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Algicidal Effect of *Serratia* sp. PDGS120915 against Harmful Dinophyceae Algae

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Abstract: Harmful algal blooms (HABs) can cause massive economic losses. In this study, the bacterial strain PDGS^{120915} produced a red pigment (prodigiosin). It was isolated from lightly contaminated stream water taken from Busan, Korea. The isolated strain was identified as *Serratia* sp. by 16S rDNA sequence analysis and morphological characteristics. Prodigiosin from *Serratia* sp. PDGS^{120915} was extracted and purified by high-performance liquid chromatography (HPLC). This pigment showed algicidal activity against dinophyceae, *Alexandrium catenella, Gymnodinium impudicum*, and *Cochlodinium polykrikoides*. The algicidal activity of this prodigiosin against dominant bloom-forming dinophyceae on the Korean coast was examined, and it exhibited high algicidal activity against *A. catenella* (83.4%), *G. impudicum* (92.1%), and *C. polykrikoides* (92.3%). Furthermore, prodigiosin from *Serratia* sp. PDGS^{120915} showed a broad range of algicidal activity against raphidophyceae (*Chattonella marina*, *Heterosigma akashiwo*), coscinodiscophyceae (*Skeletonema costatum*), and bacillariophyceae (*Nitzschia pungens*). The optimum concentration of this activity was observed at 5 ppb. Additionally, algicidal activity increased rapidly after 9-h and showed more than 80% algicidal activity at 12-h. Our research suggested that the algicidal bacterium *Serratia* sp. PDGS^{120915} and its algicidal compound, prodigiosin, could be a potential bio-agent for the prevention and control of harmful algal blooms.

Keywords: Algicide; Dinophyceae; HABs; Prodigiosin; Serratia

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Introduction

Harmful algal blooms (HABs) have been accompanied by huge economic losses through massive fish deaths and a threat with shellfish poisoning in marine and freshwater ecosystems (Hallegraeff, 1993; Landsberg, 2002; Sellner et al., 2003). Moreover, approximately 2,000 cases of human poisoning resulting from algal toxins are reported each year (Zingone and Enevoldsen, 2000). A number of methods of bloom control have been investigated. Many chemical (e.g. copper sulphate, ozone) and physical (e.g. clay/algal flocculation, ultrasonic irradiation) methods have been proposed to mitigate or control HABs (Anderson, 1997; Kim, 2006). However, most of these methods are inapplicable because of high costs and secondary pollution. Therefore, research on economic and feasible approaches for algae removal has important theoretical and practical significance (Pei et al., 2005). Recently, some studies have demonstrated that the bacteria could lyse alga cells by producing extracellular substances, such as protease (Lee et al., 2000b), hydroxylamine (Berger et al., 1979), antibiotics (Dakhama et al., 1993), and aminophenol (Yoshikawa et al., 2000; Yamanoto et al., 1998).

Bacteria that can control algal blooms are called algicidal bacteria. Many bacteria with strong algicidal activity against HAB species have been isolated and investigated (Kodani et al., 2002; Su et al., 2007; Ma et al., 2011). Algicidal bacteria have a broad range of potential industrial and environmental applications from the point view of diversity, biodegradability, low toxicity, and biocompatibility (Fiechter, 1992). The greatest advantage of biosurfactants when compared with synthetic surfactants is that they are easily biodegraded, making them environmentally acceptable in contrast to some synthetic algicides (Mulligan, 2005). Additionally, several studies have stated that algicidal bacteria may only be effective on a specific genus or species of algae (Fukami et al., 1992; Doucette et al., 1999), while others target a broader range of algal classes (Imai et al., 1995; Lovejoy et al., 1998; Kang et al., 2008; Roth et al., 2008a). Several strains of algicidal bacteria have been isolated, but few algicides have been purified. Great difficulties exist in the isolation and purification of algicidal compounds because of the apparent variation in characteristics across different species of algicidal bacteria (Skerratt et al., 2002).

