



Paralytic Toxin Producing Dinoflagellates in Latin America: Ecology and Physiology

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In this review we summarize the current state of knowledge regarding taxonomy, bloom dynamics, toxicity, autoecology, and trophic interactions, of saxitoxin producing dinoflagellates in this region. The dinoflagellates *Gymnodinium catenatum*, *Pyrodinium bahamense* and several species of *Alexandrium* are saxitoxin producers, and have been responsible of paralytic shellfish poisoning in different regions of Latin America, causing intoxications and important fisheries losses. The species distribution differ; most harmful algal blooms of *G. catenatum* are from the northern region, however this species has also been reported in central and southern regions. Blooms of *P. bahamense* are mostly reported in North and Central America, while blooms of *Alexandrium* species are more common in South America, however this genus is widely spread in Latin America. Species and regional differences are contrasted, with the aim to contribute to future guidelines for an international scientific approach for research and monitoring activities that are needed to increase our understanding of paralytic toxin producing dinoflagellates in this region.

Keywords: *Alexandrium*, dinoflagellates, *Gymnodinium catenatum*, Latin America, paralytic toxins, *Pyrodinium bahamense*, review, strains

INTRODUCTION

Neurotoxic paralytic shellfish toxins (PSTs) are produced in the marine environment mainly by dinoflagellates of three genera associated with harmful algal blooms (HABs). These include about a dozen species of *Alexandrium*, a single species of *Gymnodinium* (*G. catenatum*) and a single species of *Pyrodinium* (*P. bahamense*).

PSTs molecules comprise saxitoxin (STX) and over 57 analogs have been described (Wiese et al., 2010) that vary in toxicity, being the carbamoyl [STX, neosaxitoxin (NEO), gonyautoxins (GTX)] the most potent, followed by decarbamoyl (dcSTX, dcNEO, dcGTX) and the deoxydecarbamoyl analogs (doSTX, doGTX2, doGTX3). The least toxic analogs are the *N*-sulfocarbamoyl (B and C toxins). Only *G. catenatum* produces benzoyl analogs (GC), and out of 18 theoretical toxins (Negri et al., 2003a, 2007; Vale, 2008, 2010), 15 benzoyl analogs have been confirmed (Durán-Riveroll et al., 2017) (**Figure 1**).

Consumption of PSTs-contaminated seafood results in a variety of gastro-intestinal and neurologic symptoms known as paralytic shellfish poisoning (PSP) that depend on the toxin concentration and can lead, in extreme cases, to human death. PSTs are usually transferred to humans by the consumption of mollusks such as clams, oysters, and mussels; other toxin vectors that have been reported are gastropods, crustaceans and fish (Llewellyn et al., 2006; Deeds et al., 2008; McLeod et al., 2017). These toxins act at the nervous system level by blocking the voltage-gated sodium channels (Na_V) in mammals (Llewellyn, 2006). They can also bind to voltage-gated calcium (Ca_V) (Su et al., 2004) and potassium (K_V) channels (Wang et al., 2003). In the case of GC analogs, their binding to Na_V channels has only been demonstrated by *in silico* analyses (Durán-Riveroll et al., 2016). PSTs have been related to the death and intoxication of diverse organisms such as shrimp, fish, sea birds, turtles, and whales; however, the knowledge of toxin action in marine organisms is still scarce (Pérez-Linares et al., 2008; Núñez-Vázquez et al., 2011; Costa et al., 2012).

In Latin America (LAm), ~1,410 people have been intoxicated (94 fatalities) by PSP from 1970 to 2016 (Table 1). *Pyrodinium bahamense* has caused the highest number of intoxications (819 cases), followed by *Alexandrium* spp. (350 cases), and *G. catenatum* (241 cases). In the genus *Alexandrium* the highest mortalities have been caused by *A. catenella* (Lagos, 2003), causing 10 M USD losses in salmon industry (Mardones et al., 2015). In spite that intoxications and economic losses due to PSP are becoming an important public concern, few Latin American countries have established and/or maintained monitoring programs.

In this review, we summarize the current state of knowledge regarding PSTs producing dinoflagellates in LAm, contrasting the regional differences with the aim to contribute to future guidelines for an international scientific approach for research and monitoring activities that are needed to increase our understanding of PSP events in this region.

Gymnodinium catenatum

Gymnodinium catenatum is the only gymnodinioid known to produce PSTs. The first description of the species was in the northern region of the Gulf of California (GOLCA) in 1939 (Graham, 1943). Forty years later, in 1979, the first PSP related to this species in LAm was reported along the coasts of Sinaloa, Mexico, during an upwelling event, causing an extensive fish kill (~200 km), 19 human intoxications and 3 fatalities (de la Garza-Aguilar, 1983; Mee et al., 1986).

Although it was rarely observed after being described, from the decade of 1970 on, blooms have been reported and associated with human poisonings and fatalities in several countries (de la Garza-Aguilar, 1983; Hallegraef et al., 2012; Cembella and Band-Schmidt, 2018). An apparent increase in frequency, duration, and distribution of blooms are probably related to anthropogenic activities (Hallegraef, 1993, 1995; Hallegraef et al., 2012). To date, it has been reported in nine countries of LAm (Figure 2). In Mexican coasts there have been numerous

reports since 1990 (Band-Schmidt et al., 2010; Gárate-Lizárraga et al., 2016; Medina-Elizalde et al., 2018), associated with human intoxications and death of marine organisms (de la Garza-Aguilar, 1983; Mee et al., 1986; Núñez-Vázquez et al., 2011, 2016). HABs of this species have resulted in 241 cases of PSP (14 fatalities) in Mexico and Venezuela (Table 1), and epizootic diseases with mass mortalities of fish, seabirds, and marine mammals. Losses in shrimp cultures have also been reported. Also, prolonged sanitary closures by contamination with PSTs in shellfish, have affected commercialization, causing un-estimated but significant economic losses due to the closure of important shellfish fisheries in the upper GOLCA (García-Mendoza et al., 2016).

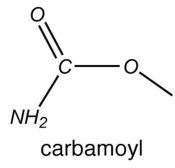
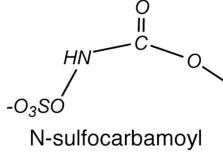

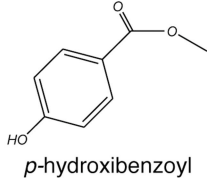
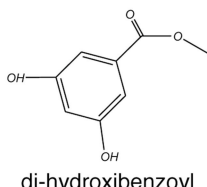
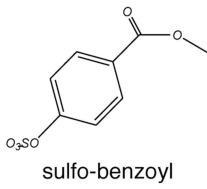
***Gymnodinium catenatum* Bloom Dynamics Mexico**

One of the most recent and lengthy HABs of this species occurred in the northern part of the GOLCA with maximum abundances of $152 \times 10^3 \text{ cell L}^{-1}$ (Medina-Elizalde et al., 2018). This bloom lasted from January to March in 2015, affecting a large number of seabirds, mammals and people (García-Mendoza et al., 2016). In Bahía Concepción (BACO), *G. catenatum* is often present without forming blooms and is more abundant during hydrographic transitional periods during spring and early fall (Morquecho and Lechuga-Devéze, 2004). BACO is one of the few bays where studies on cyst dynamics have been realized, cyst yields are low, but seem to be a constant inoculum that sustains the population for long periods (Morquecho and Lechuga-Devéze, 2004).

In Bahía de La Paz (BAPAZ), in the south of the California Peninsula, SW GOLCA, there is only one report of a HAB in February/March 2007, with abundances from 6×10^5 to $2.4 \times 10^6 \text{ cell L}^{-1}$, an average sea surface temperature (SST) of $20.9 \pm 0.7^\circ\text{C}$ and low nitrate ($1.0 \pm 0.3 \mu\text{M}$) and phosphate ($0.8 \pm 0.8 \mu\text{M}$) concentrations (Hernández-Sandoval et al., 2009). In the same bay, in 2010, this dinoflagellate was reported in low abundances ($21 \times 10^3 \text{ cell L}^{-1}$) (Muciño-Márquez, 2010).

On the NE GOLCA, in Bahía Bacoichampo, Sonora, a 24-year study was performed on HABs (1970–1994), recording 43 events, where one of the main species was *G. catenatum* (Manrique and Molina, 1997); this led to conclude that NW winds during colder months promoted blooms. They also agreed with Cortés-Altamirano (1987) that HABs had an inverse relationship with El Niño. Unfortunately, this is the only study for this region.

In April 1979 a HAB was reported in Bahía de Mazatlán (BAMAZ), Mexico, (SE GOLCA) with high abundances ($6.6 \times 10^6 \text{ cell L}^{-1}$) (Mee et al., 1986). A thermal gradient up to 5°C was registered between 0 and 10 m, associating the bloom with an upwelling event. From 1979 to 1985, several HABs occurred in this bay, being this species one of the most frequently reported (Morey-Gaines, 1982; Cortés-Altamirano, 1987). In 1997, it was concluded that blooms in this region were inhibited due to the influence of El Niño, that attenuated the upwelling of deep nutrient rich waters (Cortés-Altamirano, 2002).

Analog	R ₁	R ₂	R ₃	R ₄
STX	H	H	H	 carbamoyl
NEO	OH	H	H	
GTX1	OH	H	OSO ₃ ⁻	
GTX2	H	H	OSO ₃ ⁻	
GTX3	H	OSO ₃ ⁻	H	
GTX4	OH	OSO ₃ ⁻	H	
B1	H	H	H	 N-sulfocarbamoyl
B2	OH	H	H	
C1	H	H	OSO ₃ ⁻	
C2	H	OSO ₃ ⁻	H	
C3	OH	H	OSO ₃ ⁻	
C4	OH	OSO ₃ ⁻	H	
dcSTX	H	H	H	 decarbamoyl
dcNEO	OH	H	H	
dcGTX1	OH	H	OSO ₃ ⁻	
dcGTX2	H	H	OSO ₃ ⁻	
dcGTX3	H	OSO ₃ ⁻	H	
dcGTX4	OH	OSO ₃ ⁻	H	
GC1	H	H	OSO ₃ ⁻	 <i>p</i> -hydroxybenzoyl
GC2	H	OSO ₃ ⁻	H	
GC3	H	H	H	
GC4*	OH	H	OSO ₃ ⁻	
GC5*	OH	OSO ₃ ⁻	H	
GC6*	OH	H	H	
GC1a*	H	H	OSO ₃ ⁻	 di-hydroxybenzoyl
GC2a*	H	OSO ₃ ⁻	H	
GC3a*	H	H	H	
GC4a*	OH	H	OSO ₃ ⁻	
GC5a*	OH	OSO ₃ ⁻	H	
GC6a*	OH	H	H	
GC1b*	H	H	OSO ₃ ⁻	 sulfo-benzoyl
GC2b*	H	OSO ₃ ⁻	H	
GC3b*	H	H	H	
GC4b*	OH	H	OSO ₃ ⁻	
GC5b*	OH	OSO ₃ ⁻	H	
GC6b*	OH	H	H	

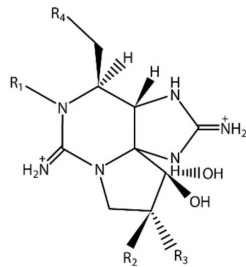


FIGURE 1 | Paralytic shellfish toxins produced by dinoflagellates. Benzoyl toxins are only produced by *Gymnodinium catenatum*. (Modified from Durán-Riveroll and Cembella, 2017).

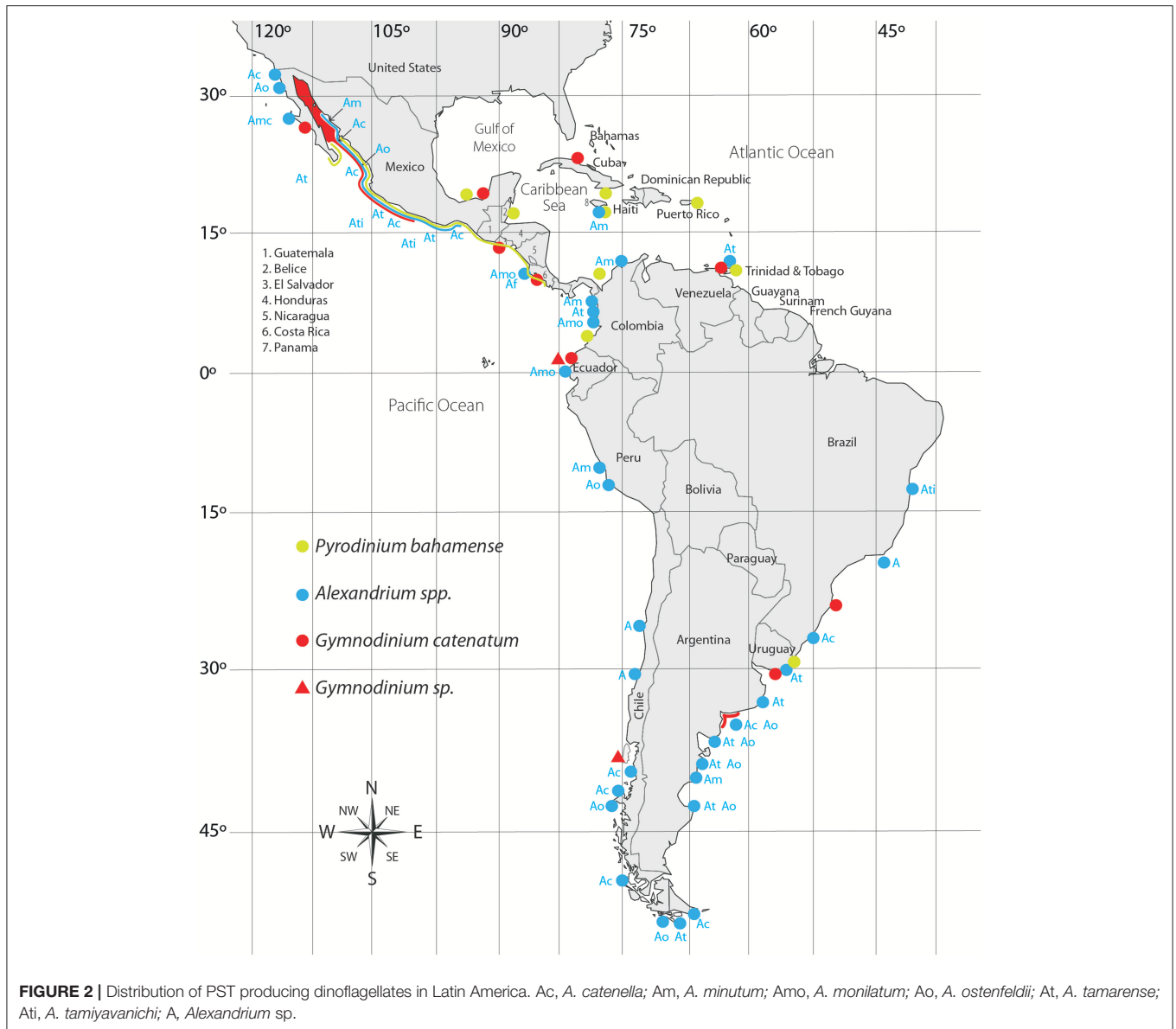
TABLE 1 | Paralytic shellfish poisoning impacts in Latin America.

