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Review

The current state of knowledge on taxonomy, modulating factors, ecological roles, and mode of action of phytoplankton allelochemicals

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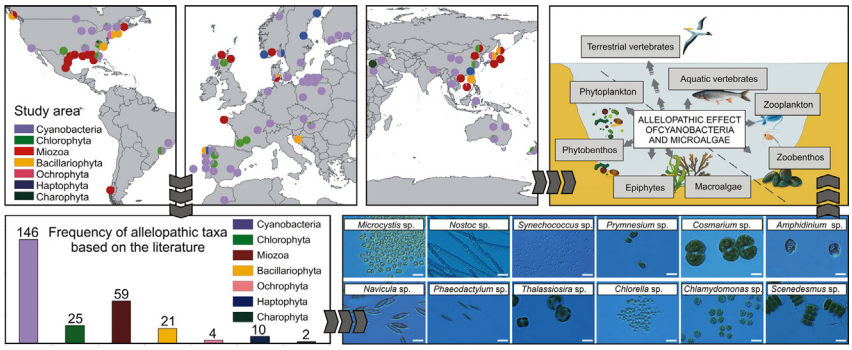
HIGHLIGHTS

- Allelopathic effects of cyanobacteria and microalgae occur in all aquatic habitats.
- Allelopathy influence ecosystem dynamics, species variability, and bloom formation.
- Studies confirm allelopathic properties in 61 genera of cyanobacteria and microalgae.
- Cyanobacteria were the most frequently examined for their allelopathic activity.
- *Synechococcus* sp. and *Karenia brevis* were the most studied organisms.

GRAPHICAL ABSTRACT



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ABSTRACT

Allelopathy is widespread in marine, brackish, and freshwater habitats. Literature data indicate that allelopathy could offer a competitive advantage for some phytoplankton species by reducing the growth of competitors. It is also believed that allelopathy may affect species succession. Thus, allelopathy may play a role in the development of blooms. Over the past few decades, the world's coastal waters have experienced increases in the numbers of cyanobacterial and microalgal blooming events. Understanding how allelopathy is implicated with other biological and environmental factors as a bloom-development mechanism is an important topic for future research. This review focuses on a taxonomic overview of allelopathic cyanobacteria and microalgae, the biological and environmental factors that affect allelochemical production, their role in ecological dynamics, and their physiological modes of action, as well as potential industrial applications of allelopathic compounds.

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Contents

1. Introduction

Allelopathy stands for any process that refers to organisms being able to produce biologically active metabolites that affect other neighboring plants or fungi (Legrand et al., 2003). It is believed that allelopathy is a strategy against competitors and predators (Sarkar et al., 2006; Granéli et al., 2008a; Fig. 1). The definition of allelochemicals includes compounds that are considered phytotoxins as well as other secondary metabolites (Leflaive and Ten-Hage, 2007).

Scientists believe that there is a greater diversity of allelopathic compounds in aquatic ecosystems than in land environments (McClintock and Baker, 2001). The impact of allelopathy on aquatic ecosystems depends on the production of active allelopathic compounds and their effective spread to target organisms (Lewis Jr., 1986). Marine organisms that produce allelopathic compounds mainly belong to the Miozoa and Haptophyta phyla (e.g., Vasconcelos and Leal, 2008; Liu et al., 2010; Poulin et al., 2018a,b; Chen et al., 2020), while Cyanobacteria dominate in freshwater and brackish environments (Gantar et al.,

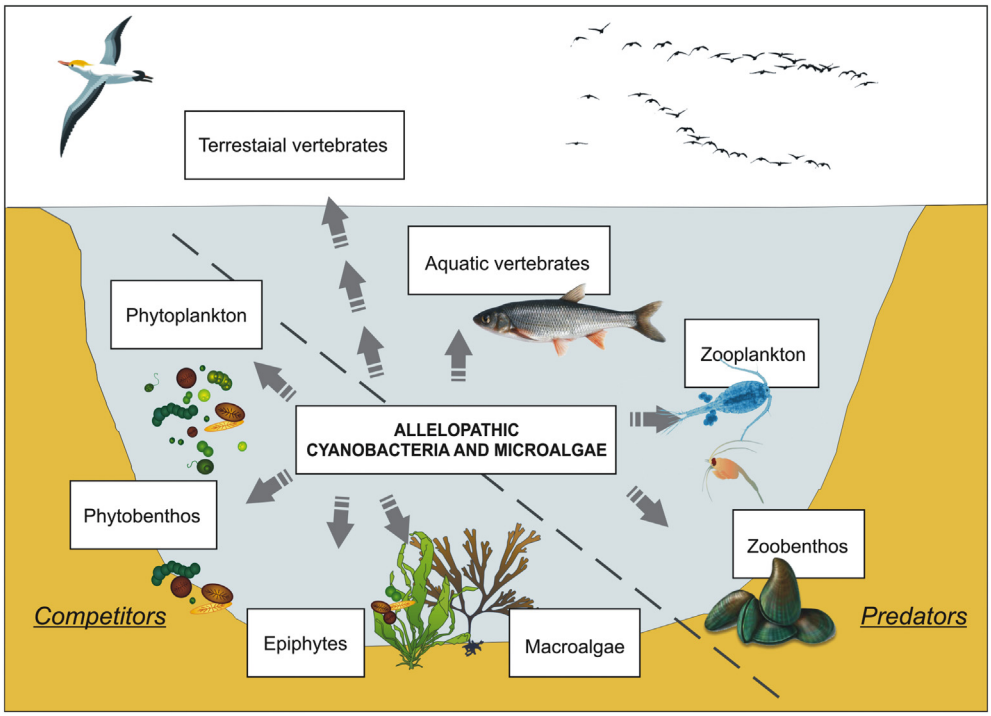

Fig. 1. Examples of possible types of allelopathic interactions of cyanobacteria and microalgae in aquatic ecosystems.

2008; Antunes et al., 2012; Kovács et al., 2018; Konarzewska et al., 2020).

Allelopathic effects also occur in benthic habitats (Leflaive and Ten-Hage, 2007), where the organisms are often at shorter distances from each other than in the pelagic zone. Moreover, in biofilms, there is direct contact between cells. In contrast to that in the terrestrial environment (Rizvi et al., 1992), a clear demonstration of allelopathic interactions in natural aquatic environments is very difficult. Therefore, studies demonstrating the allelopathic effects between aquatic marine organisms are based on laboratory experiments.

Fig. 2 presents the numbers of donor cyanobacteria and microalgae against other photoautotrophic microorganisms published in scientific papers. A total of 80 papers (Table S1 in Supplementary material) based on studies of allelopathic activity, as described in the title or keywords, were analyzed. Traditional papers that focus on interactions between cyanobacteria and microalgae were also included since some interactions were not yet unacknowledged as allelopathy (Fig. 2).

Based on our research, we showed that organisms belonging to the Cyanobacterial phylum were most often tested for their allelopathic activity globally. Moreover, the allelopathic activities of the Miozoa, Bacillariophyta, Ochrophyta, and Haptophyta phyla have been studied mainly based on species isolated from the marine environment, while the donors Cyanobacteria, Chlorophyta, and Charophyta came from freshwater and brackish ecosystems (Fig. 3). In total, 146 Cyanobacteria taxa were tested for allelopathic ability, which accounted for 55% of all organisms tested. Miozoa (representing 59 of the studied taxa), Chlorophyta (25 taxa), Bacillariophyta (21 taxa), and Haptophyta (10 taxa) were much less frequently studied. The least numerous tests for allelopathic activity were conducted for organisms belonging to Ochrophyta (*Botrydium becherianum*, *Chattonella marina*, *Heterosigma akashiwo*, and *Olisthodiscus luteus*) and Charophyta (*Cosmarium vexatum*, *Spirogyra* sp.) phyla. Among Cyanobacteria, the most commonly studied organisms for their allelopathic activity were *Synechococcus* sp., *Microcystis aeruginosa*, and *Nodularia spumigena* (11, 8, and 8 articles, respectively). Among microalgae, the highest frequency of allelopathic research concerned *Karenia brevis* (Miozoa), *Alexandrium tamarense* (Miozoa), and *Skeletonema costatum* (Bacillariophyta), which were studied in 8, 6, and 5 scientific papers, respectively (Tables 1–2).

Cyanobacteria and microalgae, with estimated numbers of 30,000 to 1,000,000 species, constitute a large group of photoautotrophs widely studied for their ecological functions in all aquatic environments (Rumin et al., 2020). Several books and papers about the allelopathic effects of aquatic photoautotrophs were published regularly decades ago (e.g., Keating, 1977, 1978; Rice, 1979; Lewis Jr., 1986; Rizvi and Rizvi, 1992; Gopal and Goel, 1993; Inderjit and Dakshini, 1994; Gross, 2003; Legrand et al., 2003; Granéli and Turner, 2006), establishing allelopathy in phytoplankton as a well-researched topic in aquatic sciences. In recent years, the number of reports on allelopathy in aquatic ecosystems has increased, demonstrating allelopathic activity in new species, describing new experimental methods (Śliwińska-Wilczewska et al., 2018, 2019) and theoretical approaches to allelopathy (Barreiro Felpeto et al., 2018), showing new factors that can affect cyanobacteria and microalgae allelopathy (e.g., Brutemark et al., 2015; Śliwińska-Wilczewska et al., 2016), and exhibiting new allelopathic compounds and new modes of action (e.g., Gomes et al., 2017; Poulin et al., 2018a,b; Chen et al., 2020; Konarzewska et al., 2020). Furthermore, Gomes et al. (2017) described the phenomenon of allelopathy between macro- and microorganisms and its ecological role in terrestrial and aquatic environments. However, to the best of our knowledge, in recent years, there have been no comprehensive reviews on allelopathy phenomena between cyanobacteria and microalgae occurring in marine, brackish, and freshwater environments.

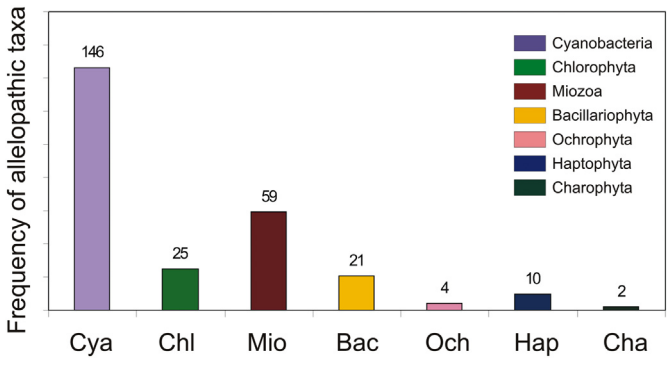

Fig. 2. The incidence of allelopathic cyanobacteria and microalgae based on the literature.

2. The role of allelopathic interactions in aquatic environments

Many studies indicate that allelopathy might be an essential factor in the species diversity, succession, and formation of cyanobacterial and microalgal blooms in freshwater, brackish and marine habitats (e.g., Figueredo et al., 2007; Poulson-Ellestad et al., 2014a,b; Barreiro Felpeto et al., 2017; Zhang et al., 2017; Poulin et al., 2018a,b; Zhu et al., 2020). The phenomenon of harmful cyanobacterial and algal blooms in recent decades has significantly increased worldwide, with the problems occurring in both freshwater and marine ecosystems (e.g., Huisman et al., 2018; Paerl, 2018). This massive proliferation of certain prokaryotic and eukaryotic phytoplankton species creates several ecological and economic problems. These problems are primarily related to the deterioration of water quality due to increases in turbidity, toxicity, and anoxia, which cause the increased mortality of many aquatic organisms. In the end, there are financial losses associated with aquaculture, fisheries, and tourism (Anderson et al., 2012; Paerl, 2018).

Keating (1977, 1978) noted for the first time that allelopathic effects could have contributed to cyanobacterial dominance in a freshwater lake. After her, several other researchers noted that the production and release of multifariously characterized metabolic substances can give a significant advantage to donors over target species and may help donor species build effective strategies in species competition and change community structure (Wolfe and Rice, 1979; Fistarol et al., 2004a; Granéli and Hansen, 2006). Many specific cases, such as those described below, could be examples.