In this study, the algicidal bacterium PDGS^{120915} was isolated from lightly contaminated stream water. Furthermore, characterization of the lytic effect was examined against several HAB species. These results were investigated to determine the potential source of algicidal bacteria or controlling HABs.

Materials and Methods

Algal Cultures

Alexandrium catenella, Gymnodinium impudicum, and *Cochlodinium polykrikoides* were supplied by the Korea Marine Microalgae Culture Center (KMCC). All algal cultures were grown in f/2 medium (Guillard and Ryther, 1962) at 20°C, pH 8, and 120 μE/m^2/sec in a 12-h light and 12-h dark cycle.

Bacterial Strain

The bacteria sample was collected from lightly polluted stream water in Busan, Korea. To screen the algicidal bacteria, the isolated strain was inoculated into logarithmic-phase algal cultures. The algicidal substance-producing bacterium designated PDGS^{120915} was obtained on Luria Bertani (LB) medium at 25°C.

Identification of Algicidal Bacteria

An isolated strain was grown at 25°C for 1 day on LB medium. Standard physiological and biochemical characteristics were examined using API kits (API 20E and APIZYM; BioMerieux, France). For the sequence analysis, bacterial genomic DNA was extracted and purified using a DNA extraction kit according to the manufacturer's instructions (Promega Co., Madison, USA). 16S rDNA was amplified by PCR using the universal primers 8F (5'- AGAGTTTGATCCATGGC-3') and 1492R (5'-GTTACCTTGTTACGACTT-3'). The obtained nucleotide sequences were analyzed by the BLASTN database (http://www.ncbi.nlm.nih.gov/BLAST) at the National Center for Biotechnology Information (NCBI). A neighbor-joining phylogenetic tree was constructed using MEGA 5.0.

Purification of algicidal compound

The bacterial cells were harvested, and pigment extraction was performed using acidified ethanol (5% HCl and 95% ethanol). Subsequently, the extracted pigments were chromatographed on an XTerra MS C18 reverse-phase column (125Å, 2.5 μm, 2.1 mm × 20 mm, Waters). HPLC was carried out with the Bio-Rad HPLC system (Bio-Rad, USA) at a 0.3 ml/min flow rate.

Characterization of Algicidal Effect

Activities of different treatments: Bacterial cells, bacterial cultures, cell-free filtrates, and purified compounds were inoculated into each algal culture. Afterward, the inoculates were cultivated in adjusted algae conditions.

Effects of growth phase of bacteria: To investigate the algicidal activities related to bacterial growth phase, the bacterial growth and algicidal activity of each time were examined.

Effects of concentration: The purified compound was inoculated into each algal culture at concentrations of 1, 3, 5, 7, and 10 ppb, and f/2 medium was used as a control. All experiments were performed in triplicate. The cultivation used the same conditions as those used for the algal culture.

Mode of activity: Isolated bacterium PDGS^{120915} was cultured in LB medium at 25°C for 24-h. Cells were harvested by centrifugation at 12,000 × g for 20 min, and supernatants were passed through 0.22-μm filters to obtain cell-free filtrates. Bacterial cultures, cell-free filtrates, and purified compounds were inoculated into each algal cell culture, respectively. Then, they were cultivated at 20°C, pH 8, and 120 μE/m^2/sec in a 12-h light and 12-h dark cycle.

Analysis of algicidal activity: To measure the algicidal activities of the isolated bacterial strain, the algal cells were quantified using a hemocytometer under a light microscope.

Lugol's iodine reagent fixed algal cell counting. The following formula was used to calculate the algicidal effect:

$$\text{Algicidal activity}(\%) = \left[\frac{(\text{Number of initial cells} - \text{Number of survived cells})}{\text{Number of initial cells}}\right] \times 100$$

Results

Physiological identification

The bacterium PDGS^{120915} was determined to be a gram-negative rod shape and reddish colony obtained on an LB agar plate. The results of its biochemical and enzymatic characteristics are shown in **Table 1**. The strain utilized citrate, fructose, galactose, glucose, maltose, mannitol, mannose, sorbitol, sucrose, and trehalose, as well as the hydrolysis of gelatin and casein. In addition, the enzyme activities were positive on lysine decarboxylase, ornithine decarboxylase, catalase, esterase, lipase, acid phosphatase, naphthol-AS-BI-phosphohydrolase, and N-acetyl-β-glucosaminidase (Ji et al., 2015).