Dinoflagellate	Locality/date	Impacts	References
<i>Alexandrium</i> spp.	Argentina/1980, 1993	<i>Public health</i> : 2 intoxicated (2 deaths) <i>Epizootic</i> : fish and bird mass mortality	Vinuesa, 1993; Vinuesa and Labal, 1996; Montoya and Carreto, 2007; Carreto et al., 1998b; Montoya et al., 1998; Ferrari, 2001; Sunesen et al., 2014.
	Chile/1972–1998, 2002, 2005, 2006, 2009, 2016	<i>Public health</i> : 348 intoxicated (27 deaths) <i>Epizootic</i> : fish cultured mass mortality. Probably related to marine mammals mass mortality	Fuentealba et al., 1981; Montebruno, 1993; Lagos, 1998; Suárez-Isla and Guzmán-Méndez, 1998; Carvajal, 2002 in FAO (2004); Guzmán et al., 2002; García et al., 2004; Hernández et al., 2016. Fuentes et al., 2008; Mardones et al., 2015; Häussermann et al., 2017; Montes et al., 2018.
<i>Gymnodinium catenatum</i>	Mexico/1979, 1988, 2015	<i>Public health</i> : 37 intoxicated (3 deaths) <i>Epizootic</i> : wild fish, shrimp (adult and larvae cultured), bird and marine mammals mass mortality	de la Garza-Aguilar, 1983; Mee et al., 1986; Cortés-Altamirano and Núñez-Pasten, 1992; Band-Schmidt et al., 2010, 2011; Núñez-Vázquez et al., 2011, 2016; Bustillos-Guzmán et al., 2016; García-Mendoza et al., 2016. Mee et al., 1986; Cortés-Altamirano and Núñez-Pasten, 1992; Alonso-Rodríguez and Páez-Osuna, 2003; Alonso-Rodríguez et al., 2004a,b; Band-Schmidt et al., 2010, 2011; Núñez-Vázquez et al., 2011, 2016; García-Mendoza et al., 2016.
	Venezuela/1979, 1981, 1991	<i>Public Health</i> : 204 intoxicated (11 deaths)	IPCS, 1984; La Barbera-Sánchez et al., 2004
	Ecuador/1998 (<i>Gymnodinium</i> sp.)	<i>Epizootic</i> : sea bird mortality	Torres, 2000.
<i>Pyrodinium bahamense</i>	Mexico/1976, 1985, 1989, 1991, 1992, 1995, 2001, 2010	<i>Public Health</i> : 476 intoxicated (18 deaths)	Saldade-Castañeda et al., 1991; Cortés-Altamirano et al., 1993; Parrilla-Cerrillo et al., 1993; Sotomayor-Navarro and Domínguez-Cuellar, 1993; Ramírez-Camarena et al., 1996, 2002; Ochoa et al., 1998; Orellana-Cepeda et al., 1998; Sierra-Beltrán et al., 1998; Meave del Castillo et al., 2006; Núñez-Vázquez et al., 2007b, 2016; Licea et al., 2008; Band-Schmidt et al., 2011; Gárate-Lizárraga et al., 2011; Sánchez-Flores, 2011; Bustillos-Guzmán et al., 2016.
	Costa Rica/1989–1990	<i>Epizootic</i> : wild fish and sea turtle mass mortality	Mata et al., 1990; Vargas-Montero and Freer, 2004.
	Guatemala/1987	<i>Public Health</i> : 70 Intoxicated (6 deaths)	Rosales-Loessener, 1989; Rosales-Loessener et al., 1989; Rodríguez et al., 1990.
	El Salvador/ 2001–2001, 2009, 2013, 2017	<i>Public Health</i> : 187 Intoxicated (26 deaths) <i>Public Health</i> : 41 Intoxicated <i>Epizootic</i> : sea turtle mass mortality	Enrique Barraza et al., 2004; Barraza, 2009 Amaya et al., 2014, 2017, 2018
	Nicaragua/2005	<i>Public Health</i> : 45 Intoxicated (1 death)	Callejas et al., 2015

In the Mexican Pacific coast, in Nayarit, two HABs were reported in December 2005. The average abundances were $1010 \times 10^3 \text{ cell L}^{-1}$, at a SST of 25°C and high nutrient concentrations (Castillo-Barrera and García-Murillo, 2007). Further south, in Bahía Manzanillo (BMANZ), Colima, HABs have increased in frequency, duration, and coverage. During winter and spring of 1999, HABs were reported with abundances of $35 \times 10^2 \text{ cell L}^{-1}$ (Blanco-Blanco et al., 1999; Morales-Blake et al., 2000). The temperature during the initiation of the bloom was 23°C , and at the highest abundance it reached 25°C . In the same bay, in spring of 2007, blooms were reported, with abundances of $3532 \times 10^6 \text{ cell L}^{-1}$, SST ranged between 24.8 and 26.3°C , salinity from 31.8 to 32.6, and dissolved O_2 from 5.1 to 6.1 mg L^{-1} (González-Chan

et al., 2007). The authors suggested that HABs were caused by upwelling events documented by satellite images.

In May 2010, the species proliferated again in BMANZ, and Bahía de Santiago (Quijano-Scheggia et al., 2012). Water temperature was 21°C at the beginning of May, with salinities of 32.5–34.6. Again, during the HAB, temperature raised from 25.5 to 27.5°C , and when temperature decreased to 22.5°C , the highest abundances ($3.7 \times 10^6 \text{ cell L}^{-1}$) were found. Also, high mean values of dissolved inorganic nitrogen (6.16 – $6.45 \mu\text{M}$), orthophosphates (0.27 – $0.51 \mu\text{M}$), and silicates (7.49 – $21.07 \mu\text{M}$) were reported, coinciding with an upwelling event in the Central Mexican Pacific that lasted 2 weeks and was more intense than previous events. Morning winds



flowed from the coast to the ocean, carrying the HAB off the coast; and in the early afternoon, the flow was in the opposite direction, causing cells to accumulated near the coast, suggesting that this dinoflagellate is present in the oceanic zone in low abundances, and that when the abundance increases, cells are transported to coastal areas during more favorable conditions, such as relaxation periods during upwellings (Quijano-Scheggia et al., 2012).

In the southern Mexican Pacific, in Bahía de Acapulco (BACA), the first record occurred in March 1999 with low abundances from 7 to 78×10^3 cell L^{-1} (Gárate-Lizárraga et al., 2009). Co-occurrence with *M. polykrikoides* was also reported during a HAB from December 2005 to February 2006, with an abundance of *G. catenatum* from 141×10^3 cell L^{-1} to 604×10^3 cell L^{-1} . In December 2007

once again there was a HAB of both species at a SST of 26 – $27^\circ C$.

In the last decade, the species has been reported in the Gulf of Mexico, with the highest densities in October 2008, between 183 and 1797 cell L^{-1} (Zamudio et al., 2013). *Gymnodinium* cf. *catenatum* was reported in oyster beds in Campeche (Poot-Delgado et al., 2015), but no HABs have occurred.

Band-Schmidt et al. (2010), reviewed the reports in the Mexican Pacific, including the GOLCA. They concluded that this dinoflagellate is more abundant during March/April, associated with a SST from 18 to $25^\circ C$, and an increase of nutrients from coastal upwelling and river runoffs. Also, that blooms are inhibited by El Niño. Later studies have confirmed these assertions.

Other Latin American Countries

In the coasts of Ecuador several HAB events occurred in the 1990s (Torres, 2000). Within the list of species, *Gymnodinium* sp. proliferated in February 1993 in the Peninsula of Santa Elena, extending for several kilometers, with a SST of 25°C and a wind speed of 8 kn. HABs of *Gymnodinium* sp. were reported in March 1993, in Estero Salado (Golfo de Guayaquil, GGUAY) and April 1997 in Isla del Muerto (Santa Clara). In August of the same year, in island Santa Clara, this species proliferated ($<5 \times 10^4$ cell L⁻¹) and remained during 5 months. In February/March 1999, abundances of 3.5×10^5 cell L⁻¹ were reported in GGUAY, with phosphates concentrations of 10.1 µg-at L⁻¹ and silicates of 170.69 µg-at L⁻¹. Nutrient values were high in comparison with previous data recorded in the same area. In January 1998 a bloom of *Gymnodinium* sp. occurred at a SST of 25–29.7°C, and was related with ENSO and associated with a bird mortality. In 1999 (April/May) blooms of *Gymnodinium* sp. were reported near shrimp farms and associated to turtle mortality (Torres, 2000). Torres-Chuquimarca (2011) reviewed HABs events from 1968 to 2009, and concluded that from March to May, HABs are recurrent in the coasts of Ecuador and again, the most frequent genus was *Gymnodinium* sp. Areas with the highest incidence of blooms and mortality of organisms were in the GGUAY (80%), particularly Estero Salado, and Río Guayas, Puna island and the coastline of the province El Oro, a region where shrimp farming is an important activity. The mortality of organisms associated to these blooms suggests that the responsible species could be *G. catenatum*.

In Brazil, this species was recorded in 1997 (Proença et al., 2001) in the estuarine complex of Paranaguá (Southern Brazil), where fisheries and aquaculture are important economic activities. From 1913 to 2000 several HAB species that impacted wildlife off the coast of Brazil were reported, including *Gymnodinium* sp., although *G. catenatum* was also reported (Odebrecht et al., 2002). From August 2002 to October 2003, it was reported in Paranaguá, among various toxic species, with a maximum abundance of 6.4×10^3 cell L⁻¹ in February (spring-fall) at 29°C (Mafra-Junior et al., 2006).

In Chile, during March–April 1999, in the archipelago of Chiloé and inland waters, a massive fish mortality that extended >1,330 km took place, from the latitude 42° to 54° S, affecting salmon farming (a loss of ~1,500 t), eels, sea stars, sea urchins, mussels, octopuses and snails (Clément et al., 2001). Mortalities were associated with *Gymnodinium* sp. ($4\text{--}8 \times 10^6$ cell L⁻¹). Also, densities of 3 to 43×10^4 cell L⁻¹ were recorded in the Magellan region (MAGR). The bloom was more intense during neap tides and strong solar radiation. A higher abundance was found in surface waters during the day, and at night at 10 m depth. The HAB originated outside the fjords and channels in the hydrographic front between the open waters (>30 salinity) and the inland waters (salinity 15–25) (Clément et al., 2001). In the archipelago of Chiloé, temperature was 1.5°C higher (15°C) than the expected, suggesting that the growth of dinoflagellates could be stimulated with high irradiance, additionally to prolonged minimal amounts of discharged fresh water in the channels and fjords, providing suitable conditions for oceanic species.

HABs were associated with the front structure of the body of water masses.

In Argentina, this species was recorded for the first time in 1964 (Balech, 1964). Until 1995, during March–April, it was observed in low densities (80 cell L⁻¹) in Mar del Plata (MPlat), but in April 1997, an abundance of 1.9×10^3 cell L⁻¹ was reported (Akselman et al., 1998). This species was also recorded on the coast of Uruguay in 1991 at the end of summer, and in autumn 1993 it was reported in both, Uruguay and MPlat. From 1991 to 2004 blooms occurred in Uruguay at a SST between 21.8 and 24.0°C and salinities between 18.4 and 32 (Méndez, 2006). In March 2003, in coastal waters of MPlat, the species was found in high abundances (8.9×10^4 cell L⁻¹) (Montoya et al., 2006). As toxin profiles differed within both locations, authors suggested that the MPlat HAB was a local event and was not caused by the transportation of the population from the estuarine region.

In Cuba, *G. catenatum* was found in the NE region coinciding with higher nutrient inputs from rivers and anthropogenic discharges. Nevertheless, during dry season, at a SST between 26.8 and 27.3°C, salinity 36.3, abundances were reported between 400 and 800 cell L⁻¹ (Leal et al., 2001). In the southern region, in Bahía de Cienfuegos, it was also reported (2.3×10^3 cell L⁻¹) at a wider SST range (between 23.6 and 27.0°C) (Moreira-González et al., 2013).

Toxin Profiles in Environmental Samples

In Mexico, two review papers have been published regarding the toxicity and toxin profile of phytoplankton and shellfish samples during HABs of *G. catenatum*. The first report included information from the Mexican Pacific coast (Band-Schmidt et al., 2010), and the second only considered data from the GOLCA (Bustillos-Guzmán et al., 2016). As in many other geographic zones, natural phytoplankton PSTs analysis linked to this species are scarce in LAM, and reports have only been done in Uruguay, Argentina and Mexico (Méndez et al., 2001; Gárate-Lizárraga et al., 2006; Montoya et al., 2006; Quijano-Scheggia et al., 2012).

Toxicity of this species is relatively low in natural phytoplankton samples and, according to reported analysis, it oscillates between 1 and 3.7 pg STXeq cell⁻¹ in BAPAZ (Gárate-Lizárraga et al., 2006), and in BMANZ from 1.4 to 10.9 pg STXeq cell⁻¹, with an average of 4.2 pg STXeq cell⁻¹ (Quijano-Scheggia et al., 2012). The PSTs analogs are predominantly sulfocarbamoyl C1/2 (73.0% in molar basis), followed by carbamoyl, STX (16.2%) and NEO (3.3%). Decarbamoyl analogs (dcGTx2/3, dcSTX) are less represented (<5%). In coastal waters of MPlat, toxin content was 122 fmol cell⁻¹ (Montoya et al., 2006), and presented a profile dominated by C1/2 (82 mol%), followed by GTX2/3 (9%), GTX4 (6%), and dcGTx2/3 (4%). The calculated toxin cell content was similar to that reported previously for Uruguayan isolates (Méndez et al., 2001). These values also agreed with the calculated cell toxin concentration related to the first lethal poisoning in Mexico, of 10 pg cell⁻¹ (Mee et al., 1986). Both reviews emphasized the low quantities of PSTs in natural phytoplankton samples of the dinoflagellate. This remark, as shown in this work, could also be extended to other zones in LAM.

Concerning the toxin profile of phytoplankton samples, two patterns can be clearly distinguished: One where sulfocarbamoyl analogs (B, C) are dominant (>50% in molar basis), and a second one, where decarbamoyl analogs (dcGTX2/3, dcSTX) dominate, representing >70% (Gárate-Lizárraga et al., 2004, 2006). The first pattern has been reported in bloom samples of Argentina (Montoya et al., 2006) and Mexico (Quijano-Scheggia et al., 2012). The second was found in samples from Mexico: Bahía Concepción (BACO) and BAPAZ (Gárate-Lizárraga et al., 2004, 2006) in the GOLCA. However, the liquid chromatography with fluorescence detection (LC-FLD) method commonly used for these analyses has some withdrawals, and miss-identification may occur depending on the extraction methods, if two or more toxins have the same retention time or if phantom peaks are present they can compromise the identification of analogs (Bustillos-Guzmán et al., 2015). These patterns have to be further confirmed and analyzed by confirmatory methods such as LC coupled to mass spectrometry detectors alone or in tandem (LC-MS or LC-MS/MS). Benzoyl analogs should also be analyzed in natural phytoplankton samples of *G. catenatum*, since it has been reported that at least 15 of them have been identified in cultured strains (Durán-Riveroll et al., 2017).

During HABs of this species in Mexico, PSTs content of several species of mollusks have been reported, including oysters, clams, and scallops (Bustillos-Guzmán et al., 2016; Quijano-Scheggia et al., 2016). Dominance of B and C, or dc analogs (dcGTX2/3, dcSTX) are usually found in mollusks (Gárate-Lizárraga et al., 2004; Hernández-Sandoval et al., 2009). In *Panopea globosa* analogs could be linked to the bloom phase, with a higher content of C toxins during the HAB occurrence, and a higher content of GTX5, dcGTX2, and dcSTX several weeks afterwards (Medina-Elizalde et al., 2018).