Lafforgue et al. (1995) pointed out that the correlation between diatom and cyanobacterial abundances was usually negative. In that study, the low biomass of *Fragilaria crotonensis* in Aydat Lake in 1984 was the effect of its growth inhibition, probably caused by extracellular metabolites produced by *Anabaena* sp. In the eutrophic lake of Japan, it was found that *Phormidium tenue* inhibited diatom growth by the production of allelopathic compounds (Takamo et al., 2003).

The effect of metabolites produced by the freshwater cyanobacterium *Scytonema hofmanii* on the growth of other cyanobacteria and green algae was widely studied by Mason et al. (1982). The authors showed that the compound produced by this cyanobacterium is an algicide that affects other cyanobacteria and green algae. Smith and Doan (1999) suggested that the production of bioactive compounds by slow-growing species, such as *Scytonema* sp., is a defense strategy against the dominance of other organisms that are able to grow rapidly. Thus, the allelopathic effects of cyanobacteria may have a significant impact on phytoplankton succession, helping to explain their frequent dominance in many aquatic environments (Schagerl et al., 2002).

Prymnesium parvum and *Chrysochromulina polylepis* can produce allelochemicals that make these species responsible for massive blooms in many aquatic ecosystems around the world (Edvardsen and Paasche, 1998). *C. polylepis* is notorious for the production of various allelopathic compounds. It was noted that during the *C. polylepis* blooms in Scandinavian waters, small predator (heterotrophic flagellates, ciliates, and

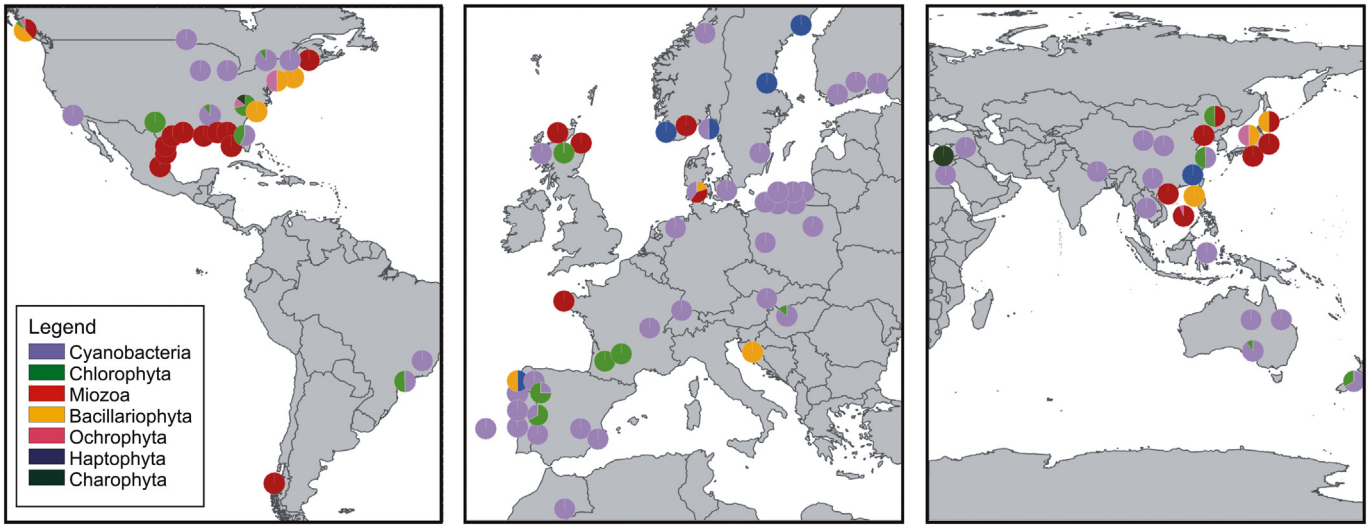

Fig. 3. Shares of allelopathic cyanobacteria and microalgae in the tested areas based on donor taxa found in the literature.

crustaceans) abundance in surface water was strongly inhibited, and the biomass of the heterotrophic bacteria was extremely low (Nielsen et al., 1990). According to Larsen and Bryant (1998), *P. parvum* dominance cannot be explained only by the high growth rates. The total absence of coexisting species during *P. parvum* blooms suggests that this species produces allelopathic compounds that negatively affect the growth of diatoms and cyanobacteria (Fistarol et al., 2003; Granéli et al., 2008a,b). These compounds eliminate potential competitors and predators (Tillmann, 2003).

The freshwater dinoflagellate *Peridinium aciculiferum* trades off its relatively large cell size and slow growth rate by the production of allelopathic compounds (Rengefors and Legrand, 2001). The lysis of the cell causes the release of nutrients that had been previously taken up by the target organism; these nutrients could then be used by the allelopathic organism (Leflaive and Ten-Hage, 2007).

Schagerl et al. (2002) showed that the extract from *Anabaena torulosa* inhibited the growth of only some species of microalgae and cyanobacteria.

The allelopathy phenomenon is also important in the context of the existence of coevolution. The existence of differences in resistance to allelopathy among coexisting target organisms suggests an adaptive coevolution process (Fistarol et al., 2003, 2004a; Suikkanen et al., 2004; Yamasaki et al., 2007). Fistarol et al. (2004b) showed that the allelopathic compounds produced by donor species (*Alexandrium tamarense*, *Karenia mikimotoi*, and *Chrysochromulina polylepis*) induced the formation of temporary cysts in target *Scrippsiella trochoidea*. Based on these results, the authors suggested that encystment may act as a defense mechanism for *S. trochoidea* to resist allelopathic compounds. There are examples of coevolution in similar systems, such as the resistance of zooplankton to phytoplankton toxins, as is the case for the freshwater crustacean *Daphnia* (Kurmayer and Jüttner, 1999; Hairston et al., 2001).

Allelopathy also costs producer species, and the trade-off between costs and benefits is not always clear (Legrand et al., 2003; Leflaive and Ten-Hage, 2007; Allen et al., 2017). Some authors, based on theoretical models of hydrodynamics, suggested that, considering the diffusion of allelopathic compounds and cell-to-cell distances in the real environment, allelopathy was far from being a successful adaptive strategy if it is not evident when blooms are already well developed (Jonsson et al., 2009). However, these models did not consider aspects such as the effectiveness of allelopathic substances at very low concentrations. This is relevant because many compounds could act as signaling molecules (Lewis Jr., 1986). For other sorts of phytoplankton toxins, theoretical models have already shown that, despite the costs of production, there are clear benefits of toxin production under certain scenarios (Chakraborty et al., 2019).

3. Abiotic and biotic factors affecting cyanobacterial and microalgal allelopathy

In the natural environment, there are many factors that can change both the production and secretion of allelochemicals (e.g., Gross, 2003; Granéli and Hansen, 2006; and Reigosa et al., 2006). Tang et al. (1995) and Reigosa et al. (1999) claim that the same factors may also affect the sensitivity of the target organism. However, only a few studies have documented the effects of biotic and/or abiotic factors on the allelopathic interaction between donor and target species. This situation could be explained by the fact that most allelopathic compounds have not yet been characterized.

3.1. Abiotic factors affecting allelopathy in aquatic ecosystems

3.1.1. Influence of light intensity

Cyanobacteria and microalgae have developed many adaptive mechanisms that allow them to expand under different light conditions (Whitton, 2008; Whitton and Potts, 2012). However, only a few studies have shown that light intensity can significantly affect the production of allelopathic compounds. Some authors reported that light intensity could influence the production of cylindrospermopsin and some other unknown allelopathic compounds in the cyanobacterium *Cylindrospermopsis raciborskii* (Dyble et al., 2006; Antunes et al., 2012). Antunes et al. (2012) showed that filtrates from *C. raciborskii* cultures display broad inhibitory activity on the green algae *Ankistrodesmus falcatus*, and increased light intensity enhanced this activity. The high light conditions coincided with the optimal growth of *C. raciborskii*. Dyble et al. (2006) showed the effect of light intensity specifically on the production of cylindrospermopsin. Maximum intracellular and extracellular cylindrospermopsin concentrations were measured in cultures grown under a light intensity of 140 μmol photons m^{-2} s^{-1}. Nakai et al. (2014) explained the variation in growth inhibition by cyanobacteria at different light intensities, claiming that it may be caused by differences in the degradation of allelochemicals. Additionally, Chetsumon et al. (1994) showed that under optimum light conditions of 200 μmol photons m^{-2} s^{-1}, the production of antibiotic compounds of cyanobacterium *Scytonema* sp. increased 2-fold. Śliwińska-Wilczewska et al. (2016) showed growth inhibition of the diatom *Navicula perminuta* after the addition of cell-free filtrate obtained from

Table 1
Study of allelopathic activity of cyanobacteria against other cyanobacteria and microalgae based on literature. Where: - means inhibiting effects, + means stimulating effect, 0 - means lack of effect.

