounds include polyphenols, alkaloids, oxylipins and others, nevertheless, marine microalgae represent a poorly explored resource. From a chemical-ecology point of view, there is a relationship between the production of bioactive molecules and the interactions affecting organisms' behavior and function. Polyphenolic compounds are a family of secondary metabolites comprising flavonoids, phenolic acids, tannins, lignans, or coumarins (Del Mondo et al., 2022). Their biological functions are well characterized in plants but poorly known in marine organisms, as for example in algae and microalgae. In benthic organisms, polyphenolic flavonoids contrast the foulers proliferation on their surfaces (Papazian et al., 2019) attracting attention for the production of alternative eco-compatible antifouling products for maritime industry after optimization of their activity *via* glycosylation and other chemical modifications (Pereira et al., 2020). Thus, these classes of compounds are also considered promising molecules for the development of new drugs and nutraceutical products, thanks to a large array of biological activity in *in vitro* and *in vivo* human experimental models, as for example antioxidant activity (Behery et al., 2013) and immune system regulation and defense against microbial pathogens (Qi et al., 2008). It must be considered that the release of these molecules into the marine environment could be primarily exerted through cell lysis by enabling certain inter- and intra- specific chemical communications (Hohlman and Sherman, 2021). This is the case of alkaloids that have been demonstrated to have an anti-grazing and deterring activity in terrestrial environments (Wink, 2019). Interestingly, specialist herbivores have evolved the capacity to store and modify these secondary metabolites, taking advantage of an extraordinary symbiotic community living in the digestive tract (Pennisi, 2017), acquiring an ecological benefit against predators (Mason and Singer, 2015; Petschenka and Agrawal, 2016). In marine environments, sea slugs accumulate several toxic compounds through their diets and modify them for their own defense (Wu et al., 2020; Wu et al., 2021). Due to the extraordinary bioactivity, alkaloids have been deeply investigated for medicinal purposes, with anti-microbial, anti-inflammatory, and anti-cancer activity demonstrated in *in vitro* and *in vivo* tests (Souza et al., 2020; Elissawy et al., 2021; Moosmann et al., 2021; Munekata et al., 2021;

Thawabteh et al., 2021). Similarly, oxylipins are considered toxic compounds involved in cell-cell communication, regulators of population dynamics, and anti-grazing activity produced, after an environmental stimulus, by the oxidation process of polyunsaturated fatty acids (Ruocco et al., 2020). Since they cover toxic and teratogenic roles in nature, oxylipins were tested on human cancer cells and *in vivo* models, demonstrating antiproliferative effect on human colon adenocarcinoma cells (Miralto et al., 1999) through the activation of apoptotic extrinsic cell death pathway triggered by the tumor necrosis factor receptor 1 (Sansone et al., 2014).

Conclusions and perspective

Despite the chemical ecology is largely investigated in terrestrial environments, in marine environments this field is still in its infancy. Although chemists have identified a large number of compounds modulating organisms' interactions, very little is known regarding chemical cues related to migrations, species recognition or assessment of predator threats. Transcriptomics, metabolomics, and proteomics are nowadays common tools that allow chemical-ecologists to look deeply into gene expression and metabolic responses to infochemicals (Dyer et al., 2018; Kellogg and Kang, 2020). Future investigations should focus the attention to understand if the same chemical cue can bring the same information to different species in a sort of chemical universal language and if there is some kind of relationship in the interpretation of chemical cues linked to phylogenetic evolution (Vet, 1999) or to ecological niche (Müller et al., 2020). An increasing number of studies suggest that anthropogenic pollutants and disturbances may severely affect the transmission and the production of infochemicals as well as the chemosensory and neurological system of aquatic organisms (Brönmark and Hansson, 2012). Ecotoxicology should focus, in the next future, on the analysis of the impacts of old and emerging contaminants on the chemical ecology of marine species, in order to predict effects at short, medium, and long term on ecosystems and ecosystemic services (Savoca et al., 2016). For example, the settlement of many marine species, both vertebrates (Ben-Tzvi et al., 2010) and invertebrates ones (Zupo et al., 2019), is triggered and facilitated by the presence of "olfactory stimuli". This settlement can be easily impaired by disturbances, as demonstrated for high pCO_2 conditions, with consequences on the recruitment of broodstock (Gerlach and Atema, 2012). Concluding, the last future perspective of chemical ecology investigations is represented by the great potential of infochemicals in biotechnological fields due to the extraordinary bioactivities observed during the past fifty years. The observation of chemical interactions among organisms allows researchers to access a more sustainable approach involving the identification of novel molecules through targeted research focusing on the most promising ecological context.

Author contributions

The manuscript has been conceived and designed by MM, GR, NR, CG, under the supervision of VZ and SG. Ecological section has been written by MM and VZ. Biotechnological section has been written by GR, CG and NR. The manuscript was reviewed and approved by all co-authors.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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