In Venezuela, from August to December 1991, in mussels (*Perna perna*) from Isla Margarita, the most abundant analog was dcSTX; NEO and GTX1-4 were also registered (La Barbera-Sánchez et al., 2004). The presence of dcGTX2/3 was attributed to *G. catenatum*, however, during this bloom cells of *A. tamarensis* were also documented. In Uruguay, during a HAB, the toxin profile in *Mytilus edulis* and the clam *Donax hanleyanus* presented N-sulfocarbamoyl analogs (C1/2, 53% in molar basis) and significant amounts of GTX2/3 and STX for the former bivalve and dc toxins, mainly dcGTX2 (~63%), for the later species (Méndez et al., 2001). Analog variation was also linked to the bloom phase, as well as the cell abundance, ingested cells or specific biotransformations of each bivalve.

Autoecology Studies

Several autoecology studies have been performed with strains of *G. catenatum* from the GOLCA and the Pacific coast of Mexico (reviewed by Band-Schmidt et al., 2010, 2016). Under laboratory conditions, this species tolerates a wide salinity, temperature, and N:P ratio. Strains are able to grow at salinities from 15 to 40; the optimal range changes with seawater source. In general, highest growth rates (from 0.28 to 0.31 div day⁻¹) occur between 28 and 38 (Band-Schmidt et al., 2004). Strains can grow at temperatures between 11.5 and 33°C, with higher growth rates (from 0.32 to 0.39 div day⁻¹) between 21 and 24°C, and maximum cell

concentration between 4,700 and 5,500 cell mL⁻¹ (Band-Schmidt et al., 2004, 2014). This species also tolerates a high range of N:P ratio (from 5.4 to 74.3 μM) with growth rates between 0.20 and 0.24 div day⁻¹, and a maximum cell concentration (5,852 cell mL⁻¹) at a N:P ratio of 23.5 (Bustillos-Guzmán et al., 2011). This wide tolerance to environmental factors probably explains partially the wide distribution of this species along the Mexican Pacific coast.

There are only two studies in LAm where photosynthetic pigments are reported. The first one determined the effect of two light intensities (120 and 350 μmol quanta m⁻²s⁻¹) on a strain from BACO [Murillo-Martínez, 2015, in (Paredes-Banda et al., 2016)], finding that, at the highest light intensity (HL) growth rates were of 0.28 ± 0.06 div day⁻¹, with maximum cell concentration of 5902 cell mL⁻¹; at a lower light intensity (LL) growth decreased in 50% (0.14 div day⁻¹) and the maximum abundance decreased by 45%. At LL the concentration of chl *a* and peridinine was higher than at HL. Also, at HL diadinoxanthine and diatoxanthine increased (18%) indicating the photoprotection in cells is higher compared with LL conditions. No differences were observed in the concentration and toxin profile under both light conditions indicating that toxin synthesis is not related with light intensity. The second study, in an isolate from Santa Catarina, Brazil, determined the pigment profile, detecting chl *a*, chl *c*2, peridinine, diadinoxanthine, and minor carotenoids (Proença et al., 2001).

Few studies have been performed in LAm to understand the effect of planktonic species on its growth and survival. In the GOLCA, grazing studies have been performed with the copepod *Acartia clausi* and the dinoflagellate *Noctiluca scintillans*, demonstrating that both are important predators of the dinoflagellate, suggesting they have an important ecological role in the regulation of its blooms (Palomares-García et al., 2006; Bustillos-Guzmán et al., 2013). It was also demonstrated the allelopathic effect of the raphidophyte *Chattonella marina* var. *marina* and the dinoflagellate *Margalefidinium polykrikoides* toward *G. catenatum*. Both species inhibited the growth of *G. catenatum* and caused changes in its morphology, and chain formation. Inhibition was stronger and occurred in a shorter time with *Chattonella*; mortality occurred with and without direct cell contact, indicating that toxic metabolites are released to the culture medium (Fernández-Herrera et al., 2016; Band-Schmidt et al., 2017). These results suggested that biotic factors affect its growth providing new insights on the interactions between this dinoflagellate and co-occurring planktonic species.

Gymnodinium catenatum Toxin Profiles Under Laboratory Conditions

In LAm, several strains of *G. catenatum* have been isolated and maintained in culture for laboratory studies (Figure 3). Toxin profiles in laboratory conditions, however, have been reported only from Brazil and Mexico. In Brazil, one isolate has been studied, isolated from Armação do Itapocoroy (AdI). In Mexico, the isolates used for autoecological studies come from Baja California Sur (BAPAZ, BACO); Sinaloa (BAMAZ); Colima (BMANZ); Bahía de Topolobampo, Sinaloa (TOPO) and Lázaro

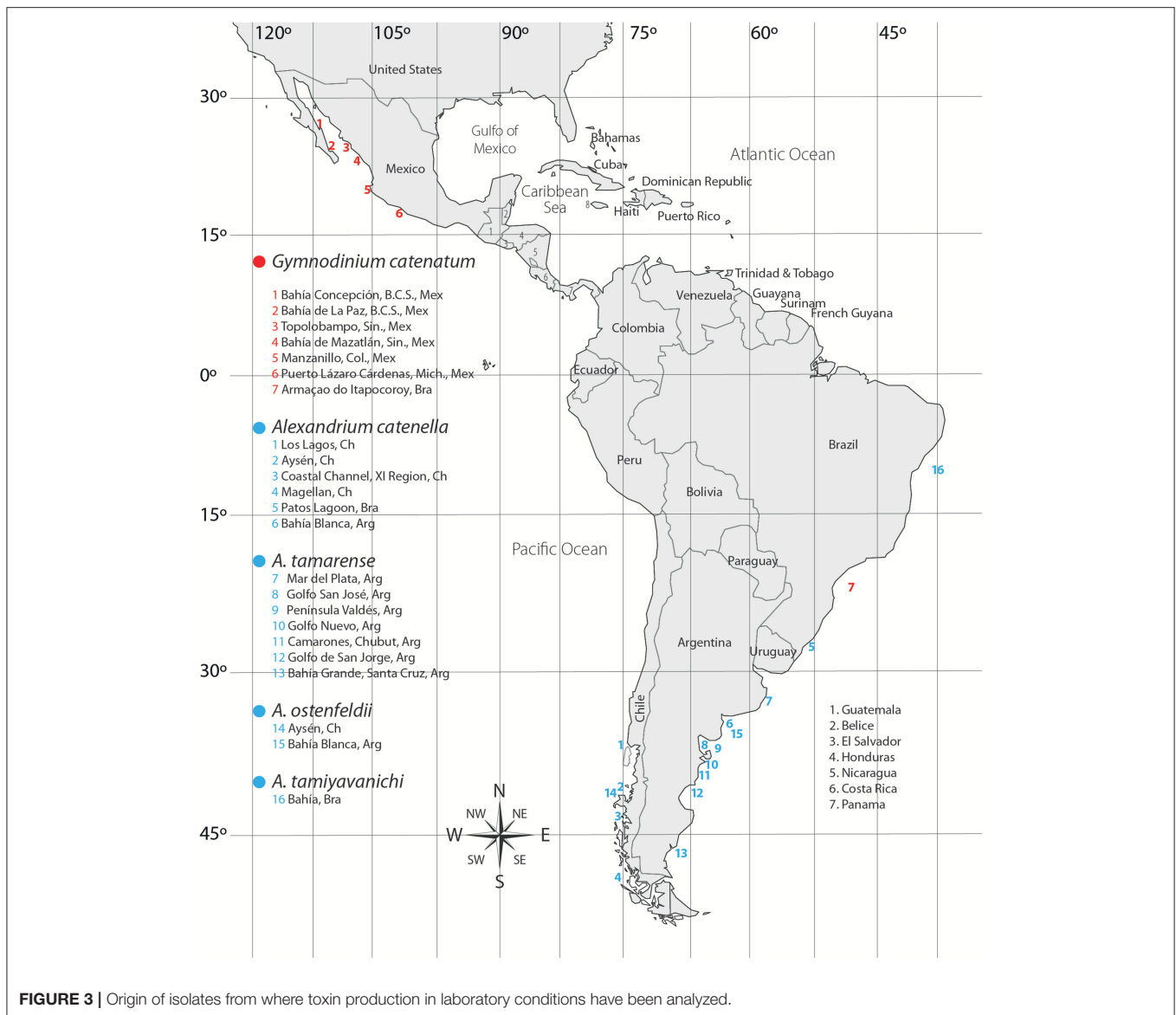


FIGURE 3 | Origin of isolates from where toxin production in laboratory conditions have been analyzed.

Cárdenas, Michoacán (CAR). In these studies, toxin analyses have been performed mostly by HPLC-FLD. This technique, though reliable for most of the common STX analogs, has some drawbacks that have been mostly reduced by several improvements of the methods. Nevertheless, it is important to keep in mind that some of these drawbacks are persistent and have led to important confusions in toxin analysis.

In 2001, laboratory studies started in Brazil. The only available standards for the analysis were GTX1-4, NEO, and STX, but none of these analogs were found in the culture samples, and peaks eluted in retention times previously reported for N-sulfocarbamoyl toxins. The production of these analogs was later proven by acidic hydrolysis of the extract and further analysis, showing a peak for GTX2/3, equivalent to the C1/2 toxins, characteristic of this species (Proença et al., 2001).

Since 2005, toxin profiles from Mexican isolates started to be studied. These isolates have been mainly from the GOLCA

region, and the Mexican Pacific. Their toxin profile included NEO*¹, dcSTX, dcGTX2/3, B1, and C1/2 (Table 2). The low molar percentages of B toxins was considered a distinctive characteristic of Mexican strains, compared to reports from Portugal and Spain (Negri et al., 2001; Ordás et al., 2004; Gárate-Lizárraga et al., 2005), but a huge variation in profiles and toxin content among strains was found, and it was also proven that they can vary with culture age and culture conditions (Gárate-Lizárraga et al., 2005).

It has been reported that the toxin content was slightly variable with culture age, but differences were not always significant (Band-Schmidt et al., 2005). As cultures aged, a decrease in the number of isolates producing NEO*, GTX2/3, C1/2, and B2 was registered, and a there was significant increase of decarbamoyl

¹In 2015, Bustillos-Guzmán and collaborators, using LC-MS/MS found that the analog reported as NEO in previous analysis could have corresponded to dcNEO.

analogs (dcSTX, dcGTX2/3) (**Table 2**). Nevertheless, in another study, no significant differences in toxin content or toxicity related to culture age were found, neither differences between strains isolated from vegetative cells and cysts. They also reported STX during certain days of the culture, a toxin that is almost never reported in Mexican isolates, which could indicate that the rest of the time it is produced in non-detectable concentrations (Band-Schmidt et al., 2006).

Later, the toxin profile of one isolate from BACO was analyzed, though the main goal was to determine its toxic capacity when fed to the copepod *A. clausi*. Toxin profile of the isolate showed only the commonly reported analogs C1/2, dcSTX, and dcGTX2/3, and no B1, B2, dcNEO or any carbamoyl toxins that were previously reported (Palomares-García et al., 2006) (**Table 2**). Also, the effects of this dinoflagellate were demonstrated on the clam *Nodipecten subnodosus*. In this case, toxins were extracted with a different acetic acid concentration (0.1 N vs. 0.03 N in former experiments) (Estrada et al., 2007). The authors found a vast amount of GTX toxins, but did not specify the analogs, and no N-sulfocarbamoyl toxins, such as B1, B2, and C1-4 were reported (**Table 2**), though these analogs have been often described as the main toxin component for the species. A year later, the effect of the PSTs were studied in the white leg shrimp, *Litopenaeus vannamei*, using an isolate from BACO (Pérez-Linares et al., 2008). Cultures were grown in f/2 medium and the toxin profile was analyzed prior to injecting the shrimp with the toxic extracts. The profile was very different from previous reports from the same isolate, probably related to differences in culture media (f/2 vs. GSe), temperature (21°C vs. 26 ± 1°C), and toxin extraction, that was performed with hydrochloric acid instead of acetic acid. The described profile for this isolate was composed by STX, NEO, GTX1/4, GTX2/3, and dcSTX (Pérez-Linares et al., 2008), and no N-sulfocarbamoyl toxins or other decarbamoyl toxins (dcNEO, dcGTX1-4) (**Table 2**), were reported. Probably, the acidic conditions of the extraction could modify the toxin profile, or the lack of N-sulfocarbamoyl standards prevented the detection of these toxins. As reported in many other countries, the presence of dcSTX, dcGTX2/3, and C1/2 are considered usual components of *G. catenatum* strains from the Pacific Mexican coasts, also, being the decarbamoylated analogs the most important in terms of toxin potency while the latest are usually the most important in terms of molar contribution (Band-Schmidt et al., 2010).

In the search for a better understanding of how the environmental factors affect the toxin profile and toxicity, *in vitro* experiments have been performed using different nutrient concentrations and temperature regimes. In 2012, the analysis of an isolate from BACO in the GOLCA, with different N:P ratios was reported (Bustillos-Guzmán et al., 2012). Toxins were extracted with 0.03 N acetic acid and a subsample was hydrolyzed to detect N-sulfocarbamoyl toxins. No significant differences in cell toxicity or toxin profile were recorded, and by the end of the experiment, an increase in total toxicity was evident in all treatments, as reported previously (see Band-Schmidt et al., 2005, 2006; Gárate-Lizárraga et al., 2005). The toxins found in these experiments were STX, NEO*, dcSTX, dcGTX2/3, B1, B2, and C1-3 (**Table 2**). This toxin profile varied slightly with previous

reports of isolates from the same geographical area, where STX and/or GTX1/4 and no N-sulfocarbamoyl toxins were described (Estrada et al., 2007; Pérez-Linares et al., 2008).

The effect of temperature in toxin profile, toxicity and growth was studied in 2014 in eight Mexican isolates from four locations in the Pacific coast: BAPAZ, BAMAZ, TOPO, and CAR (Band-Schmidt et al., 2014). All isolates produced the same ten analogs (**Table 2**), though significant differences were found among them in terms of GTX2/3 and B toxins, all of them produced higher proportions of B and C toxins. At lower temperatures (16–19°C) the production of C toxins was greater and at higher temperatures (30–33°C) B toxins represented up to 63.4% of the toxin profile, whereas at lower temperatures the maximum was 12.7% in molar basis. Decarbamoyl toxins (dcSTX, dcGTX2) were more abundant at 21°C, but since the main changes in toxin profile were within the low-potency toxins, no changes in cell toxicity related to temperature were found. An interesting relationship between dcSTX and dcGTX2 was found since both increased or decreased simultaneously (Band-Schmidt et al., 2014). This toxin profile change related to temperature, from mostly C1/2 toxins in lower temperatures to mostly B1/2 at high temperatures could be explained by enzyme activity, but more studies are necessary.