Donor cyanobacteria	Target species	Effect	References
Anabaena cylindrica	*Anabaena cylindrica*, *Cosmarium* sp., *Fragilaria* sp., *Microcystis flos-aquae Pandorina morum*, *Pandorina* sp., *Scenedesmus acutus*, *Scenedesmus armatus* var. *maior*, *Staurastrum crenulatum*	−/0	Schagerl et al. (2002)
Anabena lemmermannii	*Amphidinium* sp., *Anabaena* sp., *Aphanizomenon* sp., *Chaetoceros* sp., *Dinophysis norvegica*, *Nodularia spumigena*, *Oocystis* sp., *Paulsenella* sp., *Planktonema lauterbornii*, *Prymnesium parvum*, *Pseudanabaena* sp., *Rhodomonas* sp., *Snowella* sp., *Thalassiosira weissflogii*	−/0/+	Suikkanen et al. (2004, 2005)
Anabaena oscillarioides	*Chlorella* sp., *Microcystis aeruginosa*	–	Lam and Silvester (1979)
Anabaena torulosa	*Anabaena cylindrica*, *Cosmarium* sp., *Fragilaria* sp., *Microcystis flos-aquae Pandorina morum*, *Pandorina* sp., *Scenedesmus acutus*, *Scenedesmus armatus* var. *maior*, *Staurastrum crenulatum*	–	Schagerl et al. (2002)
Anabaena variabilis	*Chlorella vulgaris*	–	Żak et al. (2012)
Anabaenopsis elenkinii	*Anabaena cylindrica*, *Cosmarium* sp., *Fragilaria* sp., *Microcystis flos-aquae Pandorina morum*, *Pandorina* sp., *Scenedesmus acutus*, *Scenedesmus armatus* var. *maior*, *Staurastrum crenulatum*	0	Schagerl et al. (2002)
Aphanizomenon flexuosum	*Anabaena cylindrica*, *Cosmarium* sp., *Fragilaria* sp., *Microcystis flos-aquae Pandorina morum*, *Pandorina* sp., *Scenedesmus acutus*, *Scenedesmus armatus* var. *maior*, *Staurastrum crenulatum*	−/0	Schagerl et al. (2002)
Aphanizomenon flos-aquae	*Amphidinium* sp., *Anabaena* sp., *Aphanizomenon* sp., *Chaetoceros* sp., *Chlorella vulgaris*, *Dinophysis norvegica*, *Nodularia spumigena*, *Oocystis* sp., *Paulsenella* sp., *Planktonema lauterbornii*, *Prymnesium parvum Pseudanabaena* sp., *Rhodomonas* sp., *Scenedesmus quadricauda*, *Snowella* sp., *Thalassiosira weissflogii*	−/0/+	Suikkanen et al. (2004, 2005, 2006), Żak and Kosakowska (2015), Kovács et al. (2018)
Aphanizomenon issatchenkoi	*Scenedesmus quadricauda*	–	Kovács et al. (2018)
Calothrix parietina	*Anabaena spiroides*, *Ankistrodesmus falcatus*, *Calothrix parietina*, *Chlorella fusca*, *Microcystis aeruginosa*, *Nostoc muscorum*, *Oscillatoria angustissima*, *Phormidium mölle*, *Scenedesmus obliquus*, *Scytonema hofmanii*, *Synechococcus* sp.	−/0	Issa (1999)
Calothrix sp.	*Anabaena circinalis*, *Coelastrum microporum*, *Microcytis aeruginosa*, *Monoraphidium convolutum*, *Nodularia spumigena*, *Scenedesmus acutus*	−/0	Schlegel et al. (1999)
Cyanobium gracile	*Scenedesmus quadricauda*	–	Kovács et al. (2018)
Cylindrospermopsis raciborskii	*Ankistrodesmus falcatus*, *Microcystis aeruginosa*, *Scenedesmus quadricauda*	–	Antunes et al. (2012), Rzymski et al. (2014), Kovács et al. (2018)
Cylindrospermum sp.	*Anabaena cylindrica*, *Cosmarium* sp., *Fragilaria* sp., *Microcystis flos-aquae*, *Pandorina morum*, *Pandorina* sp., *Scenedesmus acutus*, *Scenedesmus armatus* var. *maior*, *Staurastrum crenulatum*	−/0	Schagerl et al. (2002)
Dolichospermum sp.	*Rhodomonas nottbecki*	–	Brutemark et al. (2015)
Fischerella sp.	*Anabaena circinalis*, *Anabaena doliolum*, *Ankistrodesmus* sp., *Chlamydomonas* sp., *Chlorella* sp., *Coelastrum microporum*, *Excentrosphaera* sp., *Lyngbya* sp., *Microcytis aeruginosa*, *Nodularia spumigena*, *Nostoc* sp., *Pseudanabaena* sp., *Monoraphidium convolutum*, *Rhizoclonium* sp., *Scenedesmus acutus*, *Scytonema* sp., *Selenastrum* sp.	−/0	Schlegel et al. (1999), Gantar et al. (2008)
Geitlerinema splendidum	*Klebsormidium* sp., *Nostoc* sp., *Pseudocapsa* sp., *Scytonema* sp.	−/0	Valdor and Aboal (2007)
Lyngbya sp.	*Ankistrodesmus* sp., *Chlamydomonas* sp., *Chlorella* sp., *Excentrosphaera* sp., *Fischerella* sp., *Nostoc* sp., *Pseudanabaena* sp., *Rhizoclonium* sp., *Scytonema* sp., *Selenastrum* sp.	−/0	Gantar et al. (2008)
Microcystis aeruginosa	*Anabaena cylindrica*, *Anabaena oscillarioides*, *Chlorella vulgaris*, *Chlorella pyrenoidosa*, *Chlorella* sp., *Cosmarium* sp., *Cylindrospermopsis raciborski*, *Cyclotella meneghiniana*, *Fragilaria* sp., *Microcystis flos-aquae*, *Monoraphidium convolutum*, *Pandorina morum*, *Pandorina* sp., *Scenedesmus acuminatus*, *Scenedesmus acutus*, *Scenedesmus armatus* var. *maior*, *Scenedesmus quadricauda*, *Staurastrum crenulatum*	−/0/+	Lam and Silvester (1979), Schagerl et al. (2002), do Carmo Bittencourt-Oliveira et al., 2015, Rzymski et al. (2014), Ma et al. (2015), Song et al. (2017), Wang et al. (2017), Kovács et al. (2018)
Microcystis flos-aquae	*Anabaena cylindrica*, *Cosmarium* sp., *Fragilaria* sp., *Pandorina morum*, *Pandorina* sp., *Scenedesmus acutus*, *Scenedesmus armatus* var. *maior*, *Staurastrum crenulatum*	0	Schagerl et al. (2002)
Microcystis panniformis	*Monoraphidium convolutum*, *Scenedesmus acuminatus*	–	do Carmo Bittencourt-Oliveira et al. (2015)
Microcystis sp.	*Peridinium gatunense*	–	Sukenik et al. (2002)
Nodularia harveyana	*Arthrospira laxissima*, *Chroococcus minutus*, *Nostoc carneum*, *Nostoc insulare*, *Synechocystis aquatilis*	–	Volk and Furkert (2006)
Nodularia spumigena	*Amphidinium* sp., *Anabaena* sp., *Aphanizomenon* sp., *Bacillaria paxillifer*, *Chaetoceros* sp., *Chlorella vulgaris*, *Dinophysis norvegica*, *Fragilaria* sp., *Nodularia spumigena*, *Oocystis submarina*, *Oocystis* sp., *Paulsenella* sp., *Prymnesium parvum*, *Pseudanabaena* sp., *Planktonema lauterbornii*, *Rhodomonas* sp., *Scenedesmus acutus*, *Scenedesmus armatus* var. *maior*, *Skeletonema marinoi*, *Snowella* sp., *Synechococcus* sp., *Thalassiosira weissflogii*	−/0/+	Schagerl et al. (2002), Suikkanen et al. (2004, 2005, 2006), Żak et al. (2012), Śliwińska-Wilczewska et al. (2016, 2019), Barreiro Felpeto et al. (2018)

(continued on next page)

Table 1 (*continued*)

Donor cyanobacteria	Target species	Effect	References
Nostoc insulare	*Arthrospira laxissima*, *Chroococcus minutus*, *Nostoc carneum*, *Nostoc insulare*, *Synechocystis aquatilis*	–	Volk and Furkert (2006)
Nostoc muscorum	*Anabaena cylindrica*, *Cosmarium* sp., *Fragilaria* sp., *Microcystis flos-aquae*, *Pandorina morum*, *Pandorina* sp., *Scenedesmus acutus*, *Scenedesmus armatus* var. *maior Staurastrum crenulatum*	−/0	Schagerl et al. (2002)
Nostoc sp.	*Anabaena circinalis*, *Anabaena cylindrica*, *Anabaena doliolum*, *Ankistrodesmus* sp., *Chlamydomonas* sp., *Chlorella* sp., *Coelastrum microporum*, *Cosmarium* sp., *Excentrosphaera* sp., *Fischerella* sp., *Fragilaria* sp., *Lyngbya* sp., *Microcytis aeruginosa*, *Microcystis flos-aquae*, *Monoraphidium convolutum*, *Nodularia spumigena*, *Nostoc* sp., *Pseudanabaena* sp., *Pandorina morum*, *Pandorina* sp., *Rhizoclonium* sp., *Scenedesmus acutus*, *Scenedesmus armatus* var. *maior*, *Scytonema* sp., *Selenastrum* sp. *Staurastrum crenulatum*	−/0/+	Schlegel et al. (1999), Schagerl et al. (2002), Gantar et al. (2008)
Oscillatoria angustissima	*Anabaena spiroides*, *Ankistrodesmus falcatus*, *Calothrix parietina*, *Chlorella fusca*, *Microcystis aeruginosa*, *Nostoc muscorum*, *Oscillatoria angustissima*, *Phormidium mölle*, *Scytonema hofmanii*, *Scenedesmus obliquus*, *Synechococcus* sp.	−/0	Issa (1999)
Oscillatoria sp.	*Anacystis nidulans*, *Ankistrodesmus falcatus*, *Chlamydomonas reinhardtii*, *Chlorella vulgaris*, *Chlorella pyrenoidosa*, *Klebsormidium* sp., *Microsytsis* sp., *Nostoc muscorum*, *Nostoc* sp., *Oscillatoria* sp., *Phormidium uncinatum*, *Phormidium* sp., *Plectonema boryanum*, *Pseudocapsa* sp., *Scytonema* sp., *Scenedesmus quadricauda*, *Selenastrum capricornutum*, *Synechococcus* sp.	−/0/+	Bagchi et al. (1993), Valdor and Aboal (2007), Leão et al. (2010), Barreiro Felpeto and Vasconcelos (2014), Barreiro Felpeto et al. (2017), Kovács et al. (2018)
Phormidium sp.	*Klebsormidium* sp., *Microcystis* sp., *Nostoc* sp., *Pseudocapsa* sp., *Scytonema* sp., *Synechococcus* sp.	−/0/+	Valdor and Aboal (2007), Dias et al. (2017)
Planktothrix agardhii	*Chlorella vulgaris*	−/0/+	Żak and Kosakowska (2015)
Planktothrix rubescens	*Anabaena cylindrica*, *Cosmarium* sp., *Fragilaria* sp., *Microcystis flos-aquae*, *Mougeotia gracillima*, *Planktothrix agardhii Pandorina morum*, *Pandorina* sp., *Scenedesmus acutus*, *Scenedesmus armatus* var. *maior Staurastrum crenulatum*	−/0	Schagerl et al. (2002), Oberhaus et al. (2008)
Pseudanabaena sp.	*Ankistrodesmus* sp., *Chlamydomonas* sp., *Chlorella* sp., *Excentrosphaera* sp., *Fischerella* sp., *Lyngbya* sp., *Nostoc* sp., *Rhizoclonium* sp., *Scytonema* sp., *Selenastrum* sp.	0	Gantar et al. (2008)
Rivularia biasolettiana	*Klebsormidium* sp., *Nostoc* sp., *Pseudocapsa* sp., *Scytonema* sp.	0	Valdor and Aboal (2007)
Rivularia haematites	*Klebsormidium* sp., *Nostoc* sp., *Pseudocapsa* sp., *Scytonema* sp.	−/0	Valdor and Aboal (2007)
Scytonema myochrous	*Klebsormidium* sp., *Nostoc* sp., *Pseudocapsa* sp., *Scytonema* sp.	−/0	Valdor and Aboal (2007)
Scytonema sp.	*Ankistrodesmus* sp., *Chlamydomonas* sp., *Chlorella* sp., *Excentrosphaera* sp., *Fischerella* sp., *Lyngbya* sp., *Nostoc* sp., *Pseudanabaena* sp., *Rhizoclonium* sp., *Selenastrum* sp.	−/0	Gantar et al. (2008)
Synechococcus sp.	*Achnanthes* sp., *Amphora coffeaeformis*, *Amphora* sp., *Anabaena* sp., *Aphanizomenon* sp., *Aphanocapsa* sp., *Aphanothece* sp., *Ankistrodesmus* sp., *Aulacoseira* sp., *Bacillaria paxillifer*, *Bacillaria* sp., *Chaetoceros* sp., *Chlorella fusca*, *Chlorella vulgaris*, *Chlorella* sp., *Chroococcus* sp., *Coelastrum* sp., *Coenocystis* sp., *Coscinodiscus* sp., *Cosmarium* sp., *Crucigenia* sp., *Cyanodictyon* sp., *Cyclotella meneghiniana*, *Cyclotella* sp., *Cylindrocystis* sp., *Desmodesmus* sp., *Dictyosphaerium* sp., *Diploneis* sp., *Fistulifera saprophila*, *Fragillaria* sp., *Gloeocapsa* sp., *Gomphonema* sp., *Grammatophora* sp., *Gymnodinium* sp., *Kirchneriella obesa*, *Koliella* sp., *Lemmermaniella* sp., *Limnothrix* sp., *Microcystis* sp., *Monoraphidium* sp., *Navicula perminuta*, *Navicula* sp., *Nitzschia dissipata*, *Nitzschia fonticola*, *Nitzschia* sp., *Nodularia spumigena*, *Nostoc* sp., *Odontella* sp., *Oocystis submarina*, *Pediastrum* sp., *Peridinium* sp., *Phacotus* sp., *Phormidium* sp., *Pinnularia* sp., *Planktonema* sp., *Planktolyngbya* sp., *Porphyridium purpureum*, *Prymnesium parvum*, *Pseudanabaena* sp., *Rivularia* sp., *Rhoicosphenia* sp., *Scenedesmus* sp., *Sphaerocystis* sp., *Snowella* sp., *Skeletonema marinoi*, *Stauroneis* sp., *Stephanodiscus* sp., *Stichococcus bacillaris*, *Stichococcus* sp., *Synechocystis* sp., *Synechococcus* sp., *Tetraedron* sp., *Tetrastrum* sp., *Ulnaria* sp., *Woronichinia* sp.	−/0/+	Paz-Yepes et al. (2013), Śliwińska-Wilczewska et al. (2016, 2017a,b, 2018, 2019), Śliwińska-Wilczewska and Latała (2018), Barreiro Felpeto et al. (2018), Bubak et al. (2020); Konarzewska et al. (2020)
Synechocystis sp.	*Chlorella vulgaris*, *Fistulifera* sp., *Porphyridium purpureum*	–	Barreiro Felpeto et al. (2019)
Tolypothrix distorta	*Klebsormidium* sp., *Nostoc* sp., *Pseudocapsa* sp., *Scytonema* sp.	−/0	Valdor and Aboal (2007)
Trichormus doliolum	*Anabaena variabilis*, *Anabaena* sp., *Microcystis* sp.	–	Von Elert and Jüttner (1997)

picocyanobacterium *Synechococcus* sp. grown only at the highest light intensity (190 μmol photons m^{-2} s^{-1}). Additionally, Barreiro Felpeto et al. (2018) demonstrated light-dependent cytolysis in the allelopathic interaction between two co-occurring bloom-forming species of cyanobacteria: the picocyanobacterium *Synechococcus* sp. and the filamentous *N. spumigena*.