Identification of algicidal substance-producing microorganism

The sequence obtained was available in GenBank under the accession number KC007128. The 16S rDNA sequence of strain PDGS^{120915} was aligned through comparison with available sequences from the GenBank database. The sequences of PDGS^{120915} shared the highest homology with *Serratia marcescens* subsp. *sakuensis* KRED^{T}. Using the 16S rDNA sequences, phylogenetic analysis was performed. The phylogenetic tree based on bacterial 16S rDNA sequences showed a close relationship between PDGS^{120915} and the genus *Serratia* (Ji et al., 2015) (**Figure 1**).

Confirmation of algicidal compound

Prodigiosin, extracted from *S. marcescens* (Castro et al., 1959), had a maximum absorption spectrum of 537–538 nm. In this study, the maximum absorption spectrum of prodigiosin extracted from *Serratia* sp. PDGS^{120915} was observed to have similar characteristics (Ji et al., 2015).

Algicidal activity of Serratia sp. PDGS^{120915} against harmful algae

The algicidal activities were investigated and divided into two parts (i.e. direct and indirect). One of the parts was treated with bacterial cells and another part with filtrates. We found that the bacterial cells had almost no algicidal activity. However, the cell-free filtrates and purified prodigiosin showed more that 80% algicidal activity, similar to that of the original bacterial cultures (**Figure 2**).

Interaction between algicidal activity and bacterial growth

The correlation between bacterial growth and algicidal activity was examined over 24-h at 2-h intervals. The results demonstrated that the algicidal activity of the PDGS^{120915} was bacterial growth-dependent; thus, the strongest algicidal activity occurred in the stationary phase (**Figure 3**).

Algicidal activity according to prodigiosin concentration

The algicidal activities at different concentrations of prodigiosin were examined. Although at 1 ppb concentration, algicidal activity was not strong, when the concentration was more than 5 ppb, the algicidal activities were over 90%. Every time the concentration increased, stronger algicidal activity was observed (**Figure 4**). Even though increase ratio was under 1% by stages between 5 and 10 ppb, this seems to be a concentration-dependent reaction.

The algicidal range of Serratia sp. PDGS^{120915}

The algicidal range of *Serratia* sp. PDGS^{120915} was examined against other HAB classes. The 5 ppb purified prodigiosin was added to each algal culture reached at the mid-exponential phase. The cultivation was adequate for the growth of each algal cell. Algicidal activity was estimated using the aforementioned equation. The algicidal activities against raphidophyceae, coscinodiscophyceae, and bacillariophyceae were as follows (**Figure 5**): *Chattonella marina* (38.9%), *Heterosigma akashiwo* (30.8%), *Skeletonema costatum* (24.7%), and *Pseudonitzschia pungens* (22.1%).

Table 1: Biochemical and enzymatical characteristics of *Serratia sp*. PDGS^{120915}

Characteristic	120915	Characteristic	120915
Spore	-	Arginine dihydrolase	-
Motility	+	Lysine decarboxylase	+
Anaerobic growth	+	Ornithine decarboxylase	+
Utilization of		Cytochrome oxidase	-
Arabinose	-	Catalase	+
Cellobiose	-	Alkaline phosphatase	-
Citrate	+	Esterase (C4)	+
Fructose	+	Esterase Lipase (C8)	+
Galactose	+	Lipase (C14)	-
Glucose	+	Leucine arylamidase	-
Lactose	-	Valine arylamidase	-
Maltose	+	Cystine arylamidase	-
Mannitol	+	Trypsin	-
Mannose	+	α-chymotrypsin	-
Melibiose	-	Acid phosphatase	+
Raffinose	-	Naphthol-AS-BI-phosphohydrolase	+
Sorbitol	+	α-galactosidase	-
Sucrose	+	β-galactosidase	-
Trehalose	+	β-glucuronidase	-
Xylose	-	α-glucosidase	-
Hydrolysis of		β-glucosidase	-
Gelatin	+	N-acetyl-β-glucosaminidase	+
Urea	-	α-monnosidase	-
Casein	+	α-fucosidase	-
Starch	-		
β-hemolysis	+		
Production of			
Acetoin	-		
H2S	-		
Indole	+		
Mixed acid	-		
Gas	-		