In 2001, new analogs reported for *G. catenatum* that brought attention to this species (Negri et al., 2001). Chromatographic peaks eluted late in the C toxin chromatograms. These peaks were later confirmed in Spanish isolates (Ordás et al., 2004), and reported as C5 and C6 compounds or possible artifacts, but it was later confirmed to be new toxin analogs containing a benzoyl ring in the lateral chain. These toxins were named GC1-3 toxins or “hydrophobic toxins” (Negri et al., 2003b). These peaks were previously noted in isolates from different countries, and in 2007 Negri and collaborators reported the widespread presence of these analogs in isolates from Australia, China, Japan, Portugal, Uruguay, and Spain, comprising between 10 and 63 mol% of the total toxin in cultured vegetative cells or cysts (Negri et al., 2007). One year later, a Portuguese strain was analyzed and several unknown oxidation products were found, in addition to the three GC toxins previously reported (Vale, 2008). Further mass spectrometry analysis confirmed the existence of a wide range of GC analogs (**Figure 1**) (Vale, 2008). In 2011, these analogs were searched for and found in Mexican isolates (Bustillos-Guzmán et al., 2011). The isolate used for these analysis was from BACO, and the toxin detection was done by HPLC-FLD, using the methodology previously described by Vale (2008) and comparing the retention times of the later peaks. The GC toxins found in this isolate were abundant and mostly composed by the sulfobenzoylated, the C-11 sulfated and the non-sulfated analogs (corresponding to the GCb series, GC1/2 and GC3 analogs, respectively). Apart from GC toxins, this analysis found the commonly reported B and C analogs but no STX or NEO, bringing out the question about previous analysis and the possibility of having misidentified dcSTX and dcNEO for STX and NEO (Bustillos-Guzmán et al., 2011). A second report of GC toxins in Mexico was from an isolate from the Pacific coast (MANZ), using nuclear magnetic resonance (NMR) in semi-purified

TABLE 2 | *Gymnodinium catenatum* toxin analogs reported under laboratory conditions.

N	Origin	Culture media	STX	NEO	GTX1/4	GTX2/3	B1	B2	C1/2	C3/4	dcSTX	dcNEO	dcGTX1/4	dcGTX2/3	GC	Reference
1	Armação do Itapocoroy, Bra	K + SE	-	-	-	-	?	?	1/1	?	?	?	?	?	?	Proença et al., 2001
3	BAPAZ, B.C.S. Mx	GSe	-	3/3	-	3/3	3/3	3/3	3/3	-	3/3	-	-	3/3	?	Gárate-Lizárraga et al., 2005
5	BACO, B.C.S. Mx	GSe	-	5/5	-	5/5	3/5	5/5	5/5	-	5/5	-	-	5/5	?	
2	BAMAZ, Sin, Mx	GSe	1/2	2/2	-	1/2	1/2	2/2	2/2	-	2/2	-	-	2/2	?	
16	BACO, B.C.S. Mx	f/2 + H ₂ SeO ₃	-	?/16	-	t	-	?/16	16/16	-	16/16	-	-	16/16	?	Band-Schmidt et al., 2005
3	BACO, B.C.S. Mx	GSe	?	3/3	-	3/3	3/3	3/3	3/3	?	-	-	-	3/3	?	Band-Schmidt et al., 2006
2	BAPAZ, B.C.S. Mx	GSe	?	2/2	-	2/2	2/2	2/2	2/2	?	-	-	-	2/2	?	
2	BAMAZ, Sin, Mx	GSe	?	2/2	-	2/2	2/2	2/2	2/2	?	-	-	-	2/2	?	
1	BACO, B.C.S. Mx	f/2 + H ₂ SeO ₃	-	-	-	-	-	1/1	1/1	-	1/1	-	-	1/1	?	Palomares-García et al., 2006
1	BACO, B.C.S., Mx	GSe	-	-	1/1	1/1	-	-	-	-	-	-	-	-	?	Estrada et al., 2007
1	BACO, B.C.S., Mx	f/2	1/1	1/1	1/1	1/1	-	-	-	-	1/1	-	-	-	?	Pérez-Linares et al., 2008
1	BACO, B.C.S., Mx	f/2 + H ₂ SeO ₃	1/1	1/1	-	-	-	1/1	1/1	1/1	1/1	-	-	1/1	?	Bustillos-Guzmán et al., 2012
1	BACO, B.C.S., Mx	f/2 + H ₂ SeO ₃	-	-	-	1/1	1/1	1/1	1/1	1/1	1/1	1/1	-	1/1	1/1	Bustillos-Guzmán et al., 2011
1	MANZ, Col, Mx	GSe	?	?	?	?	?	?	?	?	?	?	?	?	?	Durán-Riveroll et al., 2013
2	BAPAZ, B.C.S., Mx	f/2 + H ₂ SeO ₃	-	-	2/2	2/2	2/2	2/2	2/2	-	2/2	2/2	-	2/2	?	Band-Schmidt et al., 2014
3	TOPO, Sin, Mx	f/2 + H ₂ SeO ₃	-	-	2/2	2/2	2/2	2/2	2/2	-	2/2	2/2	-	2/2	?	
1	BAMAZ, Sin, Mx	f/2 + H ₂ SeO ₃	-	-	2/2	2/2	2/2	2/2	2/2	-	2/2	2/2	-	2/2	?	
2	CAR, Mich, Mx	f/2 + H ₂ SeO ₃	-	-	2/2	2/2	2/2	2/2	2/2	-	2/2	2/2	-	2/2	?	
2	BACO, B.C.S., Mx	GSe	-	-	-	2/2	2/2	2/2	2/2	2/2	-	2/2	2/2	2/2	?	Bustillos-Guzmán et al., 2012
2	BACO, B.C.S., Mx	f/2 + H ₂ SeO ₃	-	-	-	2/2	2/2	2/2	2/2	2/2	-	2/2	2/2	2/2	?	
2	BAPAZ, B.C.S., Mx	GSe	-	-	-	2/2	2/2	2/2	2/2	2/2	-	2/2	2/2	2/2	?	
2	BAPAZ, B.C.S., Mx	f/2 + H ₂ SeO ₃	-	-	-	2/2	2/2	2/2	2/2	2/2	-	2/2	2/2	2/2	?	
2	BAMAZ, Sin, Mx	GSe	-	-	-	2/2	2/2	2/2	2/2	2/2	-	2/2	2/2	2/2	?	
2	BAMAZ, Sin, Mx	f/2 + H ₂ SeO ₃	-	-	-	2/2	2/2	2/2	2/2	2/2	-	2/2	2/2	2/2	?	
1	CAR, Mich, Mx	GSe	-	-	-	1/1	1/1	1/1	1/1	1/1	-	1/1	1/1	-	1/1	
1	CAR, Mich, Mx	f/2 + H ₂ SeO ₃	-	-	-	1/1	1/1	1/1	1/1	1/1	-	1/1	1/1	-	1/1	
1	MANZ, Colima, Mx	GSe	-	-	-	1/1	1/1	1/1	1/1	1/1	-	1/1	1/1	-	1/1	
1	MANZ, Colima, Mx	f/2 + H ₂ SeO ₃	-	-	-	1/1	1/1	1/1	1/1	1/1	-	1/1	1/1	-	1/1	
3	BACO, BAPAZ, B.C.S. and CAR, Mich, Mx (mix)	GSe	?	?	?	?	?	?	?	?	?	?	?	?	?	Durán-Riveroll et al., 2017

N, number of isolates analyzed; t, trace amounts; ?/No, positive but data not shown in original publication; ?, these analogs were not searched for. Epimeric pairs have been considered together because they easily epimerise under extraction and analytical conditions, so their measurements do not necessarily reflect their original composition in plankton cells (Krock, B., personal communication).

BAPAZ, Bahía de La Paz, Baja California Sur; BACO, Bahía Concepción, Baja California Sur; BAMAZ, Bahía de Mazatlán, Sinaloa; MANZ, Manzanillo, Colima; TOPO, Bahía de Topolobampo, Sinaloa; CAR: Port of Lázaro Cárdenas, Michoacán.

Mx, Mexico. Bra, Brazil.

water-methanol fractions, where the *para*-hydroxylated benzoyl ring was visible (Durán-Riveroll et al., 2013).

In 2015, Bustillos-Guzmán and collaborators analyzed the toxin profile of *G. catenatum* from five locations along the Mexican Pacific coast that were cultivated in two different media (GSe, *f*/2 + H₂SeO₃). Analyses were performed by hydrophilic interaction liquid ion chromatography (HILIC) coupled to tandem mass spectrometry (MS/MS). In these analysis, C1/2 analogs were the most abundant, with >85% on molar basis. Decarbamoyl toxins, such as dcSTX and dcNEO represented a mean average content <5% and no differences were found between the two culture media (Bustillos-Guzmán et al., 2015). The richness of GC analogs in Mexican isolates was confirmed but due to the lack of standards, they could not be quantified, but in terms of relative abundance (peak area cell⁻¹) an interesting geographical increasing trend from strains from northern to southern regions was found (Bustillos-Guzmán et al., 2015). Also, the study was interesting since it was not possible to confirm the presence of GTX2/3 that had been reported in previous analysis done by HPLC-FLD. The same occurred for STX, and NEO, which led to the question on the existence of phantom peaks, particularly in dcNEO, which probably had been misreported as NEO. These findings raised doubts on the reliability of the most used technique in Mexico and LAm in general, especially for analogs for which reference standards are unavailable, such as GC toxins (Bustillos-Guzmán et al., 2015). For these reasons, it has been proposed that a second detection method, such as MS, should be performed in order to overcome the normal drawbacks of the identification methods.

The most recent research on GC analogs has been performed by Durán-Riveroll et al. (2017). They confirmed the production of fifteen GC analogs in the mixture of three Mexican isolates from the GOLCA, and the coasts of Michoacán, in the Pacific coast. The microalgal extract was fractionated by reverse-phase column chromatography and a MS/MS-guided fractionation was performed. Confirmation was done using MS on the search of the precursor ions and their fragments, using HILIC-MS/MS. For the analogs with same mass and mass fragments, ¹H-NMR spectroscopy was used to discriminate between them (GC4/5 and GC1a/2a). Fifteen GC analogs were identified: GC1-6, GC1a-5a, GC1b/2b, and GC4b/5b. During this study, the chromatographic behavior of the previously named “hydrophobic analogs” was analyzed, and it was revealed that GC analogs are as hydrophilic as many of the “common hydrophilic” analogs. In light of these results, authors proposed a better designation as “benzoyl analogs” and subdivide them into *para*-hydroxybenzoyl, dihydroxybenzoyl, and sulfo-benzoyl analogs (Durán-Riveroll et al., 2017). The combination of high resolution techniques, such as HILIC-MS/MS and ¹H-NMR represented an important progress on the GC analogs identification and proved the need of the use of confirmatory techniques, mostly when relatively unknown analogs are investigated.

Cell Toxin Content

Reported toxicities from different studies are shown in **Table 3**. Differences in toxicity have been found among isolates (Band-Schmidt et al., 2006), related mainly to the toxin profile: isolates

from BAMAZ have been found to be the most toxic with a higher amount of the more potent carbamoyl toxins; isolates from BAPAZ were in second place and the ones from BACO, where the least toxic. A wide variation in toxicity among isolates from the same area have also been found, which has been reported previously in other geographical areas (Bolch et al., 2001; Seok Jin et al., 2010). Also, toxicity in all isolates reached their highest point during the exponential growth phase (Band-Schmidt et al., 2006), as described for other isolates. The only other report of the toxin content in cultured cells is from a Brazilian isolate where the toxicity was estimated by mouse bioassay to be 29 pg STXeq cell⁻¹ (Proença et al., 2001).

According to previous studies, cultured dinoflagellates tend to produce less toxin per cell (cell toxin quota) due to the “forced growth” by high nutrient conditions, compared to natural populations (Cembella, 1998). In nature, cell division could take longer and toxins tend to concentrate inside the cell. Nevertheless, *in vitro* observations from *G. catenatum* cultures in Mexico have shown higher cell toxin quotas than natural populations, probably related to differences in nutrients between natural and culture conditions (Gárate-Lizárraga et al., 2005; Band-Schmidt et al., 2006). However, the experiments with different N:P ratios did not shown effects in toxicity and/or toxin profile (Bustillos-Guzmán et al., 2012).

Docking Studies

Since the properties of GC analogs, such as mammalian toxicity, receptor-binding affinities and biological action mechanisms are mostly unknown due to the lack of analytical standards and the difficulties in producing and purifying these toxins, computational tools were used as an alternative strategy for their exploration. Only one docking study on *G. catenatum* toxins has been done in LAm, by Durán-Riveroll et al. (2016). Docking modeling is a useful *in silico* tool that can reveal molecular interaction mechanisms in great detail, generating information that cannot be deduced from electrophysiological approaches (Gordon et al., 2013). Molecular docking approaches have been key in the description of the interactions of several toxins with Na_v channels, like with *μ*-conotoxins (Li et al., 2001). This approximation, even though it allows screening of many ligands for a given protein (Halperin et al., 2002; Brooijmans and Kuntz, 2003), also has certain disadvantages, related to its accuracy (Warren et al., 2006). In any case, it is possible to obtain important clarifying information about the mode of action and affinity of toxins in a protein target.

Members of the Na_v channels family are the membrane-protein targets for STX and its analogs. These interactions are mediated by the guanidinium groups in the toxin molecules, which are formed by a central carbon and three nitrogen atoms, and have a positive charge at physiological pH, directly implicated in their binding capacity to the Na_v, and allows the toxins to block the Na⁺ influx to the cell (Durán-Riveroll and Cembella, 2017). Docking studies have been useful to gain a better understanding of the blocking capacity, and due to the absence of information on GC analogs, theoretical studies are considered essential to increase the knowledge about their properties. In this study, authors found that all eighteen GC

TABLE 3 | Toxin content of cultured *G. catenatum* under laboratory conditions.

No. of isolates	Origin	Culture media	Toxicity (pg STXeq cell ⁻¹)	References
1	Armação do Itapocoroy, Bra	K + SE	28.0	Proença et al., 2001
3	BAPAZ, B.C.S. Mx	GSe	15.1	Gárate-Lizárraga et al., 2005
5	BACO, B.C.S. Mx	GSe	13.3	
2	BAMAZ, Sin, Mx	GSe	20.3	
16	BACO, B.C.S. Mx	f/2 + H ₂ SeO ₃ 17 days	25.7 ± 6.2*	Band-Schmidt et al., 2005
16	BACO, B.C.S. Mx	f/2 + H ₂ SeO ₃ 22 days	27.9 ± 17.7*	
3	BACO, B.C.S. Mx	GSe	13–47	Band-Schmidt et al., 2006
2	BAPAZ, B.C.S. Mx	GSe	36–73	
2	BAMAZ, Sin, Mx	GSe	37–101	
1	BACO, B.C.S. Mx	f/2 + H ₂ SeO ₃	60.3	Palomares-García et al., 2006
1	BACO, B.C.S. Mx	f/2 + H ₂ SeO ₃	21.8 ± 2.9	Bustillos-Guzmán et al., 2012

BAPAZ, Bahía de La Paz, Baja California Sur; BACO, Bahía Concepción, Baja California Sur; BAMAZ, Bahía de Mazatlán, Sinaloa. Mx, Mexico. Bra, Brazil. SE, Soil Extract. *Average toxicity was not significantly different.

analogs theoretically interacted with the Nav 1.4 (muscular Nav channel) residues in the two protein models used for the experiment. They also reported high affinity values (as low binding energies ΔG), for some of the GC toxins, raising the hypothesis that at least some of them could be toxic to mammals because they are able to reach key protein residues by electrostatic interactions (Durán-Riveroll et al., 2016). As the model of ion channel of Nav eukariotic structure continues improving (Shen et al., 2017) instead of using homology models of the bacterial Nav, as in this analysis, docking studies will generate more precise information. The greatest obstacle, however, is that docking programs, in order to reduce computational costs, consider the protein as a rigid body, which is far from real. The omission of conformational protein changes due to ligand binding can yield unrealistic results, and for that reason, the use of molecular dynamics (MD) is highly recommended to be used in combination with docking approach (Deeb et al., 2010), though the later greatly increases computational costs and it is more time consuming than molecular docking simulations.