Moreover, light was also shown to be important in microalgae allelopathy. Both intra- and extracellular concentrations of allelopathic compounds decreased when *P. parvum* was kept in the dark, even when the growth medium allowed the rapid growth of this species (Shilo, 1967). Barreiro Felpeto and Hairston Jr. (2013) performed experiments on *Chlamydomonas* sp. under light, nitrogen and phosphorus

Table 2
Study of allelopathic activity of microalgae against other cyanobacteria and microalgae based on literature. Where: - means inhibiting effects, + means stimulating effect, 0 - means lack of effect.

	Target species	Effect	References
Donor Miozoa			
Alexandrium catenella	*Chaetoceros gracile*, *Gymnodinium mikimotoi*, *Scrippsiella trochoidea*	−/0	Arzul et al. (1999)
Alexandrium fundyense	*Thalassiosira* cf. *gravida*	−	Lyczkowski and Karp-Boss (2014)
Alexandrium minutum	*Chaetoceros gracile*, *Gymnodinium mikimotoi*, *Rhodomonas* sp., *Scrippsiella trochoidea*, *Thalassiosira weissflogii*	−/0	Arzul et al. (1999), Fistarol et al. (2004a)
Alexandrium ostenfeldii	*Chlorella vulgaris*	−/0	Żak and Kosakowska (2015)
Alexandrium tamarense	*Ceratium lineatum*, *Ceratium* sp., *Chaetoceros gracile*, *Chaetoceros* sp., *Chattonella marina*, *Chrysochromulina ericina*, *Ditylum brightwellii*, *Dunaliella salina*, *Gymnodinium mikimotoi*, *Heterosigma akashiwo*, *Heterocapsa triquetra*, *Leptocylindrus* sp., *Phaeocystis globosa*, *Prorocentrum minimum*, *Rhodomonas salina*, *Rhodomonas* sp., *Scrippsiella trochoidea*, *Skeletonema costatum*, *Thalassiosira weissflogii*	−/0/+	Arzul et al. (1999), Fistarol et al. (2004a,b), Tillmann and Hansen (2009), Weissbach et al. (2010), Chen et al. (2015)
Amphidinium carterae	*Cylindrotheca fusiformis*	−	Chan et al. (1980)
Gonyaulax spinifera	*Cylindrotheca fusiformis*	−	Chan et al. (1980)
Heterocapsa triquetra	*Cylindrotheca fusiformis*	−	Chan et al. (1980)
Karenia brevis	*Akashiwo sanquinea*, *Amphora* sp., *Asterionellopis glacialis*, *Chaetoceros affinis*, *Chlorella capsulata*, *Leptocylindrus danicus*, *Odontella aurita*, *Peridinium* sp., *Prorocentrum mexicanum*, *Prorocentrum minimum*, *Rhizosolenia* cf. *setigera*, *Rhodomona lens*, *Skeletonema costatum*, *Skeletonema grethae*, *Stephanopyxis turris*, *Thalassiosira pseudonana*, *Thalassiosira* sp.	−/0/+	Kubanek et al. (2005), Prince et al. (2008a,b), Prince et al. (2010), Poulson-Ellestad et al. (2014a,b), Poulin et al. (2018a,b)
Karenia mikimotoi	*Prorocentrum micans*, *Scrippsiella trochoidea*	−/0	Fistarol et al. (2004b), Ji et al. (2011)
Karlodinium veneficum	*Akashiwo sanguinea*	−/0/+	Yang et al. (2019)
Prorocentrum micans	*Cylindrotheca fusiformis*, *Karenia mikimotoi*, *Skeletonema costatum*	−/0/+	Chan et al. (1980), Tameishi et al. (2009), Ji et al. (2011)
Prorocentrum minimum	*Chlorella vulgaris*	0	Żak and Kosakowska (2015)
Scrippsiella sweeneyae	*Cylindrotheca fusiformis*	−/0	Chan et al. (1980)
Donor Bacillariophyta			
Chaetoceros wighamii	*Chlorella vulgaris*	−/0	Żak and Kosakowska (2015)
Cylindrotheca closterium	*Prorocentrum donghaiense*, *Prorocentrum cordatum*, *Isochrysis galbana*, *Chaetoceros curvisetus*	−	Xu et al. (2019)
Navicula sp.	*Ostreopsis* cf. *ovata*	−	Pichierri et al. (2017)
Nitzschia longissirna	*Cylindrotheca fusiformis*	−/0	Chan et al. (1980)
Phaeodactylum tricornutum	*Cylindrotheca fusiformis*, *Phaeodactylum tricornutum*, Thalassiosira *pseudonana*	−/0/+	Sharp et al. (1979), Chan et al. (1980), Vasconcelos and Leal (2008)
Proschkinia complanatoides	*Ostreopsis* cf. *ovata*	−	Pichierri et al. (2017)
Pseudo-nitzschia sp.	*Chaetoceros* sp., *Cylindrotheca* sp., *Rhizosolenia* sp., *Skeletonema* sp.	−	Van Meerssche and Pinckney (2017)
Skeletonema costatum	*Chaetoceros muelleri*, *Cylindrotheca fusiformis*, *Heterosigma akashiwo*, *Prorocentrum micans*, *Prorocentrum minimum*, *Olisthodiscus luteus*	−/0	Pratt (1966), Chan et al. (1980), Yamasaki et al. (2007), Tameishi et al. (2009), Ji et al. (2011)
Skeletonema marinoi	*Ostreopsis* cf. *ovata*	−	Pichierri et al. (2017)
Tabularia affinis	*Ostreopsis* cf. *ovata*	−	Pichierri et al. (2017)
Thalassiosira pseudonana	*Chlorella vulgaris*, *Phaeodactylum tricornutum*	−/0	Sharp et al. (1979), Żak and Kosakowska (2015)
Thalassiosira sp.	*Ostreopsis* cf. *ovata*	−	Pichierri et al. (2017)
Donor Ochrophyta			
Botrydium becherianum	*Botrydium becherianum*, *Chlorella ellipsoidea*, *Cosmarium vexatum*, *Pediastrum boryanum*, *Pandorina morum*, *Scenedesmus incrassatulus* var. *mononae*	−	Wolfe and Rice (1979)
Chattonella marina	*Alexandrium tamarense*	−/0	Chen et al. (2015)
Heterosigma akashiwo	*Chaetoceros muelleri*, *Prorocentrum minimum*, *Skeletonema costatum*	−/0	Yamasaki et al. (2007)
Olisthodiscus luteus	*Skeletonema* sp.	−/+	Pratt (1966)
Donor Chlorophyta			
Ankistrodesmus falcatus	*Chlamydomonas reinhardtii*, *Phormidium* sp., *Selenastrum capricornutum*	−/0/+	Barreiro Felpeto and Vasconcelos (2014), Barreiro Felpeto et al. (2017)
Ankistrodesmus sp.	*Chlamydomonas* sp., *Chlorella* sp., *Excentrosphaera* sp., *Fischerella* sp., *Lyngbya* sp., *Nostoc* sp., *Pseudanabaena* sp., *Rhizoclonium* sp., *Scytonema* sp., *Selenastrum* sp.	0	Gantar et al. (2008)
Chlamydomonas reinhardtii	*Ankistrodesmus falcatus*, *Cryptomonas ozolinii*, *Microcystis aeruginosa*, *Ochromonas danica*, *Phormidium* sp., *Selenastrum capricornutum*	−/0	Barreiro Felpeto and Hairston Jr. (2013), Barreiro Felpeto and Vasconcelos (2014), Barreiro Felpeto et al. (2017)
Chlamydomonas sp.	*Ankistrodesmus* sp., *Chlorella* sp., *Excentrosphaera* sp., *Fischerella* sp., *Lyngbya* sp., *Nostoc* sp. *Pseudanabaena* sp., *Rhizoclonium* sp., *Scytonema* sp., *Selenastrum* sp.	0/+	Gantar et al. (2008)
Chlorella ellipsoidea	*Botrydium becherianum*, *Chlorella ellipsoidea*, *Cosmarium vexatum*, *Pandorina morum*, *Pediastrum boryanum*, *Scenedesmus incrassatulus* var. *mononae*	−/0/+	Wolfe and Rice (1979)
Chlorella sorokiniana	*Chlorella sorokiniana*, *Coelastrella* sp.	−	Corcoran et al. (2019)
Chlorella vulgaris	*Microcystis aeruginosa*	0	Song et al. (2017)
Chlorella sp.	*Anabaena oscillarioides*, *Ankistrodesmus* sp., *Chlamydomonas* sp., *Excentrosphaera* sp., *Fischerella* sp., *Lyngbya* sp., *Microcystis aeruginosa*, Nostoc sp., *Pseudanabaena* sp., *Rhizoclonium* sp., *Scytonema* sp., *Selenastrum* sp.	−/0	Lam and Silvester (1979), Gantar et al. (2008)
Coelastrella sp.	*Chlorella sorokiniana*, *Coelastrella* sp.	−/0	Corcoran et al. (2019)
Excentrosphaera sp.	*Ankistrodesmus* sp., *Chlamydomonas* sp., *Chlorella* sp., *Fischerella* sp., *Lyngbya* sp., *Nostoc* sp., *Pseudanabaena* sp., *Rhizoclonium* sp., *Scytonema* sp., *Selenastrum* sp.	−/0	Gantar et al. (2008)
Monoraphidium convolutum	*Microcystis aeruginosa*, *Microcystis panniformis*	−/0	do Carmo Bittencourt-Oliveira et al. (2015)

(continued on next page)

Table 2 (*continued*)

	Target species	Effect	References
Pandorina morum	*Botrydium becherianum*, *Chlorella ellipsoidea*, *Cosmarium vexatum*, *Pandorina morum*, *Pediastrum boryanum*, *Scenedesmus incrassatulus* var. *mononae*	−/0/+	Wolfe and Rice (1979)
Pediastrum boryanum	*Botrydium becherianum*, *Chlorella ellipsoidea*, *Cosmarium vexatum*, *Pandorina morum*, *Pediastrum boryanum*, *Scenedesmus incrassatulus* var. *mononae*	−/0/+	Wolfe and Rice (1979)
Platymonas sp.	*Cylindrotheca fusiformis*	0	Chan et al. (1980)
Rhizoclonium sp.	*Ankistrodesmus* sp., *Chlamydomonas* sp., *Chlorella* sp., *Excentrosphaera* sp., *Fischerella* sp., *Lyngbya* sp., *Nostoc* sp., *Pseudanabaena* sp., *Scytonema* sp., *Selenastrum* sp.	−/0	Gantar et al. (2008)
Scenedesmus acuminatus	*Microcystis aeruginosa*, *Microcystis panniformis*	−	do Carmo Bittencourt-Oliveira et al. (2015)
Scenedesmus incrassatulus var. mononae	*Botrydium becherianum*, *Chlorella ellipsoidea*, *Cosmarium vexatum*, *Pandorina morum*, *Pediastrum boryanum*, *Scenedesmus incrassatulus* var. *mononae*	−/0/+	Wolfe and Rice (1979)
Scenedesmus quadricauda	*Scenedesmus quadricauda*	0	Kovács et al. (2018)
Selenastrum capricornutum	*Ankistrodesmus falcatus*, *Chlamydomonas reinhardtii*, *Oscillatoria* sp.	0/+	Barreiro Felpeto and Vasconcelos (2014)
Selenastrum sp.	*Ankistrodesmus* sp., *Chlamydomonas* sp., *Chlorella* sp., *Excentrosphaera* sp., *Fischerella* sp., *Lyngbya* sp., *Nostoc* sp., *Pseudanabaena* sp., *Rhizoclonium* sp., *Scytonema* sp.	−/0	Gantar et al. (2008)
Uronema confervicolum	*Fistulifera saprophila*, *Gomphonema parvulum*	−/0	Allen et al. (2015), Allen et al. (2017)
Donor Charophyta			
Cosmarium vexatum	*Botrydium becherianum*, *Chlorella ellipsoidea*, *Cosmarium vexatum*, *Pandorina morum*, *Pediastrum boryanum*, *Scenedesmus incrassatulus* var. *mononae*	0/+	Wolfe and Rice (1979)
Spirogyra sp.	*Oscillatoria agardhii*	+	Mohamed (2002)
Donor Haptophyta			
Chrysochromulina polylepis	*Alexandrium ostenfeldii*, *Alexandrium tamarense*, *Ceratium furca*, *Ceratium lineatum*, *Ceratium tripos*, *Chrysochromulina simplex*, *Dictyocha speculum*, *Eutreptiella gymnastica*, *Gymnodinium mikimotoi*, *Heterocapsa triquetra*, *Heterosigma akashiwo*, *Prorocentrum micans*, *Prorocentrum minimum*, *Pyramimonas propulsa*, *Rhodomonas marina*, *Scrippsiella trochoidea*, *Skeletonema costatum*	−/0	Schmidt and Hansen (2001), Fistarol et al. (2004b)
Emiliania huxleyi	*Phaeodactylum tricornutum*	0/+	Vasconcelos and Leal (2008)
Phaeocystis globosa	*Chattonella marina*, *Chattonella ovata*, *Prorocentrum donghaiense*	−	Liu et al. (2010)
Prymnesium parvum	*Cylindrotheca fusiformis*, *Prorocentrum minimum*, *Rhodomonas* cf. *baltica*, *Rhodomonas salina*, *Thalassiosira weissflogii*	−/0	Chan et al. (1980), Granéli and Johansson (2003b), Fistarol et al. (2005), Uronen et al. (2007)
Prymnesium patelliferum	*Prorocentrum minimum*, *Rhodomonas* cf. *baltica*, *Thalassiosira weissflogii*	0	Granéli and Johansson (2003b)