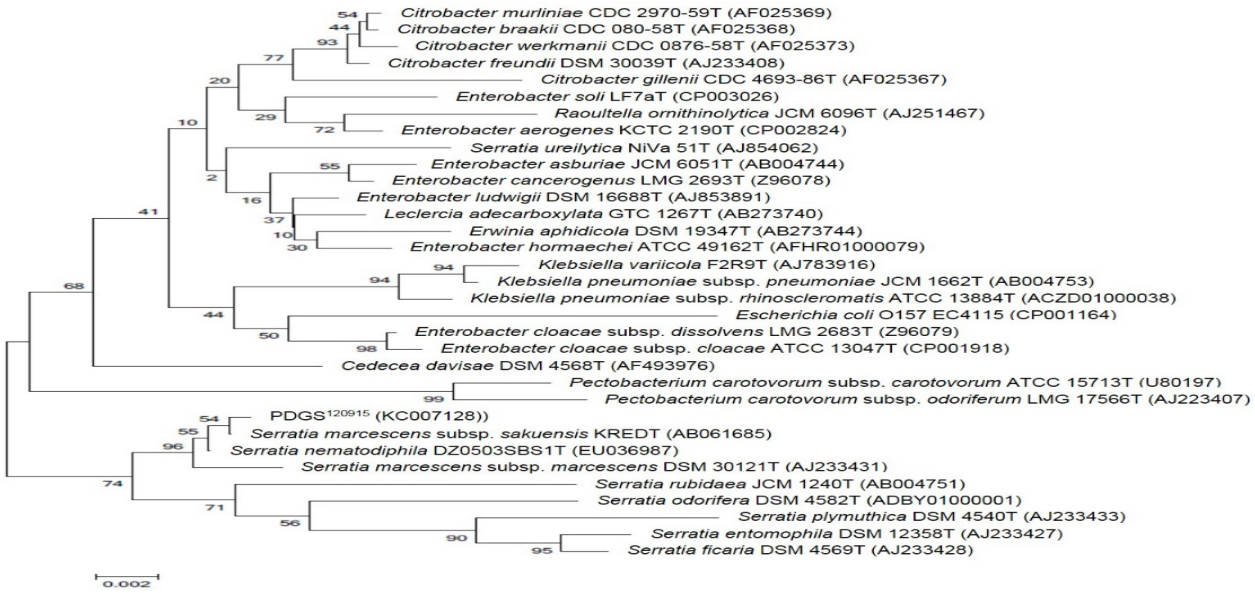

Figure 1: Neighbour-joining tree based on 16S rRNA sequence, showing relationships between PDGS[120915] and highly homologous group. Numbers at the nodes are levels of bootstrap support, based on neighbor-joining analyses of 1,000 resample datasets.