Molecular Studies

The first study of genetic variation among strains of *G. catenatum* from Asia, Europe, and Australia was published by Bolch and collaborators in 1999. Populations from Japan, Spain, and Portugal showed higher genetic similarities than with those from Australia, where a recent dispersal could have happened (Bolch et al., 1999). In LAm, molecular analyses of the species are scarce. In 2008 the LSUrDNA sequences and morphology of strains from the GOLCA were reported, where a single nucleotide polymorphism was identified in sequences from strains from BACO, suggesting a mutation or genetic isolation (Band-Schmidt et al., 2008). Authors proposed that the Western Pacific population could be an ancestral population of this species. In 2013, the gene expression and histological injuries in the Japanese oyster *Crassostrea gigas* when exposed to *G. catenatum*

toxins were analyzed, determining changes in the transcription level cell-cycle regulation genes and epithelial damages associated to inflammatory responses, concluding that the toxins induced DNA damage in this mollusk (García-Lagunas et al., 2013).

The origin of STX genes and the relationship between copy number and genome size in *G. catenatum* has not been well established, recently Mendoza-Flores et al. (2018) carried out a study to determine the origin of *sxtA* (domains *sxtA1* and *sxtA4*) and their gene copy number. The phylogenetic tree with partial sequences of *sxtA1* of *G. catenatum* showed a separated subclade of toxic and non-toxic *Alexandrium* species, while sequences of *sxtA4* showed two well-supported clades within the dinoflagellates group, separating *G. catenatum* from *Alexandrium* species. Authors concluded that *G. catenatum* did not acquire *sxtA* gene by horizontal gene transference from *Alexandrium*. Moreover, differences in copies number of *sxtA1* and *sxtA4* between *G. catenatum* and *Alexandrium* species were observed.

Pyrodinium bahamense

Pyrodinium bahamense is an important member of PST-producing marine dinoflagellates, especially in tropical waters, and has caused more human illnesses and fatalities than any other PST producing dinoflagellate (Usup et al., 2012). This species was originally described from New Providence Island, Bahamas (Plate, 1906). For many years, two varieties were assigned to the genus: the Indo-Pacific variety designated “*compressum*,” and the Atlantic-Caribbean variety “*bahamense*.” However it was demonstrated that the range of distribution of both varieties extended beyond these original locations (Martínez-López et al., 2007; Morquecho, 2008), and that both varieties co-occur in several areas (Glibert et al., 2002; Gárate-Lizárraga and González-Armas, 2011). In addition to several morphological attributes, one of the primary differences between both varieties was the

absence of toxin production in var. *bahamense* (Steidinger et al., 1980). However, a recent re-evaluation found no consistent morphological or molecular traits that could be used to separate the varieties, since toxin production was also demonstrated in var. *bahamense* (Landsberg et al., 2006; Mertens et al., 2015).

Its distribution in the Pacific coast extends from southern GOLCA to Colombia (Martínez-López et al., 2007; Rodríguez-Salvador and Meave del Castillo, 2007; Morquecho, 2008; Gárate-Lizárraga and González-Armas, 2011; Usup et al., 2012). In the Atlantic coast it has been reported from the Gulf of Mexico to Uruguay (Licea et al., 2013; Limoges et al., 2015; Mertens et al., 2015; Poot-Delgado et al., 2015; Cusick et al., 2016). HABs have been linked in several occasions to human poisoning (Rosales-Loessener, 1989; Rodríguez et al., 1990; Saldade-Castañeda et al., 1991; Núñez-Vázquez et al., 2011; Gárate-Lizárraga et al., 2012; Callejas et al., 2015) as well as to epizootic events (fish and sea turtles) (Núñez-Vázquez et al., 2011; Amaya et al., 2018) (Table 1). The first HAB of this dinoflagellate in LAm was reported in the coast of Guatemala in 1987, causing 175 intoxications and 26 fatalities (Rosales-Loessener, 1989). PSP cases produced by this species have affected several Latin American countries, notably in the southern Mexican Pacific, and Central America (Figure 2).

Bloom Dynamics Mexico

Vegetative cells of *P. bahamense* were reported for first time in 1942 in Mexico (Osorio-Tafall, 1943). In several occasions, this species has been registered from the coasts of Michoacán to Chiapas (Figure 2) (Cortés-Altamirano et al., 1993; Orellana-Cepeda et al., 1998). In winter 1995, a HAB was recorded on the SW coast, affecting invertebrates, fish, and causing the death of 145 turtles (Orellana-Cepeda et al., 1998).

In the GOLCA, it was recorded for the first time in May 2005, in the lagoon system of Topolobampo-Santa María-Ohuira, with an abundance of 100 cell L⁻¹. Cysts were also recorded (Martínez-López et al., 2007). Shortly afterwards, vegetative cells in the island San José in BAPAZ were reported (Morquecho, 2008). The author mentioned that the relatively low frequency of cysts of *P. bahamense* in this zone may indicate the influence of warm water from the tropical Pacific, and therefore it is likely that El Niño event contributed to the transport of vegetative cells or cysts from Central America. High temperatures prevailed in summer (July-October) when outbreaks occurred close to San José Island. From July to November 2010, in the southern peninsula of Baja California, it was found with abundances between 800 and 1110 cell L⁻¹ at a SST of 28–28.5°C and salinity of 35.2 (Gárate-Lizárraga and González-Armas, 2011). These contributions widen the northern distribution of this species in the Pacific coastline of LAm. The presence of this dinoflagellate from July to November was considered unusual, and again authors attributed this to El Niño event. It was suggested that this is an invasive species and that it was probably transported by surface tropical waters moving within the GOLCA (Cortés-Altamirano et al., 2006; Gárate-Lizárraga and González-Armas, 2011). Also, the species was recorded in coastal lagoons of

Sinaloa (Alonso-Rodríguez et al., 2015). To date, no HABs of *P. bahamense* have been reported in this region.

During December 1989 and February 2002, in the southern Pacific coast of Mexico, HABs of this species were registered (Licea et al., 2008). Environmental conditions based on satellite images reported a positive thermal anomaly of 1.5°C between southern Mexico and Costa Rica. The dinoflagellate was recorded on the coast of Oaxaca from September 2009 to June 2010, with abundances from April to June 2010 of 4 × 10³ cell L⁻¹ and 3.3 × 10⁴ cell L⁻¹, respectively. The SST ranged from 27.4 to 31.3°C and from 28.4 to 30°C, respectively (Alonso-Rodríguez et al., 2015).

In 2001, in BACA, cysts were reported (Meave del Castillo et al., 2006). Ten years later, in July 2010 vegetative cells were recorded at low abundances, from 1 × 10³ to 1462 × 10⁶ cell L⁻¹ (Gárate-Lizárraga et al., 2012).

Based on a cyst study in the Gulf of Tehuantepec, it was suggested that the species has been present in this region since 1860, and that cells have been transported recently from the Indo-Pacific population (Sánchez-Cabeza et al., 2012). They mentioned that, since 1950, its influx increased in this region, due to La Niña events, however historical data of strong El Niño anomalies, recorded from 1892 to 1983, indicated there was a minimum cyst flow. Emphasizing that in 81% of cases these fluxes coincided with heavy rain (>400 mm) and high nutrients, and that high cyst flow was correlated with lower temperatures (<24.5°C). The authors proposed that low SST (conditions during La Niña) could favor the dinoflagellate growth. When a rapid transition to high SST conditions occur, rainfall increased with an input of large amounts of nutrients, making it possible to maintain the bloom. At the termination of the bloom, cysts could be incorporated into the sediments. They suggested that this situation may occur during strong upwelling conditions, hypothesis that needs to be confirmed. It was also suggested that the exceptional records in the coastline and offshore waters of the Mexican central Pacific during the 1999–2000 La Niña could suggest a link with the recurrence of HABs (Hernández-Becerril et al., 2007).

In the southern Gulf of Mexico, according to data recorded from 1966 to 1996, in coastal lagoons this species is widely distributed throughout the year (Gómez-Aguirre, 1998). In Laguna de Términos, the highest reported abundance has been 3 × 10³ cell mL⁻¹, and blooms are more frequent in autumn-winter. HAB formation could be associated with seawater fluxes and northern winds that remove the water column. Mangrove forests could also provide suitable conditions for cell accumulation (Gómez-Aguirre, 1998). In the Gulf of Mexico, this dinoflagellate is limited to the SE region (Aké-Castillo and Poot-Delgado, 2016).

Other Latin American Countries

In November 2005 and March 2006, in the coast of El Salvador, satellite images showed a positive thermal anomaly of 1.5°C between southern Mexico and Costa Rica during a HAB of *P. bahamense* (Licea et al., 2008). In December 2005, its abundance reached 489 × 10⁵ cell L⁻¹ and in March 2006 it decreased to 15 cell mL⁻¹. The authors mentioned that blooms could be influenced by SST, strong winds and heavy precipitation.

From November to June 2010 in the same area, a bloom of ~13 km was recorded with abundances of 15.3×10^6 cell L⁻¹. Offshore concentrations were of 22×10^3 cell L⁻¹ (Licea et al., 2012). They stated that HABs of this dinoflagellate in Central America are influenced by smaller scale gyres, upwelling and local hydrographic conditions. Cysts were detected in March and August 2012 in the Gulf of Fonseca (Alvarado et al., 2014).

In November 2005, a HAB was detected on the Pacific coast of Nicaragua, with a maximum abundance of 17.3×10^6 cell L⁻¹, being likely that this HAB was a reflection of a major climate event scale that covered a wide area of the Central Pacific (Chow et al., 2010).

Toxin Profiles in Environmental Samples

Data regarding toxicity and toxin content for *P. bahamense* is scarce. Only two reports on toxin profiles in natural samples exist. The first one is from El Salvador, during a bloom in 2005–2006 that caused human intoxications and mortality of sea turtles (Licea et al., 2008). The second report is from phytoplankton samples of a HAB in the coast of Guerrero, Mexico in 2010. Sulfocarbamoyl analogs dominated (>80 mol%), followed by STX and GTX3, with a contribution of 12.0 and 6.8 mol%, respectively (Gárate-Lizárraga et al., 2012).

In 1987, during a HAB in Guatemala, the clam *Amphichaena kindermanni* presented mainly B1 toxin, accompanied by small amounts of STX and NEO (Rodríguez et al., 1990). The net toxicity calculated from the concentrations of these three toxins corresponded to 7,500 mg STX dihydrochloride 100 g⁻¹; 93.7 times above the maximum level for most regulations in Latin American countries that limits PSTs content at 80 µg STXeq 100 g⁻¹ (400 MU 100 g⁻¹) for human consumption. During this event, 175 people were intoxicated, and 26 people died (Rosales-Loessener, 1989).

In 1991 and 1993, in Uruguay, toxin profile of *M. edulis* was linked to HABs of this species. The mollusk presented C1/2 (up to 53 mol%), with significant amounts of GTX2/3, and STX, while *D. hanleyanus* presented decarbamoyl analogs, mainly dcGTX2 (~63 mol%) (Méndez et al., 2001).

In Mexico, most of the human intoxications related with this species have been due to the consumption of diverse bivalve species (Saldate-Castañeda et al., 1991; Cortés-Altamirano et al., 1993; Gárate-Lizárraga et al., 2012). In 1995, in BACA, STX, GTX2, dcGTX2/3, dcSTX as well as B1 were reported in the oyster *C. iridescens* (Núñez-Vázquez et al., 2007a). In 2010, a dominance of sulfocarbamoyl analogs (59 mol%), mainly B1/2 and C1, followed by STX (12%) and GTX3 (6.8%) were recorded in *C. mexicana*, in the same bay (Gárate-Lizárraga et al., 2012), with toxin concentrations ranging from 579.0 to 894.7 µgSTX 100 g⁻¹. In 2001, in the coasts of Chiapas, STX, NEO, GTX2/3, B1 were detected in *D. gracilis*, and STX, GTX2/3 and B1 in *M. capax* (Núñez-Vázquez et al., 2007a). No data on toxin concentrations were given.

During a bloom in Nicaragua, 45 people developed symptoms of PSP with one fatal case in 2005. The toxin profile of *A. tuberculosa* presented STX as the dominant toxin with small quantities of NEO and B1 (Callejas et al., 2015).

Molecular Studies

Limited genetic information exists regarding *P. bahamense*. Morphological differences, as well as the LSUrDNA sequences were analyzed in vegetative cells and cysts of both varieties: *compressum* and *bahamense*, from distinct geographic regions such as Jamaica, Puerto Rico, Guatemala and Colombia (Mertens et al., 2015). No morphological differences between vegetative cells of the isolates were found. Cyst morphology, however, showed differences between specimens from Indo-Pacific and Atlantic-Caribbean regions. Results agreed with ribosomal sequences, where a distinct ribotype was identified for each geographical region. Based on these results, the authors suggested that it is a species complex.

As many other dinoflagellates, this species has bioluminescence capacity. Molecular diversity based on 18S rRNA and on the luciferase gen (*lcf*) was examined, using single cell isolates from Florida, USA and Puerto Rico. Phylogenetic analysis revealed that all sequences clustered together and were closely related to *Alexandrium* spp. With *lcf* sequences from Florida and Puerto Rico, two distinct clusters formed, defined by a set of core amino acid substitutions, and the inclusion of *lcf* sequences from the Indo-Pacific strain resulted in a third cluster. *Lcf* sequences of *P. bahamense* were more closely related to *Pyrocystis* spp. than *Alexandrium* spp. suggesting a much greater variation than that seen in bioluminescent species with known gene variants (Cusick et al., 2016).

Alexandrium Species

One of the most studied harmful algal blooming genera worldwide is the genus *Alexandrium*. More than 30 species have been defined and at least half of them are known to be toxic or have harmful effects (Anderson et al., 2012). Three different families of known toxins are produced by species of this genus: STX, spirolides, and goniodomins. In LAm this genus is widely distributed (Figure 2), and several toxic species have been reported: *A. catenella*, *A. minutum*, *A. monilatum*, *A. ostenfeldii*, *A. tamarensis*, and *A. tamiyavanichi*. There are also reports of *A. peruvianum*, however Kremp et al. (2014) proposed that *A. peruvianum* should be considered as a synonym of *A. ostenfeldii* due to inconsistent morphological and gradual genetic divergence of groups, together with no evidence of compensatory base changes indicating reproductive isolation (Kremp et al., 2014). For the purpose of this review *A. peruvianum* is considered as a synonym of *A. ostenfeldii*.

HABs of *Alexandrium* are mostly reported in South America and the main responsible species are *A. catenella* (Chile) and *A. tamarensis* (Uruguay, Argentina). The intensity and frequency of these HABs have increased since 1990, causing severe economic losses in the fishing and aquaculture sector (Álvarez et al., 2009; Menezes et al., 2010; Aguilera-Belmonte et al., 2011, 2013; Mardones et al., 2015).