limitations to test its allelopathic effect on selected cyanobacteria and microalgae (*Microcystis aeruginosa*, *Cryptomonas ozolinii*, and *Ochromonas danica*). Among those resource-limiting regimes, light limitation had the greatest allelopathic effect on target species.

3.1.2. Influence of temperature

Relatively little is known about how temperature affects the allelopathic activity of cyanobacteria and microalgae. An increase in the allelopathic activity of the cyanobacterium *C. raciborskii* under high temperature was reported by Antunes et al. (2012), who showed that filtrate obtained from *C. raciborskii* growing at 30 °C exhibited the strongest allelopathic effect. Van Rijssel et al. (2007) also reported an increase in the hemolytic activity of *Phaeocystis pouchetii* caused by an increase in temperature from 4 °C to 15 °C. Ma et al. (2015) showed that the growth of *C. vulgaris* cocultured with *M. aeruginosa* was promoted at 20 °C but was inhibited at higher temperatures, i.e., 25 °C. Additionally, Śliwińska-Wilczewska et al. (2016) and Barreiro Felpeto et al. (2019) indicated that the production of allelopathic substances by picocyanobacteria *Synechococcus* sp. and *Synechocystis* sp. is regulated by temperature. The addition of cell-free filtrate from *Synechococcus* sp. cultures grown at higher temperatures showed stronger inhibition of growth in the diatom *N. perminuta* (Śliwińska-Wilczewska et al., 2016). Similarly, Barreiro Felpeto et al. (2019) demonstrated that filtrate from *Synechocystis* sp. inhibited the growth of selected microalgae species (*Porphyridium purpureum*, *Fistulifera* sp., and *Chlorella vulgaris*), and the negative effect of the cyanobacterium was stronger at the highest temperatures (20 °C) at which *Synechocystis* sp. was grown. Noaman et al. (2004) observed that *Synechococcus leopoliensis* exhibited different antimicrobial activities against the gram-positive bacterium *Staphylococcus aureus* depending on the temperature, which was optimal at 35 °C. This work showed that the temperature range for growth was 15–45 °C, whereas the temperature range for antimicrobial agent production was 20–40 °C. The difference between the optimal temperatures for growth and allelopathic compound production was also studied by Issa (1999). This author determined the biomass, chlorophyll *a* content, protein content, and secondary metabolite concentration of the cyanobacteria *Oscillatoria angustissima* and *Calothrix parietina* that were grown at high temperatures. The highest rate of allelopathic compound production was recorded at 25 °C, whereas biomass, chlorophyll *a* content, and protein content reached the optimum at 30 °C. Ame et al. (2003) described that the production of microcystin was favored at temperatures higher than 23 °C. Conversely, maximum cylindrospermopsin production by the cyanobacterium *C. raciborskii* was reported at 20 °C (Griffiths and Saker, 2003). The production of cyanobacterin Lu-1 by *Nostoc linckia* is also temperature-dependent (Gromov et al., 1991). Additionally, Lehtimaki et al. (1997) found that low temperatures (7, 10, 16 °C) resulted in lower rates of nodularin production by the cyanobacterium *N. spumigena*; the highest production rates for this toxin were observed at higher temperatures. Therefore, it is believed that the predicted increase in temperature caused by global climate change may favor the formation of massive cyanobacterial and algal blooms by increasing the production of harmful secondary metabolites (O'Neil et al., 2012; Ma et al., 2015).

3.1.3. Influence of availability of nutrients

Some studies have addressed the relationship between nutrient limitation and allelopathic activity of different phytoplankton species (Granéli and Johansson, 2003a,b; Fistarol et al., 2005; Allen et al., 2017; Śliwińska-Wilczewska and Latała, 2018). Śliwińska-Wilczewska and Latała (2018) showed that nutrient-enriched conditions enhanced allelochemical production in *Synechococcus* sp. The toxicity of the dinoflagellate *Protogonyaulax tamarensis* was also enhanced by an excess of nutrients (Boyer et al., 1987). The cyanobacterium *C. raciborskii* exhibits the greatest allelopathic activity under phosphorus deficiency (Antunes

et al., 2012). It was also reported that *T. doliolum* cultured under phosphorus deficiency produced and released approximately 200 times more allelopathic compounds per biomass unit than *T. doliolum* cultured under excess phosphorus (Von Elert and Jüttner, 1997). Nutrient deficiency also stimulated the production of toxins by *Nostoc* sp. (Kurmayer, 2011) and *Microcystis aeruginosa* (Krüger et al., 2012). Bloor and England (1991) observed a similar trend in the cyanobacterium *Nostoc muscorum*, wherein the highest allelopathic activity was recorded under the influence of phosphorus limitation. DellaGreca et al. (2010) noted that the production of allelopathic fatty acids by the green alga *Chlorella vulgaris* increased under phosphate limitation. Myklestad et al. (1995) found that the growth of the diatom *Skeletonema costatum* was strongly inhibited after filtrate addition obtained from *P. parvum* culture grown in phosphate deficiency. Granéli and Johansson (2003b) showed that both N and P deficiencies increased *P. parvum* toxicity.

A more developed framework to study the relationships between nutrients and secondary metabolites, such as toxins and allelochemicals, consists of the C:N:P stoichiometry (Barreiro Felpeto and Hairston Jr., 2013; Van de Waal et al., 2014, Brandenburg et al., 2020). Many of the allelochemicals from secondary metabolism are rich in nitrogen. Therefore, high N:P ratios tend to induce an increase in their rates of production. At the same time, phosphorus limitation, by reducing cell division rates, enhances the accumulation of toxins inside the cells (Brandenburg et al., 2020).

All aspects related to nutrients are important, especially in the current context of anthropogenic-induced eutrophication occurring in many freshwater and coastal marine ecosystems in the world (Thornton et al., 2013).

3.1.4. Influence of pH

Several studies have recorded an effect of pH on allelopathic activity. Ulitzur and Shilo (1964) already reported an effect of pH on the production of toxins by *Prymnesium parvum*. These authors observed that an increase in pH from 8 to 9 resulted in an increase in *P. parvum* cytotoxic activity. Schmidt and Hansen (2001) also found that the production and excretion of harmful secondary metabolites by cyanobacteria and microalgae are pH-dependent. Furthermore, Ray and Bagchi (2001) reported that the allelopathic effect of the cyanobacterium *Oscillatoria laetevirens* increases with increasing pH. Noaman et al. (2004) also noted that the pH of the medium strongly influenced the growth of picocyanobacterium *S. leopoliensis* and its production of secondary metabolites. Yamasaki et al. (2007) also suggested the influence of pH on allelopathic activity. However, it is not yet clear to what extent the correlation between allelopathic effects and an increase in pH is spurious and if the true relationship is with increased growth and biomass levels (which will increase the pH if there is no strong buffering system or the addition of extra CO_2).

3.1.5. Influence of salinity

Salinity is an important factor that influences the distribution of phytoplankton species in some coastal areas and shallow reservoirs. Brutemark et al. (2015) noted that the allelopathic potential of the bloom-forming cyanobacterium *Dolichospermum* sp. was higher in the medium with a salinity of 3‰ and lower in the freshwater medium. However, the intracellular toxin concentration was the highest at a salinity of 6. The authors concluded, based on their experimental findings, that salinity played significant roles in *Dolichospermum* sp. growth, allelopathic properties, and toxicity. Śliwińska-Wilczewska et al. (2016) also indicated that the production of allelochemicals is dependent on salinity to a significant degree. The authors investigated the influence of the picocyanobacterium *Synechococcus* sp. allelopathic activity on the diatom *Navicula perminuta* by adding the cell-free filtrate obtained from *Synechococcus* sp. cultures that were grown under different salinity conditions (8, 16 and 32‰). The largest decline in diatom growth was observed after the addition of the filtrate obtained from *Synechococcus* sp. grown at a salinity of 8‰, the lowest salinity out of all tested plants. Van Meerssche and Pinckney (2017) demonstrated that cryptophyte and diatom abundances in the natural phytoplankton community were negatively correlated with the abundance of *Pseudonitzschia* sp. and with the concentration of domoic acid. Furthermore, the growth inhibition effect was noticeably dependent on salinity.

3.2. Biotic factors affecting allelopathy in aquatic ecosystems

3.2.1. Taxonomic identities of the donor and target organisms

Granéli et al. (2008a) recorded approximately 40 phytoplankton species with known allelopathic properties. Here, we present literature reports confirming allelopathic properties in 61 different genera of cyanobacteria and microalgae (24 genera of Cyanobacteria, 8 of Miozoa, 10 of Bacillariophyta, 4 of Ochrophyta, 13 of Chlorophyta, 2 of Charophyta, and 4 of Haptophyta). It should also be noted that among these genera, different species and even strains belonging to the same species might show differences in their allelopathic activity (Tables 1–2). Examples of cyanobacteria and microalgae in which allelopathic activity was confirmed are shown in Fig. 4.

The production of allelopathic compounds by phytoplankton was found in several phyla, such as Cyanobacteria, Miozoa, Bacillariophyta, Ochrophyta, Chlorophyta, Charophyta, and Haptophyta. Typically, donor organisms can affect several, but not all, target organisms. Similarly, target organisms are susceptible to several but not all allelopathic compounds released by donor species. In many studies, it was noted that the intensity of the allelopathic effect varies depending on the taxonomic identity (including differences between strains) of the donor and target organism (Schagerl et al., 2002; Volk and Furkert, 2006; Gantar et al., 2008; Barreiro Felpeto and Vasconcelos, 2014; Poulson-Ellestad et al., 2014b; Konarzewska et al., 2020).