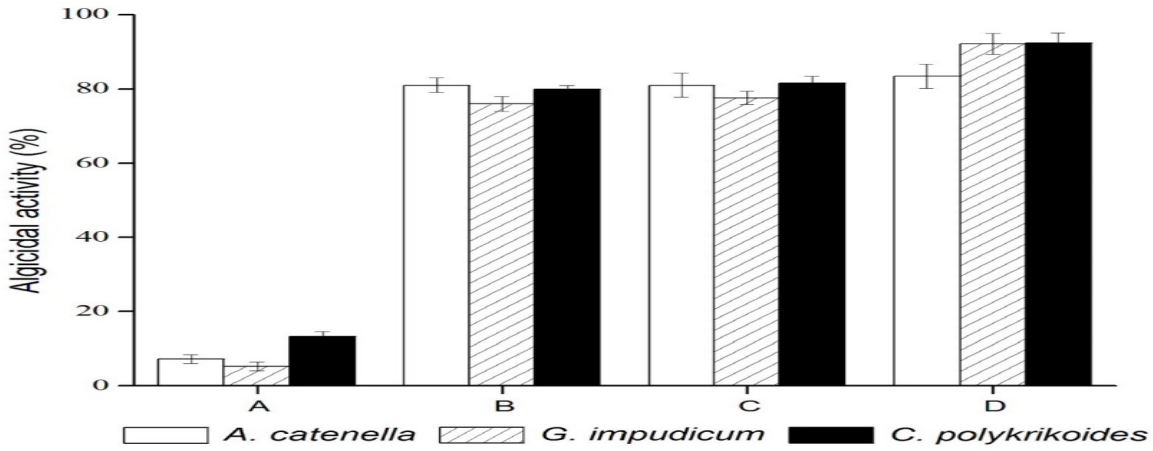

Figure 2: The algicidal activity of different treatments. (A) Re-suspended bacterial cells, (B) Bacterial culture, (C) Cell-free filtrates and (D) prodigiosin.

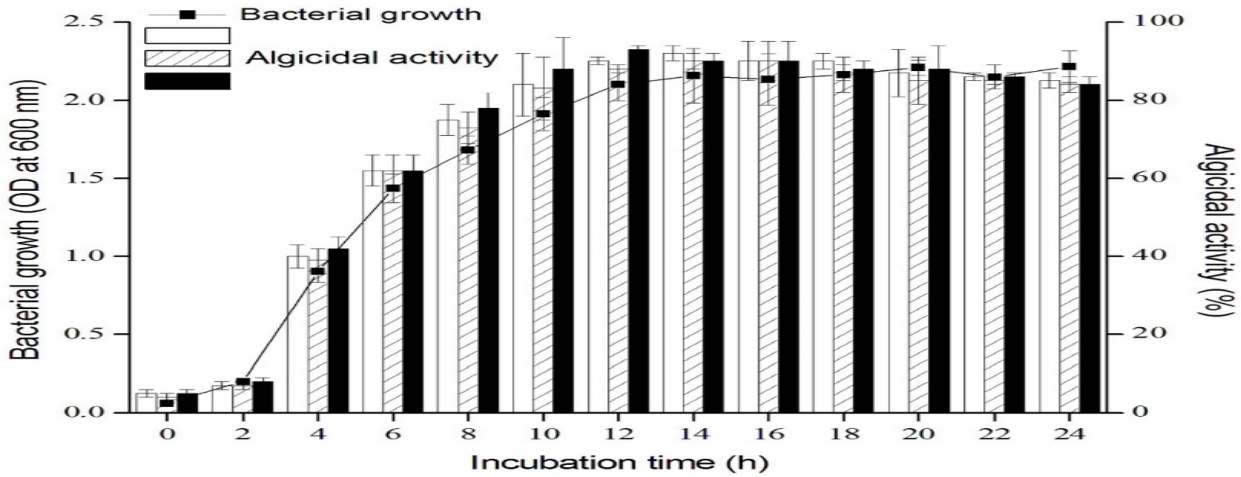

Figure 3: Correlation between bacterial growth and algicidal activity..