A total of 350 cases have corresponded to the consumption of seafood associated with HABs caused by *Alexandrium* species in South America (Table 1). Chile is the most affected country; HABs in this area have also caused massive mortalities of

invertebrates, fish, both wild and cultivated, as well as seabirds and whales.

Bloom Dynamics

Chile

In Chile, the main *Alexandrium* species reported is *A. catenella*. From 1972 to 1994, outbreaks in the MAGR and Aysén regions (AYSR) were attributed to this species. HABs have increased in their frequency, extension, duration and intensity (Guzmán et al., 2002, 2010). Until this date the distribution limits of this species were: Cailin in the southern sector of Los Lagos region, and in the north Seno Ponsonby, in the MAGR. In October 1972, after a period of high irradiance and thermohaline stratification, a HAB lasted for 5 weeks, with densities from 2.4 to 6×10^5 cell L^{-1} at the surface, and 157×10^2 and 3201×10^2 cell L^{-1} in the sub-surface layer (5–10 m), respectively. The same hydrographic conditions were recorded in Bahía Bell in 1973, when this species bloomed. In subsequent years (1972–1994) HABs continued emerging (Guzmán et al., 2002). The authors suggested that blooms occurred in response to global changes related to El Niño, which causes a decrease in salinity and stronger stratification, proposing that blooms are related to the terminal period of La Niña and the initiation of intense El Niño episodes. The authors concluded that this dinoflagellate is able to bloom under calm conditions, high insolation and a stable water column.

There is a list of data of HABs of this species from 1994 in the MAGR, with maximum abundance values of 30,902 cell L^{-1} , and in the AYSR of 5,808 cell L^{-1} . Cells are found from spring to autumn, when high temperatures trigger the blooms (Guzmán et al., 2002). From 1993 to 1998, also in AYSR, several dinoflagellates were identified, including *A. catenella*. Temperature ranged from 5.2 to 16.2°C; the lowest temperatures were recorded in 1996, and the highest in 1994 and 1998. HABs coincided with a temperature from 11 to 14°C, mainly between December and April, being more frequent in February (Cassis et al., 2002). Data suggested that 1998 was an anomalous year that presented an extensive HAB that covered the entire south of the country in March, overlapping with positive anomalous values. This event caused 20 human poisonings, two fatalities and losses of over USD 10 M to the salmon industry (Mardones et al., 2015).

From 1995 to 2002, several outbreaks with marked seasonality were reported in inland waters of the NW Patagonia (Molinet et al., 2003). Blooms occurred mainly from January to March, with a tendency to expand its distribution northwards. These events were attributed to the presence of cysts banks, and associated to thermal oscillations in adjacent ocean waters that affected the circulation in inland waters. Cyst dispersion was associated to the drift of surface waters, caused mainly by winds and circulation of inland waters (Molinet et al., 2003). Also, the structure of the water column suggested that these HABs originated from the mixture of Antarctic and sub-Antarctic surface waters, derived by wind action. Cyst germination is considered relevant in the recurrent HABs in inland seas, as well as in the fjords and MAGR channels (Uribe et al., 2010). In 2005 and 2006, another bloom in the X region occurred at 12°C (Fuentes et al., 2008). Data suggested that stratification

conditions favored dinoflagellates growth and coincided with the presence of PSTs (Díaz et al., 2014).

In March 2009, a HAB covered a wide geographical area from 46° to 43° 45' S. During late February in Easter Island, this dinoflagellate reached a maximum of 2230 cell mL^{-1} ; in March, in the same geographic region it reached 12×10^2 cell mL^{-1} , and in Cuptana 6×10^3 cell mL^{-1} . These data demonstrated an expansion of the northern distribution of this species with respect to their historical distribution range, being the first record of *A. catenella* in oceanic waters of the Pacific coast SE outside Chiloé Island. The new distribution suggested a cell transport toward inland waters through Chacao channel. Cells probably also reached Chiloé water fjord and channels, by oceanic water masses (Mardones et al., 2010). Northern distribution of this species continues expanding, during the last intense bloom of *A. catenella*, in the late summer of 2016, PSP-affected areas reached for the first time as far north as Los Ríos (39°S) (Hernández et al., 2016).

In the Southern Austral Ecosystem, this species was associated to temperatures between 9 and 13°C and salinities of 28 and 33 (Cruzat et al., 2018), with higher abundances at 10°C. The high genetic diversity in terms of population differentiation suggested a possible recent dispersion. Many factors could be influencing this dispersion, as the frequent use of transportation related with aquaculture operations, ocean currents, and natural dispersion. In the AYSR there has been a tendency of intense HABs in summer. Cysts play a key factor for repopulation during spring-summer and they can be re-suspended by the advection of the water column (Pizarro et al., 2018). In southern Chile fjords, resting cyst of *A. catenella* are sparse and there have been doubts on their importance in the recurrence of massive toxic dinoflagellate blooms in the region. Mardones et al. (2016) under laboratory conditions demonstrated with strains isolated from this region that moderate vegetative cell abundances (>400 cell mL^{-1}) can produce high amounts of cysts which have a short dormancy period (minimum 69 days). These results are in agreement with the finding by Díaz et al. (2014) of empty cysts found a few months (~3 months) after a bloom event, representing less than 10%. Mardones et al. (2016) suggest that the short cyst dormancy for Chilean strains explains the rapid cyst depletion from the sediments of the inner fjords. However, dense cyst aggregation cysts can be accumulated and preserved in selected areas of the fjords. Authors point out the need to investigate the oceanographic conditions that lead to massive outbreaks.

Argentina

In the Argentine sea, *A. tamarensis* is the most frequently reported harmful dinoflagellate species. During 1980–1984, several HABs of this species were reported. In 1980 a high abundance (1.8×10^6 cell L^{-1}) restricted to a hydrographic frontal system was found outside PVAL, characterized by high nutrients and turbulence (Carreto et al., 1985). The initial outbreaks expanded widely, and covered most of the Argentine coasts, in the frontal area, where vegetative cells, cysts, and high levels of toxicity are found. Also, a decoupling zooplankton-phytoplankton arrangement was found, being the main predator the dinoflagellate *Polykrikos schwartzii*

(Carreto et al., 1985). In 1981, a HAB lasted 4 months (September to December), and was also restricted to a frontal system. In areas with stratified waters, cysts were found in sediments and were re-suspended during the mixing of the water column. Also seedbeds of hypnozygotes were observed which are known to serve as dispersion centers and increase the extension of toxic areas (Carreto et al., 1985). In 1995, during an annual cycle, cysts were found most of the year in coastal waters in MPlat (151–2758 cysts cm^{-3}) (Carreto et al., 1998a). *In situ* germination was the main source of vegetative cells that were initially found in August at 30 m (80 cells L^{-1}) depth and in September at 0 m (15×10^3 cells L^{-1}). A broad temperature range was recorded, from 9°C to 20°C in summer, during a well-developed thermocline. It has been suggested that the presence of vegetative cells in winter could be attributed to the biological mechanism that controls cyst germination before temperature rises (Carreto et al., 1998a). A retrospective analysis of HAB and toxicity concluded that most records of this species occur in a wide coastal strip from 34° to 47° S at a depth between 50 and 100 m. Maximum abundances are reported in the frontal system of the Patagonian tidal region. Advection transport from external waters toward the coast explained the accumulation of cells in the intertidal zone. The Patagonian current contributed to the northward spread of cysts, the thermocline, hydrographic fronts and ocean currents were also key factors for their growth and distribution (Carreto et al., 1998a).

In Golfo Nuevo (GNVO) this species was recorded in August 1995 (Gayoso, 2001), at a lower temperature (9°C), with a peak in September of the same year of 6.1×10^3 cell L^{-1} . Cysts were recorded in surface sediments (300 cysts cm^{-3}). Heavy precipitation in winter and high solar radiation during spring could have influenced the formation of HABs. However, during blooms in July and December 2000, with a maximum abundance of 21.8×10^3 cell L^{-1} , and temperature from 9 to 12.5°C, a multiple linear regression of the cell abundance with environmental variables (solar radiation, temperature, wind speed, rainfall, and nutrients), did not show a high correlation (Gayoso and Fulco, 2006), remaining to determine the factors that influence its blooms in this region.

Waters in the north coast of the Patagonian region, are ecosystems poor in nitrates (Montoya et al., 2010). On the other hand, phosphate concentrations are relatively high throughout the year, reason why the N:P ratio is heavily imbalanced with respect to the Redfield ratio. On the contrary, nitrate concentration is high in the sub-Antarctic waters and the Patagonian current mainly in southern latitudes, where N limitation was not found during summer. Therefore, it is assumed that the nutrient ratio and cell toxin content from natural populations of *A. tamarensis* are correlated with the availability of nutrients in the southern region of South America, and the toxin content is inversely correlated with water temperature.

Other *Alexandrium* species, such as *A. catenella*, *A. excavatum* and *A. ostenfeldii* have been reported in Argentina. During spring/summer of 1980 PSTs were detected for the first time in GNVO (Esteves et al., 1992). The responsible species was *A. excavatum*, with abundances from 7.5×10^5 to 3.1×10^3 cell

L^{-1} during an upwelling event. The SST was 15°C and prevailing winds were from the SW ($>20 \text{ km h}^{-1}$). In late December northern winds dominated, the average temperature was $18.3 \pm 0.9^\circ\text{C}$ and salinity was 33.9. Nitrate concentration remained constant, $0.3 \pm 0.1 \mu\text{g-at L}^{-1}$. However, in February nitrates, phosphates and ammonium raised to 1.9, 7.1, and $9.3 \mu\text{g-at L}^{-1}$, respectively.

In the Beagle Channel, during 2006 and 2007 *A. catenella*, *A. tamarensis* and *A. ostenfeldii* were observed (Almandoz et al., 2011). Temperature ranged from 4.9 to 10.1°C, and salinity from 30.7 to 31.2. In 2006, nitrate and phosphate were higher in winter (15.2 and $1.4 \mu\text{M}$, respectively). The highest abundance of *A. tamarensis* was detected in spring 2006 with 11.7×10^5 cell L^{-1} (Almandoz et al., 2011). Outbreaks in the Beagle Channel of this dinoflagellate, have been proposed to have a relationship with the decrease in the ozone layer (Benavides et al., 1995). In the same region, in July 2005 and December 2006, *A. ostenfeldii* had a low abundance (5860 and 3850 cell L^{-1} , respectively). Temperature and salinity varied between 7.5 and 10°C and 30–30.5. Considering the apparent absence of records of this species in the Antarctic waters, the Beagle channel is considered as the most southerly distribution of *A. ostenfeldii* (Almandoz et al., 2014).

Other Latin American Countries

In El Salvador, in September 2014 an intense HAB of *M. cf. polykrikoides* co-occurred with *Alexandrium cf. globosum*. Fish deaths were reported and attributed to *M. polykrikoides* (Alvarado et al., 2015).

In the Pacific coast of Colombia, in Bahía Tumaco and in the island Gorgona, in April/May 2001, an *A. tamarensis* bloom with maximum abundances of 7.5×10^6 cell L^{-1} occurred (García-Hansen et al., 2004). A year afterwards, in March 2002, another event was recorded from northern Cabo Corrientes to Bahía Solano, with a lower abundance (1.6×10^6 cell L^{-1}). In both occasions, temperature was between 24 and 24.6°C, and salinities between 33 and 34. These parameters were abnormal, since temperature was three degrees lower and salinity was 2.5 higher than the average for this region. The authors assumed that these conditions reflected upwelling events, and suggested that this could be a recently introduced species.

In Venezuela, *A. tamarensis* was recorded forming HABs since 1972, during March and June with abundances of 1×10^6 cell L^{-1} . Cells were also detected in mussel's viscera, in raft-cultures in the Gulf of Cariaco. In 1975, in April-March, this species proliferated with other dinoflagellates. This HAB was associated with the predominance of trade winds that influenced the water circulation, causing coastal upwellings. Another bloom occurred in the NW coast of island Margarita in May 1977, intoxicating 171 people.

In February 2010 and May 2014, in Peruvian shellfish extraction areas, HABs of *Alexandrium* were reported. In May 2012 *A. ostenfeldii* bloomed at a temperature between 18 to 23°C, phosphate concentration ranged from 0.7 to $11.6 \mu\text{M}$ and nitrate concentrations from 0.8 to $9.8 \mu\text{M}$. In 2015, *A. minutum* was reported for the first time off the coast of Peru, with a maximum abundance of $16 \times 10^6 \text{ L}^{-1}$, suggesting that this species was

transported by ballast water or that its presence had not been detected previously (Baylón et al., 2015).

In Brazil, the distribution of *A. tamarensis* apparently expanded into the southern hemisphere during the last two decades. The first HAB was documented in 1996 (Persich et al., 2006). Through satellite images, a cold water front that moved from northern Uruguay to Brazil was detected, which may have been the transportation vector. The high similarity among toxic profiles of *Alexandrium* strains from Brazil and Uruguay, suggested a Uruguayan origin of the Brazilian strain. Also, the low number of cysts in Brazilian sediments supported the hypothesis of a recent dispersal from Uruguay. The authors concluded that the southern Brazilian coastline may have experienced additional outbreaks of PSP originated from local cyst germination or by recent populations that were transported by the Uruguayan coastal current (Persich et al., 2006). In 2007, *A. minutum* was registered on the coast of Rio de Janeiro, with abundances from 4.3×10^5 to 1×10^2 cell L⁻¹; cysts were also registered (Menezes et al., 2007).

In Uruguay, frequent HABs of *A. tamarensis* were registered during the 90s. From 1991 to 1993, recurrent blooms were reported in early spring, near La Paloma, with abundances of 80×10^3 cell L⁻¹. In the coastal area, in a transition zone between the stream and the Malvinas current, abundance was of 355×10^2 cell L⁻¹ with a SST from 11 to 15°C (Méndez et al., 2001). A wide and strong thermal-saline front during spring-winter coincided with the HABs; blooms initiated when the discharge of the Río de la Plata decreased, as well as the front of the Falklands current (Méndez et al., 1996). From 1991 to 2004, HABs of *A. tamarensis* and *G. catenatum* have been reported, blooms of *Alexandrium* occurred at abundances of 10×10^3 cells L⁻¹, temperatures between 11 and 14°C, and salinities of 32.2.

Toxin Profiles in Environmental Samples

Alexandrium catenella

Paralytic toxins have affected ~35% of the Southern Pacific coast of Chile (Oyaneder-Terrazas et al., 2017). In 1996, samples of the mussel *M. chilensis* from the regions XI and XII, were analyzed, and in general they showed a molar dominance of GTX analogs, with a dominance of GTX2/3 in samples collected in the XI region, whereas GTX1/4 were the major analogs in the XII region (Lagos et al., 1996). The more potent analogs STX and NEO represented, together, 12 and 16 mol%, for the XI and XII region, respectively. A clear contrasting pattern was observed for the XII region when comparing *M. chilensis* profiles between years with a dominance of STX and NEO (45–46 mol%) in 1992 (Lagos et al., 1996). In several bivalves collected in 2012 in the AYSR (Region XI) a clear dominance of GTXs analogs was evident in most bivalves (García et al., 2015). Record toxicity values have been found in the AYSR with maximal values oscillating between 22,000 and 28,340 µg STX eq 100 g⁻¹ (Guzmán et al., 2002; Molinet et al., 2003).