Fistarol et al. (2004b) showed that two different strains of *C. polylepis* (CCMP 289 and K-0259) demonstrated different allelopathic effects on *Scrippsiella trochoidea*. The filtrate obtained from CCMP strain 289 caused significantly higher mortality of *S. trochoidea* than the filtrate obtained from strain K-0259. The allelopathic effects on different strains were also demonstrated for *Cylindrospermopsis raciborskii*. The *C. raciborskii* LS118 and LS124 strains strongly inhibited the activity of PSII in the green algae *Coelastrum sphaericum*, while strain LS117 did not show any allelopathic effects (Figueredo et al., 2007). Konarzewska et al. (2020) showed that three different *Synechococcus* sp. phenotypes (CCBA124 – the green strain, CCBA120 – the red strain, and CCBA132 – the brown strain) had significant allelopathic effects on 18 target cyanobacteria and microalgae species. It was also noted that *Synechococcus* sp. CCBA132 had the strongest effects on the tested cyanobacteria, green algae, and diatoms. Moreover, Paz-Yepes et al. (2013) examined the allelopathic interaction between marine unicellular cyanobacteria of the genus *Synechococcus*. The authors demonstrated the growth impairment of *Synechococcus* sp. CC9311 and *Synechococcus* sp. WH8102 when they were cultured in the presence of *Synechococcus* sp. CC9605 and the McC-like gene cluster were involved in these interactions.

3.2.2. Cell size

The surface-volume relationship in phytoplankton is a very important variable in phytoplankton physiology. Schmidt and Hansen (2001) found a negative correlation between the effect and the cell size of the target species and their sensitivity to *C. polylepis* metabolites. Lyczkowski and Karp-Boss (2014) also showed that the filtrate obtained from *Alexandrium fundyense* cultures negatively affected the diatom *Thalassiosira* cf. *gravida*, and the effect was dependent on the cell size of the target species. Generally, it is assumed that the growth rate is inversely proportional to the cell size; therefore, larger cells are characterized by slower metabolism (Amato et al., 2005). Conversely, the high metabolism rate of small cells may lead allelopathic compounds to enter a target cell faster than they would a larger target cell. Lyczkowski and

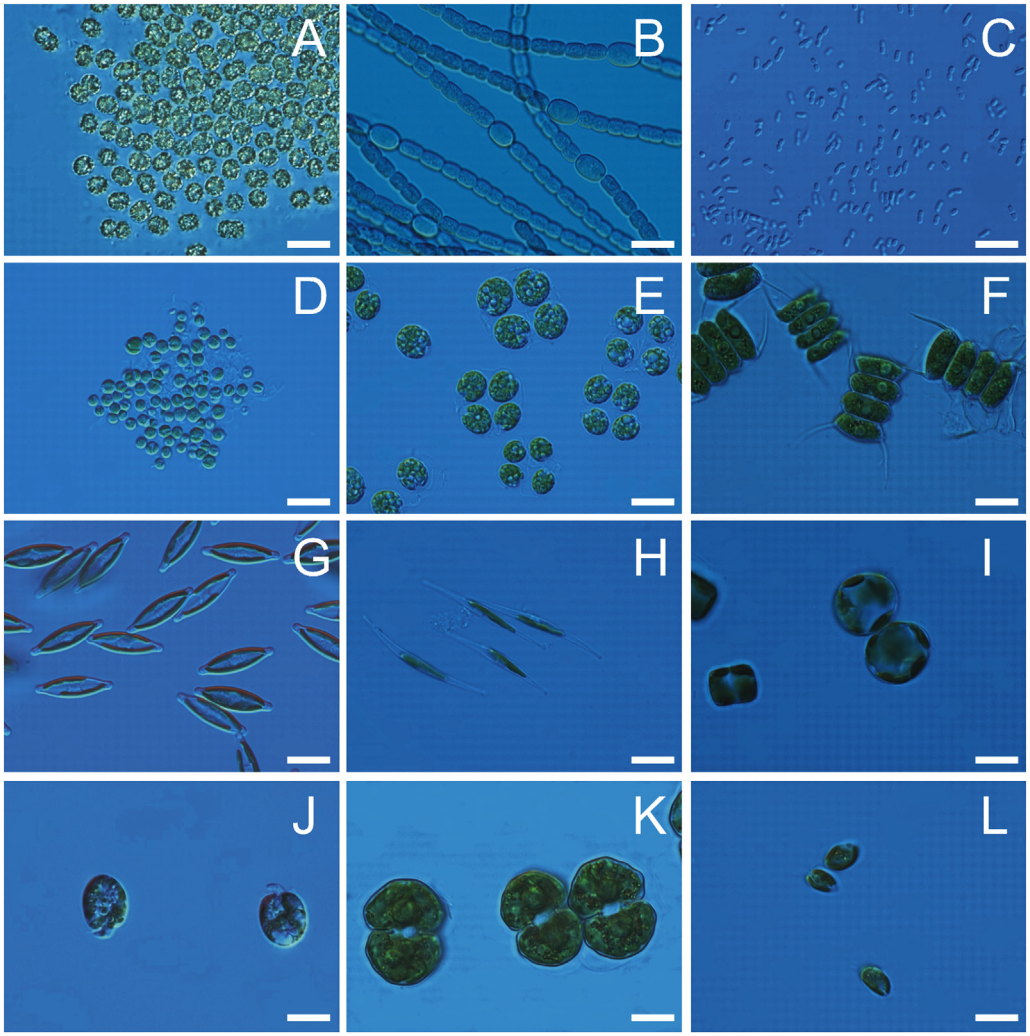

Fig. 4. Examples of allelopathic cyanobacteria and microalgae: *Microcystis* sp. (A), *Nostoc* sp. (B), *Synechococcus* sp. (C), *Chlorella* sp. (D), *Chlamydomonas reinhardtii* (E), *Scenedesmus* sp. (F), *Navicula* sp. (G), *Phaeodactylum tricornutum* (H), *Thalassiosira* sp. (I), *Amphidinium carterae* (J), *Cosmarium* sp. (K), *Prymnesium parvum* (L). Scale bars = 10 μm.

Karp-Boss (2014) observed that higher amounts of culture filtrate were needed for the allelopathic effect to be observed on larger cells. Schmidt and Hansen (2001) suggested that larger target microalgae require longer exposure times than smaller target microalgae cells and need to be affected by allelopathy. Ma et al. (2011) noticed that many allelopathic compounds damage the outer cell membranes, a process that will also be more effective with a higher surface-to-volume relationship.

3.2.3. Cell abundances and growth phase

Allelopathy is based on the production and release of chemicals into the environment; therefore, its effect should be dependent on the abundances of donor and target cells (Schmidt and Hansen, 2001; Tillmann and John, 2002; Tillmann, 2003). Higher abundances of allelopathic cyanobacterial and microalgal cells result in the increased potential exposition of target species to their harmful effects (Schmidt and Hansen, 2001; Tillmann, 2003). The increase in allelopathic interactions associated with increased donor cell abundance was demonstrated on various phytoplankton groups, such as prymnesiophytes and dinoflagellates (Schmidt and Hansen, 2001; Tillmann and John, 2002; Tillmann, 2003). Other studies have shown that the allelopathic effects of donors *P. parvum* and *Alexandrium* sp. decreased as the concentration of target organisms increased (Tillmann, 2003). Conversely, it has been found that some species may lose their activity in the stationary growth phase, even if the cell density is still very high (Schmidt and Hansen, 2001). Allelopathic activity is observed in both high and low densities of cyanobacteria and microalgae. Most likely, the lack of a clear correlation between allelopathic activity and cell density may reflect the regulation of allelopathic compound production in different growth phases, which depends on the metabolic routes that produce each specific allelopathic compound.

The growth phase determines the balance between primary and secondary metabolism; hence, it is essential to understand the production of allelochemicals. In principle, depending on the route that leads to the production of the allelochemical, its production rate would be higher in one phase or another.

There are a series of works showing stronger allelopathic activity in the exponential growth phase. Suikkanen et al. (2004) showed that the filtrate obtained from the *N. spumigena* culture taken during the exponential growth phase had adverse allelopathic effects on both *Thalassiosira weissflogii* and *Rhodomonas* sp. However, the filtrate from the stationary growth phase of *N. spumigena* did not show any significant impact. Similarly, the exudates from *Synechococcus* sp. and *N. spumigena* cultures in the stationary phase did not have adverse allelopathic effects on *B. paxillifer*, *C. vulgaris*, *O. submarina*, and *S. marinoi* (Śliwińska-Wilczewska et al., 2019). Additionally, Yamasaki et al. (2007) noted that the filtrate obtained from *Skeletonema costatum* cultures from different stages of growth had different effects on the growth of *Heterosigma akashiwo*, *Chaetoceros muelleri*, and *Prorocentrum minimum*. The filtrate obtained from *S. costatum* culture from the exponential growth phase significantly inhibited the growth of *H. akashiwo*

and *C. muelleri*, while the filtrate from the *S. costatum* stationary growth phase only moderately inhibited the growth of these species. With the same experimental design, these authors studied *H. akashiwo* as a donor species. The filtrate obtained from *H. akashiwo* from the exponential growth phase significantly inhibited the growth of *S. costatum* and *C. muelleri*. Additionally, Kubanek et al. (2005) noted the growth inhibition of *Asterionellopsis glacialis* when the *Karenia brevis* culture filtrate obtained from the exponential growth phase was added to *A. glacialis* culture. Conversely, the filtrate from *K. brevis* cultures from the stationary growth phase did not cause any significant changes in the cell numbers of *A. glacialis*. Schmidt and Hansen (2001) showed that old *C. polylepis* cultures did not affect *Heterocapsa triquetra*. Some authors have suggested that in the exponential growth phase, allelopathic activity is caused by the production of groups of allelopathic compounds rather than single substances (Arzul et al., 1999).

Contrary to all the above, there are also studies reporting greater activity in the stationary growth phase. Issa (1999) observed that the maximum antimicrobial activities of cyanobacteria *Oscillatoria* sp. and *Calothrix* sp. were recorded in the early stationary growth phase. Furthermore, the maximum allelopathic activity of *Synechococcus leopoliensis* was observed on the 15th day of culture incubation (Noaman et al., 2004). Moreover, it was found that *C. raciborskii* produces cylindrospermopsin only in the stationary growth phase (Griffiths and Saker, 2003). Arzul et al. (1999) also noted that the addition of *Alexandrium* sp. filtrate obtained from the exponential growth phase did not affect the diatoms, while strong inhibition was observed after the addition of the filtrate from the stationary phase.

4. Mode of action of allelopathic compounds

The functionality of allelopathic compounds is highly diverse. Donor species can affect target organisms in many different ways. Allelopathic compounds secreted by certain cyanobacteria and microalgae affect target organisms by inhibiting fluorescence and photosynthesis processes (e.g., Von Elert and Jüttner, 1997; Smith and Doan, 1999; Legrand et al., 2003; Leflaive and Ten-Hage, 2007; Śliwińska-Wilczewska et al., 2016), producing cell membrane lysis (e.g., Fistarol et al., 2004a,b; Granéli and Hansen, 2006; Pichierri et al., 2017), inhibiting enzymatic activity, impeding RNA synthesis and DNA replication, inducing temporary cyst formation, and blocking cell motility and division (Kearns and Hunter, 2001; Uchida, 2001; Ianora et al., 2006; Leflaive and Ten-Hage, 2007; Granéli et al., 2008b). However, in most cases, the mechanism of action of allelopathic compounds is still not well known (Rodríguez-Ramos et al., 2007). Therefore, it is important to characterize allelopathic interactions in controlled laboratory conditions to investigate the nature of released substances and their effect on target organisms.