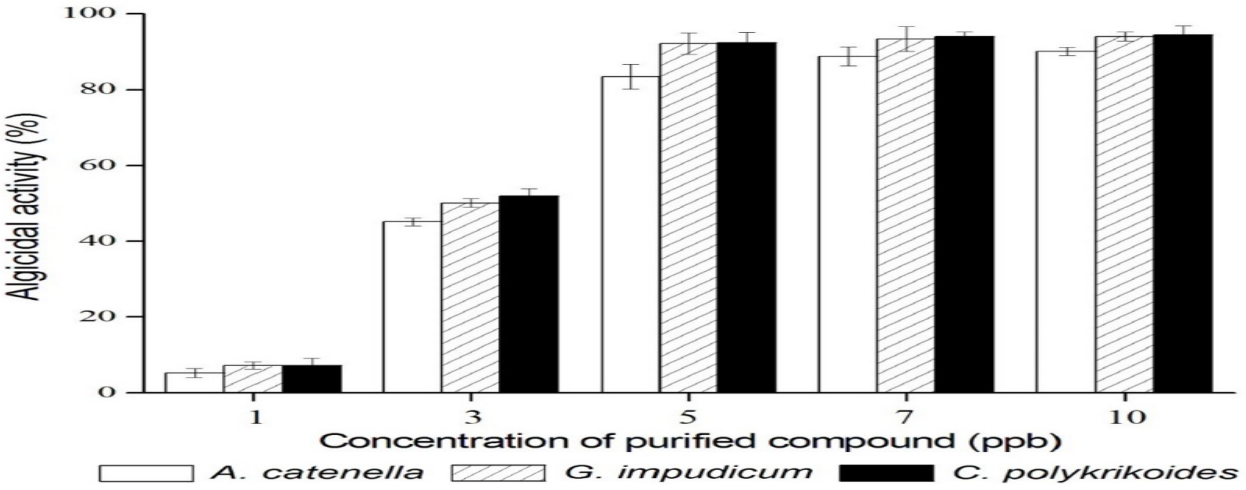

Figure 4: The algicidal activity of different concentration of prodigiosin against HAB.

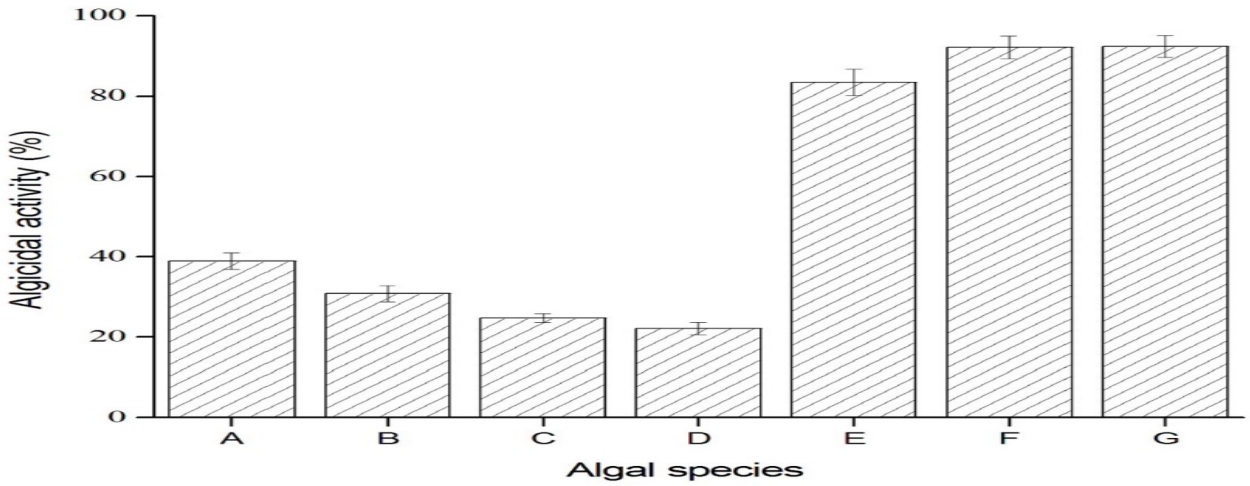

Figure 5: The algicidal range of prodigiosin against various HAB species. The 5 ppb purified prodigiosin was added to each algal culture at the mid-exponential growth phase. (A) *Chatonella marina*, (B) *Heterosigma akashiwo*, (C) *Skeletonema costatum*, (D) *Nitzschia pungens*, (E) *Alexandrium catenella*, (F) *Gymnodinium impudicum* and (G) *Cochlodinium polykrikoides.*