Compartmentalization of PSTs showed that GTX analogs are mainly found in the digestive tract. The case of *M. chilensis* is relevant since in the adductor muscle 99% (in molar basis) NEO was found, whereas in the mantle and digestive glands, GTX1/4 were detected. In a recent study of the PSTs content

in regulated and non-regulated aquatic organisms from regions with a variable presence of *A. catenella* (Oyaneder-Terrazas et al., 2017), the analogs GTX1/4, GTX2/3, NEO, dcSTX, STX were detected. Dominant analogs in rocky strata-dwelling species were 58.8 mol% STX, followed by 15.4 mol% GTX2/3, 4.8 mol% NEO, and 3.3 mol% dcSTX; while in sandy bottom-dwelling species, 77.7 mol% of GTX2/3 were detected, 19.3 mol% STX, 2.1 mol% NEO and 0.9 mol% dcSTX. Data clearly showed the variability of toxin profiles in this zone and that this variation is not only associated to the sampling season, but also to the distinct basal analogs produced by this dinoflagellate as reported previously (Varela et al., 2012) and the bivalve species.

In phytoplankton samples, sulfocarbamoyl toxins C1/2 and B1 represented 70% in molar basis of the total analogs, followed by carbamoyl analogs GTX1/4 (24 mol%), contributing in smaller proportions GTX2/3 (~3 mol%). NEO, STX, dcGTX2/3 and dcSTX were found in trace levels. Cell toxicity was estimated in ~15 pg STXeq cell⁻¹ (Oyaneder-Terrazas et al., 2017). The authors pointed out that this was a characteristic toxin profile for species blooming during January and March in the austral fjords of Chile. In other seasons the toxin profile differed, for instance, toxin profiles in spring predominantly had, in molar basis, β-epimers (C2, GTX4, GTX3), and in autumn α-epimers (C1, GTX1, GTX2) (Oyaneder-Terrazas et al., 2017), which is a bit surprising since it has been proven that these enantiomers do not reflect the original composition in plankton due to their easy epimerization under extraction and analytical conditions (Bustillos-Guzmán et al., 2015). Size fractionated plankton samples obtained from the XI region of Chile only presented sulfocarbamoyl analogs C1/2 in concentrations <0.7 ng µL⁻¹ (Pizarro et al., 2018). The authors pointed out the low abundance of *A. catenella* during the cruise. In autumn, during an exceptional toxic event in the Beagle Channel in 1991/1992, the cell toxicity was calculated, also via mouse bioassay, to be 325 pg STXeq cell⁻¹ (Benavides et al., 1995).

In El Rincón, Argentina in 2015 during a bloom of *Pseudonitzschia*, cells of *A. catenella* and *A. ostensfeldii* were found in low numbers (up to 1×10^3 cell L⁻¹). Phytoplankton net tows (NT) samples presented PST in low concentrations ranging between 114.4 ng NT⁻¹ and 2593.8 ng NT⁻¹. Toxin profiles were dominated by GTX1/4; C1/2 and GTX2/3 were also detected (Guinder et al., 2018).

Alexandrium tamarensis

In Argentinian coasts, based on historical data and on shellfish toxicity, it was suggested that *A. tamarensis* could grow offshore and that cells were transported inshore toward shellfish populations. This phenomena also occurred in the Uruguayan coast, where shellfish reached toxicity values between 80 and 10,000 µg STXeq 100 g⁻¹, whereas in the Argentinian coast the toxicity values were higher, with exceptional values up to 50,000 µg STXeq 100 g⁻¹ (Carreto et al., 1998b). Toxin profile in phytoplankton samples during a bloom from MPlat to Bahía Grande, were dominated by GTX1/4 analogs (from 69.1 to 93.6 mol%), with an exception of a sample from MPlat, where GTX2/3 represented 88.5 mol% (Montoya et al., 2010). Sulfocarbamoyl toxins (C1/2) were scarce, and their contribution

was <8.5 mol%. Cell toxicity varied between 9.8 and 93.0 pg STXeq cell⁻¹. Toxin profiles contrasted with those obtained from culture strains, where sulfocarbamoyl analogs represented >60 mol%. Therefore, cell toxicity from field samples, in general, was higher when compared with cultured strains (1.8–10.3 pg STXeq cell⁻¹) grown in nutrient replete conditions. These results were confirmed with NT samples from the Argentinian coast containing *A. tamarensis* cells and minor quantities of *A. aff. minutum*, which again showed a higher concentration of GTXs (Fabro et al., 2017). Gonyautoxin concentrations (GTX1/4) ranged between 0.3 and 1104 ng NT⁻¹ and GTX2/3 ranged between 0.1 and 31.7 ng NT⁻¹. Cell quotas of total GTX estimated for *A. tamarensis* species complex plus *A. minutum* were <0.8 pg cell⁻¹. N-sulfocarbamoyl toxins (C1/2) were also detected at low concentrations. The high potency carbamoyl analogs STX and NEO were the least frequent analogs (Fabro et al., 2017).

Mussels (*M. edulis*) were sampled during two blooms, in spring and autumn. In both occasions, the toxin profile in mussels was dominated by GTX1/4 and to a lesser extent by C1/2 that constituted >80 mol% (Carreto et al., 2004). However, toxin profile changed according to the mussel toxin content. Thus whereas GTX1/4 represented more than 60 mol% during the maximum toxicity and detoxification rate period, an important increase of STX and GTX2/3 was observed at a low toxin content. Toxin profile changes reflected the compositional shifts resulting from differential toxin retention and toxin bioconversions within the mussel (Oshima, 1995). Maximum values of toxicity in the mussel were between 450 and 500 μg STXeq 100 g⁻¹.

Other *Alexandrium* Species

In Trinidad and Tobago, PSTs were first reported in 1999 in the mussel *Perna viridis* from Chaguaramas (Yen et al., 2004). STX, dcSTX, GTX1/4, GTX2/3 and dcGTX2/3 were detected, with the last three toxins being the most abundant. During 2000, STX, dcSTX, NEO, GTX2/3, and dcGTX2/3 were detected, with the last three analogs in the highest concentrations. No causative organism was identified. Known PSTs-producing dinoflagellates in this region are *A. catenella*, *A. tamarensis*, *G. catenatum*, and *P. bahamense* (Heileman and Siung-Chang, 1990; Sánchez-Suárez and Troncone-Osorio, 1994; La Barbera-Sánchez et al., 2004).

Although *A. minutum* has been reported in Peru and Argentina, to our knowledge, no further toxin research on this species has been performed. In Brazil only one bloom in the coast of Rio de Janeiro in 2007 was analyzed, being NEO (73.8 mol%), GTX2/4 (22.6 mol%), and STX (3.6 mol%) the reported toxins (Menezes et al., 2007).

In the northern coast of Chile, phytoplankton toxin profiles related to *Alexandrium* blooms did not present PSTs (Álvarez et al., 2009). However, the mollusks *Semimytilus algosus* and *Argopecten purpuratus* presented low quantities of PSTs, between 27.5 and 34.4 μg STXeq 100 g⁻¹ (determined by mouse bioassay). The toxin profile was characterized by the presence of C2 and GTX2/3 in both bivalves, concluding that *A. catenella* was unlikely to be the responsible species for these PSP events.

Autoecological Studies

Few strains of the genus *Alexandrium* have been isolated and autoecological studies of the group are scarce in LAm (Figure 3). Since Chile has been historically adversely affected by their blooming off its coasts, it is in this country where most of studies have been performed, followed by Argentina and Brazil.

Alexandrium catenella

The effect of temperature, salinity, L:D cycle, cyst or vegetative strains, and nutrients on the growth of *A. catenella* from diverse regions of Chile have been determined (Table 4) (Navarro et al., 2006; Aguilera-Belmonte et al., 2011, 2013; Ávila et al., 2015). In general, this species tolerates temperatures between 10 and 16°C, producing cell concentrations above 50,000 cell mL⁻¹ at 15°C with growth rates from 0.54 to 0.73 div day⁻¹ (Navarro et al., 2006; Aguilera-Belmonte et al., 2011, 2013); indicating that growth is temperature-dependent. Studies for the same species from other geographical sites have reported a higher optimal temperature for growth 20–25°C (Siu et al., 1997), the optimal temperature in this study being 14°C demonstrated its great capacity of this species to adapt to a wide range of temperatures. Maximum biomasses are reached between 15 and 65 days; this wide time difference could be related to the L:D cycle used in the different culture conditions or could be inherent to strain differences (Table 4) (Navarro et al., 2006; Aguilera-Belmonte et al., 2011, 2013). Their salinity tolerance is also wide; growing under laboratory conditions at salinities from 15 to 35. Chain formation was observed mainly during the first week of culture, reducing their presence (>7%) when cultures reached ~5,000 cell mL⁻¹ (Navarro et al., 2006). With these studies, a wide range of tolerance to salinity and temperature was proved, which helps explain, at least partially, its ecological success.

The effect of temperature on the cell dry weight was also determined. Maximum biomass was inversely proportional to temperature, with values of 117.3 ± 0.9, 120.3 ± 3.2, 90.9 ± 0.6 and 23.3 ± 1.4 μg mL⁻¹ at 10, 12, 14, and 16°C, respectively, with a direct relationship between cell dry weight and cell abundance. Cell dry weight was greater in the initial phase, decreased during the exponential phase, and increased again toward the terminal phase. The highest values for individual cell dry weights were obtained at 14°C (9.6 ± 1.1 ng cell⁻¹, day 3) and at 10°C (9.5 ± 0.9 ng cell⁻¹, day 3). The lowest were obtained at 12°C (5.9 ± 0.3 ng cell⁻¹, day 3) and at 16°C (5.8 ± 1.7 ng cell⁻¹, day 6). The authors suggested that the increase of cell weight during the growth phase could be explained by the presence of thecae of dead cells that added to the total weight of the culture and also to the increase in cell size (Navarro et al., 2006).

These results suggested this species has also a wide photo-acclimation and that it presents a lower range of thermal tolerance in relation to strains from other geographic regions. The optimal temperature range correlated well with ambient water temperatures in southern Chile, in which important blooms have been reported. Noteworthy differences have been detected in growth among populations from different geographical origins obtained from the same toxic event, concluding that abiotic factors can differentially affect the

TABLE 4 | Ecophysiology studies of *Alexandrium* species in Latin America.

Species	Strain code	Culture conditions	Photoperiod L:D h	Temp (°C)	Salinity	Abundance (cel mL ⁻¹)	Growth rate (div day ⁻¹)	Geographic area/date of isolation	References
<i>Alexandrium catenella</i>	ACC02	L1 59.53 ± 0.25 μmol/m ² s	14:10	10	30	29,460 ± 460	0.18 ± 0.00	Aysén Region, Chile 1994	Navarro et al., 2006
				12		34,850 ± 1,641	0.11 ± 0.00		
				14		24,000 ± 448	0.30 ± 0.01		
				16		6,389 ± 300	0.10 ± 0.03		
	PFB36	L1 50 μmol photons/m ² s	16:08	15 ± 1	nd	52,320 ± 6,122	0.54 ± 0.04	San Pedro Island, Los Lagos Region, Chile March 2009	Aguilera-Belmonte et al., 2011
	PFB37				nd	24,608 ± 884	0.52 ± 0.02	Quemada Island, Aysén Region, Chile March 2009	
	PFB38				nd	48,581 ± 6,963	0.73 ± 0.02	Cailin Island, Los Lagos Region, Chile March 2009	
	PFB39				nd	43,520 ± 1,227	0.58 ± 0.01	Asasao Bay Los Lagos Region, Chile March 2009	
	PFB41				nd	54,288 ± 3,982	0.55 ± 0.02	Luz Island, Aysén Region, Chile March 2009	
	PFB42				nd	45,632 ± 2,563	0.42 ± 0.02	Jorge Island, Aysén Region, Chile March, 2009	
PFB45				nd	49,104 ± 2,400	0.56 ± 0.03	Aysén Bay, Aysén Region, Chile March, 2009		
AY2	L1 with silicates 24 μE/m ² s N:P (24:1) N:P (12:1) N:P (3:1)		14:10	15	30	5,093	0.49*	Aysén Region	Garrido et al., 2012
PFB37	L1 medium 65 μmol photons/m ² s	16:8	10 ± 1	15	22,205 ± 4190	0.35 ± 0.04	Quemada Island, Aysén Region, Chile March 2009	Aguilera-Belmonte et al., 2013	
PFB38									
				15 ± 1	35	22,080 ± 2,437	0.47 ± 0.05		
				15 ± 1	15	14,750 ± 452	0.61 ± 0.04		
				10 ± 1	35	24,608 ± 884	0.52 ± 0.03		
				10 ± 1	15	17,954 ± 5,164	0.34 ± 0.02	Cailin Island, Los Lagos Region, Chile March 2009	
				15 ± 1	35	44,800 ± 7,250	0.39 ± 0.05		
				15 ± 1	15	40,760 ± 3,123	0.48 ± 0.03		
				10 ± 1	35	52,671 ± 4,650	0.73 ± 0.03		
PFB41				10 ± 1	15	14,869 ± 1,099	0.25 ± 0.02	Luz Island, Aysén Region, Chile March 2009	

(Continued)

TABLE 4 | Continued

Species	Strain code	Culture conditions	Photoperiod L:D h	Temp (°C)	Salinity	Abundance (cel mL ⁻¹)	Growth rate (div day ⁻¹)	Geographic area/date of isolation	References
PFB42				15 ± 1	35	15,287 ± 1,391	0.35 ± 0.04		
				15	15	11,006 ± 2,337	0.28 ± 0.02		
				10 ± 1	35	52,038 ± 1,554	0.56 ± 0.03	Jorge Island, Aysén Region, Chile	
				10 ± 1	15	24,211 ± 2,260	0.34 ± 0.03	March 2009	
				15 ± 1	35	38,005 ± 3,880	0.42 ± 0.04		
				15 ± 1	15	36,713 ± 1,713	0.29 ± 0.03		
				35	35	45,632 ± 2,563	0.42 ± 0.02		
		AC090610-QU-Q	L1 medium	16:8	10	>3,000	0.08	sediment cysts	Ávila et al., 2015
			24 μmol photons/m ² s		15	>3,000	0.12	Punta Yenecura, zona Sur de Quellón	
					20	<1,500	0.10	(43°08'44.2'' S;	
				10	2,324	0.12	73°39'30.6'' W) Región de Los Lagos, Chile		
				10	2,018	0.12	Summer 2010		
				30	3,788	0.18			
				31	2,000	0.05			
		L1 medium	12:12			2,000	0.07		
		24 μmol photons/m ² s				2,000	0.07		
		L1 medium	16:08						
		24 μmol photons/m ² s							
		L1 medium	08:16						
		24 μmol photons/m ² s							
		L1	??			> 2,800	0.08		
		L1/2	??			> 2,800	0.07		
		L1/10	??			< 1,000	0.06		
		L1/15	??			< 1,000	0.06		
		L1/-N-P	??			< 1,000	0.06		
	Strain cross: Q09 x CERES8	L1	12:12	17	30	?	0.36	Los Lagos, Quellón x North Aysén, Ceres Island	Mardones et al., 2016
	Strain cross: Q09 x K7	100 μphotons PAR/m ² s							
		L1/-N	12:12	17	30	?	0.52	Los Lagos, Quellón x South Magallanes	Mardones et al., 2016
		100 μphotons PAR/m ² s							
<i>A. tamararensis</i>	MDQ1096	45 μmol photons/m ² s	12:12	18	??	1,924	0.28	Mar del Plata, Argentina	Frangópulos et al., 2004

*. maximum values.

population dynamics of toxic genotypes, making it extremely difficult to predict the ecological behavior of this species in the field in terms of the intensity of a potential outbreak (Aguilera-Belmonte et al., 2011, 2013).