4.1. The allelopathic effect on photosynthesis

Photosynthesis is a fundamental physiological process in primary producers, which is why it is an important target for inhibition by allelopathic competitors (Gross, 2003; Ma et al., 2015). Literature data indicate that many allelopathic compounds cause damage to thylakoid membranes, resulting in less chlorophyll content in cyanobacterial and microalgal cells (Gleason and Paulson, 1984) and inhibiting electron transport in photosystem II (Chauhan et al., 1992). Von Elert and Jüttner (1997) showed that allelopathic compounds obtained from *T. doliolum* cultures inhibit the flow of electrons in PSII of other cyanobacteria. Sukenik et al. (2002) reported that the addition of filtrate from *Microcystis* sp. affected the net photosynthesis and oxygen production of *Peridinium* sp. Other studies have shown that several species of cyanobacteria of the *Fischerella* genus can produce fischerellins that inhibit PSII activity (Gross et al., 1991). The chemical structure of this compound was described by Hagmann and Jüttner (1996) and was examined in detail in the context of PSII inhibition by Srivastava et al. (1998). The authors concluded that fischerellin was a compound that inhibited four different sites in PSII. Moreover, it was reported that fischerellin A inhibited PSII in cyanobacteria and eukaryotic algae but not in purple bacteria (Srivastava et al., 1998). This observation may indicate that this compound generally disrupts membrane activity in photosynthesis. This effect will be allowed by the hydrophobic nature of fischerellin, which is able to pass through cell membranes and accumulate in the thylakoids of target organisms Srivastava et al. (1998). Earlier than fischerellin, another allelopathic compound inhibiting PSII was isolated from the cyanobacterium *Scytonema hofmanii*; this allelochemical was cyanobacterin, described by Gleason and Paulson (1984). This compound could impede the flow of electrons in quinone A (Mallipudi and Gleason, 1989). Gleason (1990) showed that cyanobacterin damaged the thylakoids of *Euglena gracilis* but did not affect the growth of heterotrophic organisms. Two compounds, cyanobacterin LU-1 and LU-2, are produced by *Nostoc linckia* and affect oxygen production during the light phase of photosynthesis of cyanobacteria by inhibiting electron transport in PSII (Gromov et al., 1991; Vepritskii et al., 1991). Singh et al. (2001) showed that microcystin inhibited the growth of *Nostoc muscorum* and *Anabaena* sp. This inhibition was also associated with a reduction in photosynthesis. Ma et al. (2015) described in detail how the allelopathic compounds produced by the cyanobacterium *Microcystis aeruginosa* inhibited the photosynthesis and photosynthetic parameters of the green algae *C. vulgaris*. Śliwińska-Wilczewska and Latała (2018) and Śliwińska-Wilczewska et al. (2016, 2018, 2019) demonstrated that the picocyanobacterium *Synechococcus* sp. had allelopathic activity on photosynthetic parameters, which resulted in the inhibition of growth of tested green algae, diatoms, and unicellular red algae. Note that the study of Smith and Doan (1999) showed that many allelochemicals are generally soluble in organic solvents, insoluble in water and have low molecular weight; such properties facilitate penetration of the membrane of the thylakoids where photosynthesis occurs. These results emphasize broader modes of action of allelochemicals on target organisms than synthetic inhibitors (Duke et al., 2001).

Furthermore, chlorophyll fluorescence measurements can point to changes in photosystem II (PSII) activity by calculating the maximum quantum yield of PSII—F_v/F_m (where F_v—the difference between the maximum and minimum fluorescence and F_m—the maximum fluorescence). This is a highly sensitive method for examining cyanobacterial and algal responses to stress (Suresh Kumar et al., 2014; Machado et al., 2015) that may also be caused by allelopathic activity (Sukenik et al., 2002; Prince et al., 2008a,b; Song et al., 2017; Śliwińska-Wilczewska et al., 2017a, 2018, 2019; Barreiro Felpeto et al., 2019). Low values of the quotient F_v/F_m indicate low activity in PSII (Suresh Kumar et al., 2014). Sukenik et al. (2002) were among the first to study allelopathic effects using the pulse amplitude modulation (PAM) method; the analysis of fluorescence parameters showed that the addition of the cell-free filtrate from *Microcystis aeruginosa* reduced the F_v/F_m value in *Peridinium* sp. by 35%. The authors suggested that the allelopathic effect was due to slower electron transfer to PSI. Śliwińska-Wilczewska et al. (2016, 2017a, 2018, 2019) and Konarzewska et al. (2020), as well as Barreiro Felpeto et al. (2019), reported that picocyanobacteria *Synechococcus* sp. and *Synechocystis* sp., respectively, showed an allelopathic effect detected through the chlorophyll fluorescence parameter F_v/F_m of target cyanobacteria and microalgae. Song et al. (2017) reported a negative allelopathic effect of *Microcystis aeruginosa* on *Chlorella vulgaris* photosynthesis efficiency. Furthermore, Figueredo et al. (2007) noted that filtrate obtained from *C. raciborskii* inhibited PSII of target species. In that study, it was also found that *Microcystis aeruginosa* was the most allelochemically sensitive organism among the tested organisms, whereas slight inhibitions of photosynthesis were reported in *Microcystis wesenbergii*, *Monoraphidium contortum*, and *Coelastrum sphaericum*. Conversely, *Navicula* sp. was not susceptible to the compounds produced by *C. raciborskii*. These different sensitivities and responses to allelopathic activity could be explained by the

Table 3
Selected allelopathic compounds produced by cyanobacteria and microalgae.

Allelopathic compounds	Donor organisms	Reference
Cyanobacteria		
7-Deoxysedoheptulose	*Synechococcus elongatus*	Brilisauer et al. (2019)
12-Epi-hapalindole E isonitrile	*Fischerella muscicula*	Leão et al. (2012)
Anatoxin	*Planktothrix agardhii*, *Planktothrix isothrix*	Puschner (2018)
Aplysiatoxin	*Lyngbya majuscula*, *Nostoc muscorum*, *Schizothrix calcicola*, *Symploca muscorum*	Mynderse et al. (1977), Puschner (2018)
Apratoxin A	*Lyngbya majuscula*	Luesch et al. (2001)
Calothrixin A and B	*Calothrix* sp.	Rickards et al. (1999)
Coibamide A	*Leptolyngbya* sp.	Medina et al. (2008)
Crossbyanols A—D	*Leptolyngbya crossbyana*	Choi et al. (2010)
Cyanobacterin	*Scytonema hofmanii*	Mason et al. (1982)
Cyanobacterin LU-1 and LU-2	*Nostoc linckia*	Gromov et al. (1991), Vepritskii et al. (1991)
Debromoaplysiatoxin	*Lyngbya majuscula*	Kuiper-Goodman et al. (1999)
Fischerellin A and B	*Fischerella muscicola*	Burja et al. (2001)
Hapalindole A	*Hapalosiphon fontinalis*	Moore et al. (1984), Leão et al. (2012)
Hemolysin	*Synechococcus* sp.	Puschner (2018)
Homoanatoxin-a	*Oscillatoria formosa*, *Raphidiopsis mediterranea*	Puschner (2018)
Kalkitoxin	*Lyngbya majuscula*	Berman et al. (1999)
Lyngbyatoxin A	*Lyngbya majuscula*	Burja et al. (2001)
Majusculamide A—D	*Lyngbya majuscula*	Burja et al. (2001)
Microsporin A	*Nostoc* sp.	Burja et al. (2001)
Microviridin	*Microcystis viridis*	Puschner (2018)
Muscorid A	*Nostoc* sp.	Burja et al. (2001)
Noscomin	*Nostoc commune*	Jaki et al. (1999)
Nostocarboline	*Nostoc* sp.	Becher et al. (2005)
Nostocyclamide	*Nostoc* sp.	Todorova and Jüttner (1995)
Nostocyclamide M	*Nostoc* sp.	Jüttner et al. (2001)
Nostocin A	*Nostoc spongiaeforme*	Hirata et al. (1996)
Oscillatoxin-a	*Oscillatoria nigroviridis*	Puschner (2018)
Portoamide A—D	*Phormidium* sp.	Leão et al. (2010)
Scytophycin A and B	*Scytonema ocellatum*, *Scytonema hofmanii*, *Scytonema pseudohofmanii*	Puschner (2018)
Spumigin	*Nodularia spumigena*, *Sphaerospermopsis torques-reginae*	Mazur-Marzec et al. (2015), Sanz et al. (2015)
Tanikolide	*Lyngbya majuscula*	Burja et al. (2001)
Tenuecyclamide C	*Nostoc spongiaeforme*	Leão et al. (2012)
Thionsulfolipid	*Synechococcus* sp.	Kunimitsu et al. (1993)
Chlorophyta		
5-Aminolevulinic acid (ALA)	*Chlorella* sp.	Sasaki et al. (1995)
α-Linoleic acids	*Botryococcus braunii*	Chiang et al. (2004)
Abscisic acid (ABA)	*Chlorella vulgaris*, *Stichococcus bacillaris*	Maršálek et al. (1992)
Acetic acid	*Chlorella vulgaris*, *Chlorella pyrenoidosa*	Dakshini (1994)
Chlorellin	*Chlorella vulgaris*	Pratt et al. (1944)
Free fatty acids (FFAs)	*Platymonas viridis*, *Chlorella minutissima*	Liu et al. (2016)
Glycolic acid	*Chlorella* sp., *Tetraselmis gracilis*	Tolbert and Zill (1956), Rigobello-Masini et al. (2012)
Hydrocarbons	*Botryococcus braunii*	Liu et al. (2016)
Indole-3-acetic acid (IAA)	*Chlorella pyrenoidosa*, *Scenedesmus armatus*	Liu et al. (2016)
L-ascorbic acid (AA)	*Chlorella pyrenoidosa*, *Prototheca* sp.	Running et al. (2002)
Lactic acid (LA)	*Chlorella vulgaris*, *Chlorella pyrenoidosa*, *Scenedesmus incrassatulus*	Dakshini (1994), Kambourova et al. (2006)
Linoleic acids	*Botryococcus braunii*	Chiang et al. (2004)
Oleic acids	*Botryococcus braunii*	Chiang et al. (2004)
Palmitic acids	*Botryococcus braunii*	Chiang et al. (2004)
Portoamide	*Chlorella vulgaris*	Berry (2011)
Pyruvic acid	*Chlorella vulgaris*, *Chlorella pyrenoidosa*	Dakshini (1994)
Bacillariophyta		
Domoic acid	*Amphora coffeaeformis*, *Nitzschia navis-varingica*, *Pseudonitzschia australis*, *Pseudonitzschia delicatissima*, *Pseudonitzschia pseudodelicatissima*, *Pseudonitzschia pungens*, *Pseudonitzschia seriata*	Maranda et al. (1990), Villac et al. (1993), Lundholm et al. (1994), Lundholm and Moestrup (2000)
Glycolic acid	*Phaeodactylum tricornutum*	Rigobello-Masini et al. (2012)
Polyunsaturated aldehydes (PUAs)	*Skeletonema marinoi*, *Thalassiosira* sp.	Ianora et al. (2011)
Miozoa		
Brevetoxin A, B	*Gymnodinium breve*, *Karenia brevis*	Nicolaou et al. (1995, 1998), Kubanek et al. (2005)
Dinophysistoxin-1	*Prorocentrum lima*	McLachlan et al. (1994)
Karlotoxin	*Karlodinium micrum*	Adolf et al. (2006)
Haptophyta		
Acrylic acid	*Phaeocystis* sp.	Sieburth (1960)
Prymnesin 1 and 2	*Prymnesium parvum*	Igarashi et al. (1999)
Ochrophyta		
Free fatty acids (FFAs)	*Ochromonas danica*, *Nephrochloris salina*	Liu et al. (2016)
Lactic acid (LA)	*Nannochloropsis salina*	Talukder et al. (2012)

differences in morphology and physiology. Since the fluorescence measurement is correlated with gross photosynthesis, Figueredo et al. (2007) concluded that the reduction in photosynthetic activity might have affected the growth of target organisms. Gantar et al. (2008) showed that extracts from *Fischerella* sp. inhibited fluorescence of *Chlamydomonas* sp., and the inhibition, measured by PAM, was dependent on the concentration of the extract and on the time of exposure, indicating the inhibition of PSII. The compound suspected of having allelopathic activity produced by *Fischerella* sp. was an alkaloid. Detailed studies on allelopathic and photochemical interactions were also conducted by Prince et al. (2008b), who analyzed the effect of the dinoflagellate *K. brevis* on the F_v/F_m fluorescence parameters of 5 target organisms (*Akashiwo* cf. *sanguinea*, *Amphora* sp., *Asterionellopsis glacialis*, *P. minimum*, and *S. costatum*). It was noted that the extract obtained from *K. brevis* resulted in the inhibition of the fluorescence parameters of all examined microalgae. This effect was dependent on the growth phase of the donor organism. A dramatic decrease in PSII performance was recorded in *S. costatum*, with 68% lower F_v/F_m than the control. Prince et al. (2008b) showed that PSII inhibition occurred after 1 h of exposure to allelochemical compounds produced by *K. brevis*, while growth inhibition was measured after 2–4 days of the experiment. Then, the measurement of PSII performance may be more sensitive for the detection of allelopathic effects than measures of cell population growth.