Discussion

During the past several decades, HABs have tended to increase worldwide and have negative influences, such as killing fish, shellfish, and other marine life in the ocean ecosystem (Friedman and Levin, 2005). Sprinkling clay to mitigate HABs is the only method used in practice, but it has limitations in its application to the marine ecosystem. Therefore, many researchers have examined biological control methods for HABs, such as the algicidal effect (Fukami et al., 1992; Iwata et al., 2004) and the interaction between marine bacteria and phytoplankton (Furuki and Kobayashi, 1992; Fukami et al., 1997). We found that a potent algicidal strain, PDGS^{120915}, isolated from the lightly contaminated stream water in Busan, Korea. Based on 16S rDNA sequence analysis, this strain was identified as the genus *Serratia*. Yang et al. (2013) also isolated a strain belonging to that genus, which can effectively lyse the algal cells of the *Microcystis aeruginosa*, which is a species of freshwater *cyanobacteria*. However, no reports have documented a bacterial strain belonging to *Serratia* that can lyse the toxic algal cells of *A. catenella, G. impudicum*, and *C. polykrikoides*, which are widely included as HABs and distributed in the coast of Korea.

In general, the algicidal mode of bacteria could be summarized as either direct or indirect attacks (Mayali and Azam, 2004; Pokrzywinski et al., 2012). Direct attacks mean that algicidal bacteria make contact with the algal cells and lyse them, while indirect attacks are algicidal activity dependent on active compounds produced by the microorganism (Mayali and Azam, 2004). Only a few compounds from algicidal bacteria have been characterized. These compounds comprise peptides or enzymes (Chen et al., 2011; Imamura et al., 2000; Lee et al., 2000; Paul and Pohnert, 2011; Wang et al., 2012), biosurfactants (Wang et al., 2005), pigments (Nakashima et al., 2006; Sakata et al., 2011), and antibiotic-like substances (Dakhama et al., 1993). In the present study, PDGS^{120915} exhibits indirect attacks against *A. catenella, G. impudicum*, and *C. polykrikoides*. These results determined different treatments for the algal cells. It was indicated that our

strain released an algicidal compound into the culture broth, and we identified this compound as prodigiosin. The algal cell rupture from cellular swelling was observed after the treatment of prodigiosin. It is presumed that the intervention of the ion channel of prodigiosin leads to increasing water inflow within the intracellular space, causing the rupture of cells due to cellular swelling. This result is similar to that of Kim et al.'s research (Kim et al., 2008).

Several reports describe the algicidal activity of prodigiosin, and a preliminary test for prodigiosin's algicidal activity has been carried out. Jeong et al. (2005) reported that when prodigiosin from *Hahella chejuensis* was used to treat *C. polykrikoides* culture, the algal cells were rapidly burst. Takuji et al. (2006) reported that PG-L-1, a prodigiosin-like pigment, had potent algicidal activity against *C. marina* and *H. akashiwo.* In our studies, we purified prodigiosin from *Serratia* sp. PDGS^{120915} and examined the algicidal activity against the dominant algal bloom-forming species *A. catenella, G. impudicum*, and *C. polykrikoides*. Our results showed that prodigiosin from *Serratia* sp. PDGS^{120915} could be a useful bio-compound for mitigating or controlling HABs. However, further investigation of how to use it and the killing process that takes place in natural conditions is required. Additionally, in order to evaluate the benefits of algicidal agent spraying, we are considering the necessary addition of a mesocosm study.

The cost of algicidal agent spraying is divided into direct and indirect costs. Direct costs are all expenses involved in spraying. (i.e. production charges, transportation charges, equipment and vessel charges, labor costs, etc.). Indirect costs refer to the negative effects on marine ecosystems and organisms. We have obtained 0.81 kg/ton of prodigiosin from a wild-type strain. An expendable production cost (LB media) except equipment for separation and extraction is 2,320,000 won (unit price/ton). As a result of calculation in the presumable working concentration range at 10–100 ppb, the processing cost per ton (m^3) of sea water is 28.6–286 won (*in vitro* test). If decreasing production costs and increasing production yield are achieved through the investigated optimal production conditions, we expect a reduction of the processing cost per ton (m^3). This information will be an important factor for the potential application of algal control.

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