Another mode of allelopathic effects is altering the pigment content in phytoplankton cells. Suikkanen et al. (2006) demonstrated significant differences in the cellular chlorophyll contents of *Rhodomonas* sp. and in the filtrates of *Aphanizomenon flos-aquae* and *N. spumigena* compared with the control. Śliwińska-Wilczewska et al. (2017a) also showed that filtrates from the picocyanobacterium *Synechococcus* sp. caused significant reductions in the chlorophyll contents of *Phormidium* sp. and *Rivularia* sp. cells and increased the carotenoid contents of *A. flos-aquae* and *Nostoc* sp. Similarly, Barreiro Felpeto et al. (2018) and Konarzewska et al. (2020) demonstrated that *Synechococcus* sp. cell-free filtrate caused reductions in the chlorophyll *a* contents of target cyanobacteria and microalgae. These observations may indicate that cyanobacteria produce allelopathic compounds that protect against photosynthesis. In addition, the increased carotenoid contents of target species may represent their protective responses to allelochemicals.

4.2. The allelopathic effect on the cell membrane

Lysis of cell membranes is another possible mode of action of allelopathic compounds. Granéli and Hansen (2006) described that some dinoflagellates (*Alexandrium* sp. and *Heterocapsa circularisquama*) and prymnesiophytes (*Prymnesium parvum* and *Chrysochromulina polylepis*) caused lysis of the cells of most of their competitors. Fistarol et al. (2004a,b) showed that filtrate obtained from *Alexandrium tamarense* produced cell lysis, pigmentation loss, and an increased number of empty cells in *Scrippsiella trochoidea*. Pichierri et al. (2017) demonstrated some essential cytosolic anomalies of *Ostreopsis* cf. *ovata* exposed to *Proschkinia complanatoides* and *Navicula* sp. filtrates. This dinoflagellate showed a lack of mobility, the formation of abnormal vesicle-like structures, and contraction of the cytoplasm. Barreiro Felpeto et al. (2018) reported that filtrate from *Synechococcus* sp. had an effect on the morphology of *N. spumigena*, consisting of the collapse of large portions of filaments. Śliwińska-Wilczewska et al. (2019) showed that exudates from *Synechococcus* sp. also negatively affected microalgae morphology, and the most apparent cell physical damage was observed for the diatom *S. marinoi*. Valdor and Aboal (2007) noted that cell-free filtrate obtained from *Oscillatoria* sp. caused disentangling of the filaments of *Pseudocapsa* sp. and *Nostoc* sp. Moreover, Gantar et al. (2008) found that *Chlamydomonas* sp. demonstrated morphological and structural changes after exposure to allelopathic compounds from *Fischerella* sp. In that study, electron microscopy revealed the degeneration of thylakoids and the loss of certain cell structures, including the nucleus.

4.3. Other modes of action of allelopathic compounds

Cyanobacteria and microalgae can produce a variety of compounds that inhibit enzyme activity (Gross, 2003; Leflaive and Ten-Hage, 2007). Jüttner and Wu (2000) showed that 20% of cyanobacteria isolated from freshwater biofilms from Taiwan inhibited α-glucosidase activity. An α-glucosidase inhibitor was isolated from *Spirogyra varians* (Cannell et al., 1987). A low molecular weight compound isolated from cyanobacterium *Anabaena* sp. inhibited α-amylase (Winder et al., 1989). Phenolic compounds such as chlorogenic acid, caffeic acid, and catechinic acid may inhibit phosphorylase activity and cinnamic acid, while their derivatives may inhibit ATPase hydrolysis activity (Mendes and Vermelho, 2013).

Other studies indicate that allelopathic compounds can also inhibit RNA synthesis and DNA replication (Doan et al., 2000, 2001). An alkaloid isolated from *Fischerella* sp., 12-epi-Hapalindole E isonitrile, and calothrixin A, isolated from *Calothrix* sp., inhibited RNA synthesis in *Bacillus subtilis* (Doan et al., 2001). These compounds were shown to directly inhibit the RNA polymerase of *Escherichia coli* (Doan et al., 2001). Calothrixin A also inhibits DNA replication (Doan et al., 2000). Pichierri et al. (2017) detected genotoxic damage in the DNA of the dinoflagellate *Ostreopsis* cf. *ovata* exposed to *Proschkinia complanatoides* and *Navicula* sp. filtrates.

Detailed studies on how lipid composition is affected by the stress caused by allelopathic compounds were carried out by Poulson-Ellestad et al. (2014b) and Poulin et al. (2018b). Poulson-Ellestad et al. (2014b) noted that allelopathic compounds produced by *Karenia brevis* increased the oxidative stress of *Thalassiosira pseudonana*. Poulin et al. (2018b) described that allelopathic compounds produced by the dinoflagellate *K. brevis* significantly altered the lipidomes of *Asterionellopsis glacialis* and *T. pseudonana*. Membrane-associated lipids of living *T. pseudonana* cells became permeable after exposing them to the compounds produced by *K. brevis*. This implies that allelopathic compounds affect lipid biosynthesis. On the other hand, Barreiro Felpeto et al. (2019) showed that the lipid contents increased in several species (*P. purpureum*, *Fistulifera* sp., and *C. vulgaris*) after exposure to *Synechocystis* sp. allelochemicals. The authors suggested that the increase in lipid content in target cells could be a reaction similar to what was observed under stress conditions.

5. Chemical identities of allelopathic compounds and the possible perspective of their application

Allelochemicals are generally produced in low amounts, which is problematic in terms of their chemical characterization, i.e., difficulties in producing high biomass levels and time-consuming preparative and analytical methods (Leflaive and Ten-Hage, 2007). In addition, the effect of environmental factors on the metabolic pathways of cyanobacteria and microalgae is very strong (Leflaive and Ten-Hage, 2007). Therefore, many studies do not undertake isolation and chemical characterization of allelopathic compounds.

In recent years, interest in bioactive compounds produced by cyanobacteria and microalgae has increased considerably (e.g., Berry et al., 2008; Leão et al., 2009, 2010, 2012; Costa et al., 2014; Konarzewska et al., 2020). The activity of secondary metabolites is described in terms of their potential and specific modes of action (Berry, 2011; Leão et al., 2012; Mendes and Vermelho, 2013; Zhu et al., 2020). Toxins can also be classified as allelopathic compounds because they have a negative impact on coexisting plants and animals (Leflaive and Ten-Hage, 2007). Additionally, compounds produced by cyanobacteria and microalgae can be chiral and present in two active forms (enantiomers). Furthermore, in many cases, one of the enantiomers may have toxic properties, while the other may be inactive or antagonistic; however, knowledge on these aspects is still limited (Skulberg, 2000). Table 3 lists some cyanobacterial and microalgal allelopathic compounds. Known cyanobacteria and microalgae toxins, i.e., anatoxin-a, anatoxin-a

(s), BMAA (β-*N*-methylamino-L-alanine), cylindrospermopsin, MAA (mycosporine-like amino acids), microcystin, nodularin, and saxitoxin, were excluded from the table, and only specific and selected allelochemicals were listed. For in-depth reviews about cyanobacterial and microalgal toxins, see Carmichael (1986), Codd et al. (1989, 1997), and Puschner (2018).

Cyanobacteria are one of the most morphologically, physiologically and metabolically diverse groups among gram-negative, prokaryotic and photosynthetic organisms (Whitton, 2008). This is due to the adaptations they developed to colonize most of earth's ecosystems, from ocean, freshwater, and brackish aquatic environments to terrestrial environments (Whitton and Potts, 2012). A consequence of this is their ability to produce and secrete many different secondary metabolites (Table 3). There are also reports of the ability to secrete allelopathic compounds by different microalgae belonging to the Chlorophyta, Bacillariophyta, Miozoa, Haptophyta, and Ochrophyta phyla (Table 3). However, the presence of different metabolites still needs to be confirmed since the literature reports on compounds produced by cyanobacteria and microalgae are still insufficient.

An important report pointing out the potential of compounds secreted by plants for broad practical applications was given by Gottfried Fraenkel in his work, "The Raison D'Être of Secondary Plant Substances" (Fraenkel, 1959). Five years later, Ehrlich and Raven (1964) suggested that secondary metabolites could protect plant organisms from herbivores or other predators. Over the next five decades, scientists have described the allelopathic effects of cyanobacteria and microalgae on other plants, insects and invertebrates in the context of their potential use in the agriculture, medicine and pharmaceutical industries (e.g., Tan, 2007; Berry et al., 2008; Rey et al., 2009; Berry, 2011; Liu et al., 2016; Brilisauer et al., 2019).

Cyanobacterial and microalgal allelochemicals can be used as herbicides and insecticides (Ishibashi et al., 2005; Doi et al., 2006; Berry et al., 2008; Brilisauer et al., 2019). It is estimated that the United States spends more than a few billion dollars a year on the commercial use of herbicides and insecticides (Peng et al., 2003). Therefore, in recent decades, scientists have focused on examining the roles of active compounds as biological pest controllers (Farooq et al., 2011). Additionally, scientists have focused on the application of cyanobacterial and microalgal allelochemicals as natural compounds used to control mosquito larvae (Nassar et al., 1999; Harada et al., 2000; Rey et al., 2009). Literature data indicate that combined mosquito-borne illnesses (e.g., malaria, yellow fever, dengue fever, various forms of meningitis, West Nile fever virus) have killed millions of people worldwide and have become extremely serious problems (Gubler, 1998). Therefore, it is suggested that allelochemical compounds produced by certain cyanobacteria (e.g., *Microcystis aeruginosa*) and microalgae (e.g., *Akashiwo sanguinea*) may be a potential source of protection against mosquitoes.

Cyanobacterial and microalgal allelochemicals can also be used in medicine and the pharmaceutical industry. The antimicrobial, antifungal, and antiviral activities of allelochemicals produced by different cyanobacteria (i.e., *Fischerella* sp., *Lyngbya* sp., *Phormidium* sp., *Pseudanabaena* sp., *Spirulina* sp., and *Scytonema* sp.) as well as microalgae (*Porphyridium* sp., *Rhodella* sp., *Chlorella* sp., and *Gyrodinium* sp.) were demonstrated (Gustafson et al., 1989; Patterson and Boils, 1995; Hagmann and Jüttner, 1996; Oufdou et al., 2001; Hernández-Corona et al., 2002; Garima et al., 2013; Liu et al., 2016). Moreover, Martins et al. (2008) and Costa et al. (2014) showed that some picocyanobacteria from the genera *Cyanobium*, *Synechococcus*, and *Synechocystis* were able to induce cytotoxic effects in human cancer cell lines. Moreover, secondary metabolites secreted by the filamentous cyanobacteria *Lyngbya* sp. were used as antitumor activity elements and were tested in clinical trials (Burja et al., 2001; Simmons et al., 2005).

The secondary metabolites described above are only a part of examples of compounds that can potentially be used in the agriculture, medicine, and pharmaceutical industries. Currently, studies in this field are being developed rapidly all over the world.

6. Conclusions

The production of allelopathic compounds is an adaptation by some cyanobacteria and microalgae that could provide a competitive advantage over other primary producers or could be a predatory trait. This production may play a relevant role in aquatic ecosystems, especially during the success of phytoplankton communities. The main abiotic factors influencing allelopathy are the availability of macronutrients, light and temperature. Essential biotic factors influencing allelopathy are the taxonomic positions of the donor and target organisms (including differences even between strains), growth phase and population abundances. The modes of action of allelopathic compounds are diverse. They can produce membrane lysis or inhibit photosynthesis, enzyme activity, RNA synthesis or DNA replication. However, in most cases, the mechanism of action is insufficiently understood or completely unknown. Many cyanobacterial and microalgal secondary metabolites may have commercial potential, mostly in the pharmaceutical industry but also in agriculture. The chemical nature of most allelochemicals is still unknown, as are their metabolic mechanisms of action. Further research on this topic is probably the most urgent need for allelopathy studies, both for achieving a better understanding of the role of allelochemicals from evolutionary and ecological perspectives and for the development of industrial applications.

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CRediT authorship contribution statement

Sylwia Śliwińska-Wilczewska: Trial design, Test Management, Writing, and Revising.

Kinga Wiśniewska: Data Analysis, Supplementary Test, Software, Checking Findings.

Zofia Konarewska: Literatures Collecting, Methodology, Checking Findings.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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