In 2015, Ávila and collaborators evidenced the effects of salinity, temperature, photoperiod and nutrients in cultures established from cysts. Cysts were isolated from Punta Yencura, Los Lagos region, in Chile. Different experiments were designed, and only one parameter was tested at the time (salinity, temperature, photoperiod, nutrients) (details in **Table 4**). Maximum biomasses were never above 4,000 cell mL⁻¹ and was reached between 28 and 51 days of culture; maximum abundances were found at 10 and 15°C and salinities of 30-31 with growth rates from 0.12 to 0.18 div day⁻¹. No clear effect of the L:D cycle was observed on cell abundance, whereas growth rate was higher at 16:08 and 08:16 L:D. Higher abundances were obtained with L1 and L1/2 media, but where much lower than biomasses obtained with strains obtained from vegetative cells in other studies. This difference could also be explained by the lower light intensity used (Ávila et al., 2015) (**Table 4**). With strain crosses obtained from cysts collected in Los Lagos and AYSR during the massive HAB event, Mardones et al. (2016) using the same medium with and without N, and higher light intensities also obtained high growth rates (0.36 and 0.52 div day⁻¹) (**Table 4**).

There is only one report of allelopathy regarding *Alexandrium* species from LAM. This study was performed with a strain of *A. catenella* from southern Chile (Arzul et al., 1999). The allelopathic and hemolytic effect of this, and other toxic *Alexandrium* species from Europe and Asia were determined on *Gymnodinium mikimotoi*, *Scrippsiella trochoidea*, and *Chaetoceros gracile*. Filtrates of *A. catenella* reduced the growth of *G. mikimotoi* and *C. gracile*, particularly in the exponential phase of culture, which was related with toxicity and haemolytic activity. No effect on *S. trochoidea* was observed. This information supported the environmental observations, where blooms of the later usually follow a PSP outbreak caused by *A. catenella* (Arzul et al., 1999).

Alexandrium tamarense

The growth rate under different N and P regimes in *A. tamarense* from MPlat was determined. The strain was compared with strains of *A. tamarense*, *A. minutum*, and *A. anderssoni* from Spain. The Argentinian isolate presented the lowest affinity for P. The half saturation coefficient (K_s) and the P concentration to which the specific culture cell growth rate was zero (K_{min}) under P limitation were 1.68 and 0.48, respectively, which were higher than the K_s and K_{min} of the other strains. The lower affinity for P indicated that the Argentinian isolate has a lower competitive ability under P limitation. The average abundance for this strain under non-nutrient limitation was 1,924 cell mL⁻¹, with growth rates from 0.22 to 0.28 div day⁻¹ (**Table 4**). These values were also lower than those reported previously for *A. catenella*, with the exception of a strain obtained from cyst germination (Frangópulos et al., 2004).

Other *Alexandrium* Species

Another study reported a negative experimental effect on copepod nauplii larvae, and larvae of gastropods and tintinnids. Exudates of *A. tamiyavanichii* decreased the survival of copepod larvae, suggesting that the dinoflagellate has an impact on the trophic chain (Silva et al., 2013).

Toxin Profiles in *Alexandrium* Species Under Laboratory Conditions

Several studies on toxin profiles have been performed with *Alexandrium* species in LAM, mostly in countries where the blooms of species of this genus are common and are an important threat for the economic activities.

Alexandrium catenella

This species is particularly important along the Chilean coasts, and many research groups have performed toxin analysis in cultures for more than one decade. Data from toxin profiles, toxicity and toxin content are available in **Tables 5, 6**, and the origins of the isolates are indicated in **Figure 3**.

One of the first autoecological studies performed in LAM was done to determine the role of temperature in growth rate, cell density and toxicity (Navarro et al., 2006). Cells of *A. catenella* isolated from the AYSR were cultured in L1 medium at four temperatures: 10, 12, 14, and 16°C. Toxins were extracted with 0.1 M HCl and later HCl 1 M was added. Toxicity was measured using patch clamp electrophysiology with human embryonic kidney cells expressing STX-sensitive rat skeletal muscle Na_v channels. Toxin content was variable during the experiment, but an inverse relationship was noted between temperature and toxin content, with the highest toxin content found at 10°C, and the lowest at 16°C. According to Cembella (1998), low temperatures contribute to higher PSTs levels, making *Alexandrium* strains from higher latitudes more toxic, which is probably related to effects on metabolic processes (Navarro et al., 2006).

Among the toxinological studies performed on *Alexandrium* species in LAM, Brazilian isolates have been analyzed. Persich et al. (2006) worked on *Alexandrium* isolates and reported the species as *A. tamarense*, but later molecular studies confirmed them as *A. catenella* (Menezes et al., 2018). Five isolates were cultured from cysts and one from vegetative cells, in f/2 medium at 20°C. Toxins were extracted with 0.05 M acetic acid and analyzed by LC-FLD with post-column derivatization. Toxin content ranged from 42 to 199 fmol cell⁻¹ and toxicity varied between 7.1 to 65.9 pg STXeq cell⁻¹, except for the culture originated from vegetative cells, which showed higher toxicity, mainly due to the higher GTX4 content (Persich et al., 2006).

Krock et al. (2007) analyzed the toxin composition of an isolate from the coastal Channel, XI Region of Chile. Toxins were extracted in 0.03 M acetic acid and analyzed by LC-FLD and LC-MS/MS. For the first time both techniques were used for comparison and precision. Detected toxins were C1/2, GTX1/7, B1, GTX2/3, NEO, and B2, in descending order according to their concentration. STX, dcSTX, dcGTX2/3, and C3/4 were present only in trace amounts (<1 mol%). *Alexandrium catenella* is considered the predominant, or even exclusive, source of PSTs in central Chile, and its toxin profile agreed with other profiles from

TABLE 5 | *Alexandrium* toxin analogs reported under laboratory conditions.

Isolate(s)	Origin	Culture media	STX	NEO	GTX1/4	GTX2/3	B1	B2	C1/2	C3/4	dcSTX	dcNEO	dcGTX1/4	dcGTX2/3	References
A. catenella															
6	Patos Lagoon, Bra	f/2	1/1	1/1	1/1	1/1	-	-	1/1	-	-	-	-	1/1	Persich et al., 2006
1	Coastal Chamel, XI Region, Ch	L1	t	1/1	1/1	1/1	1/1	1/1	1/1	Tr	Tr	-	-	Tr	Krock et al., 2007
7	South Chiloé to south Aysén, Ch	L1	2/7	2/7	7/7	7/7	3/7	3/7	3/7	1/7	-	-	-	-	Aguilera-Belmonte et al., 2011
7	Los Lagos, Ch (cysts)	L1	T6/7	7/7	7/7	7/7	t1/7	t1/7	7/7	T5/7	t7/7	-	-	-	Varela et al., 2012
2	Aysén, Ch (cysts)		t1/2	2/2	2/2	0/2	0/2	*2/2	0/2	0/2	t1/2	-	-	-	
3	Aysén, Ch (veg. cells)		t3/3	3/3	3/3	3/3	*3/3	3/3	3/3	3/3	t1/3	-	-	-	
2	Megellan, Ch (veg. cells)		0/2	2/2	2/2	0/2	0/2	2/2	2/2	0/2	0/2	-	-	-	
1	Adjacent shelf front, Bahía Blanca, Arg	½ K	1/1	1/1	1/1	1/1	-	-	1/1	-	-	-	-	-	Guinder et al., 2018
A. tamarense															
1	Mer del Plata, Arg	f/2	1/1	1/1	1/1	1/1	-	-	1/1	-	-	-	-	1/1	Carreto et al., 1996
6	Patos Lagoon, Bra	f/2	1/1	1/1	1/1	1/1	-	-	1/1	-	-	-	-	1/1	Persich et al., 2006
6	Golfo Nuevo, Arg	f/2	t1/6 1/6	t3/6 1/6	6/6	6/6	-	-	6/6	-	-	-	-	-	
3	Golfo San José, Arg		t1/3 1/3	3/3	3/3	3/3	-	-	3/3	-	-	-	-	-	
1	Península Valdés, Arg		1/1	1/1	1/1	1/1	-	-	1/1	-	-	-	-	-	
3	Mer del Plata, Arg (Nat)		1/3	1/3	3/3	3/3	-	-	3/3	-	-	-	-	-	
1	Península Valdés, Arg (Nat)		-	-	1/1	1/1	-	-	-	-	-	-	-	-	
1	Camarones, Chubut, Arg (Nat)		-	-	1/1	1/1	-	-	-	-	-	-	-	-	
1	Bahía grande Santa Cruz, Arg (Nat)		-	-	1/1	1/1	-	-	-	-	-	-	-	-	
2	Golfo de San Jorge, Arg	½ K	2/2	2/2	2/2	2/2	2/2	2/2	2/2	-	-	-	-	-	Krock et al., 2015
A. ostenfeldii															
1	Aysén, Ch	L1	1/1	-	-	1/1	-	-	-	-	*t1/1	-	-	-	Salgado et al., 2015
3	Adjacent shelf front, Bahía Blanca, Arg	½ K	3/3	-	-	3/3	-	-	3/3	-	-	-	-	-	Guinder et al., 2018
A. tamiyavanichi															
1	Bahía, Bra	f/2	1/1	1/1	1/1	1/1	-	-	?	?	?	?	?	1/1	Menezes et al., 2010

T, trace amounts; *, trace amounts in one of the isolates.

Ch, Chile; Arg, Argentina; Bra, Brazil.

Nat, Natural samples (for comparison)

Enantiomeric pairs are expressed together because they easily epimerize under extraction and analytical conditions, so their measurements do not necessarily reflect their original composition in plankton cells (Krock B, pers. comm.).

TABLE 6 | Toxin content of cultured *Alexandrium* under laboratory conditions.

N	Origin	Culture media	Toxicity (pg STX eq cell ⁻¹)	Toxin content (fmol STX cell ⁻¹)	References
A. catenella					
1	Morlaix river, Fr	f/2	0.5		Arzul et al., 1999
1	Canal Costa, Ch		1.39		
1	Onagawa Bay, Jap		7.2		
1	Aysén region, Ch	L1		27.8 (10°C)	Navarro et al., 2006
1	Aysén region, Ch			13.3 (12°C)	
1	Aysén region, Ch			7.82 (14°C)	
1	Aysén region, Ch			3.5 (16°C)	
1	Aysén, Ch	f/2		5–8	Uribe et al., 2008
7	South Chiloé to south Aysén, Ch	L1		8.5–96.9	Aguilera-Belmonte et al., 2011
7	Los Lagos, Ch (cysts)		Max: 63.65; min: 3.51	42.6–295.5	Varela et al., 2012
2	Aysén, Ch (cysts)			41.6–235.9	
3	Aysén, Ch (veg. cells)			41.1–79.0	
2	Magellan, Ch (veg. cells)			64.5–67.2	
3	Aysén, Ch	L1		Min nd (10°C, 15 and 35 sal) Max 239 (10°C and 35 sal)	Aguilera-Belmonte et al., 2013
1	Los Lagos, Ch			Min 8.54 (15°C and 35 sal) Max 95.8 (10°C and 35 sal)	
A. tamarense					
1	Mar del Plata, Arg				Carreto et al., 1996
6	Patos Lagoon, Bra	f/2	7.1–65.9	42–199	Persich et al., 2006
6	Golfo Nuevo, Arg	f/2	1.8–6.5	13.3–35.4	Montoya et al., 2010
3	Golfo San José, Arg		1.1–5.8	17.2–26.9	
1	Península Valdés, Arg		10.3	51.3	
3	Mar del Plata, Arg (Nat)	Natural samples	9.8–62.8	45.5–164.0	
1	Península Valdés, Arg (Nat)		80.2	225.52	
1	Camarones, Chubut, Arg (Nat)		86.8	228.7	
1	Bahía grande Santa Cruz, Arg (Nat)		93.0	261.4	
2	Golfo de San Jorge, Arg	½ K	74–60		Krock et al., 2015
A. ostenfeldii					
1	Aysén, Ch	L1		105.8 ± 72.2	Salgado et al., 2015
A. tamiyavanichi					
1	Bahia, Bra	f/2		16.9	Menezes et al., 2010

Fr, France (for comparison); Ch, Chile; Arg, Argentina; Bra, Brazil.
Nat, Natural samples (for comparison).

populations from the Pacific Ocean in the northern hemisphere (Krock et al., 2007).

Aguilera-Belmonte et al. (2011) compared the phenotypic and genotypic characteristics, including toxin profiles of seven isolates from the same HAB event, but from different geographical zones. Isolates were cultured in L1 medium at 15 ± 1°C. Toxin analysis was performed by LC-FLD on 0.05 M acetic acid extracts. *N*-sulfocarbamoyl analogs were detected after hydrolysis. All isolates had different toxin profiles, but most of them showed high proportions of GTX1/4 followed by GTX2/3. In three out of seven isolates they reported B1, B2, and C toxins (43 mol%). In two, NEO and STX (29 mol%) (Aguilera-Belmonte et al., 2011), showing large intraspecific variability, as reported within a variety of dinoflagellates, even among clones from the same geographic area (Tillmann et al., 2009;

Seok Jin et al., 2010). In addition, they found a cosmopolitan distribution of the morphospecies within the North American Clade, though interesting differences were found in their toxin profiles (Aguilera-Belmonte et al., 2011).

Research on these isolates continued, but the aim of this study was to analyze four combined conditions: two temperatures (10 and 15°C) and two salinities (15 and 35). Samples were extracted with 0.05 M acetic acid. Toxins were analyzed by UPLC-FLD, and samples from the four replicates were pooled to cover intrinsic variability among them (Aguilera-Belmonte et al., 2013). Toxin content varied widely among isolates, treatments, salinities and culture age. During stationary phase, most isolates accumulated toxins (from 1.4 to 4.5 times) compared to the exponential phase, with three exceptions of the sixteen analyses (19%). Concerning the toxin profile, NEO, GTX2/3 and GTX1/4

TABLE 7 | Abiotic factors during HABs of *G. catenatum*, *P. bahamense*, and *A. catenella* in different geographic regions of Latin America.

Species	Country/ocean	Location/date	Abundance (cells L ⁻¹)	Temp (°C)	Salinity	Hydrographic conditions	References
<i>Gymnodinium catenatum</i>	Mexico/North East Pacific (Gulf of California)	N GOLCA Mar 1939	1 × 10 ⁶	14–17	35.07–35.5		Graham, 1943
		BACO Spring, early fall 1990, 1999, 2000, 2002	1.8 × 10 ² –5.7 × 10 ⁵	18–26	34.2–36	Hydrographic transitional periods	Morquecho and Lechuga-Devéze, 2004; Gárate-Lizárraga et al., 2006
		BAPAZ Feb–Mar 2007	6 × 10 ⁵ –2.4 × 10 ⁶	20.9 ± 0.7		NO ₂ 0.22 ± 0.05 μM NO ₃ 1.04 ± 0.33 μM PO ₄ 0.81 ± 0.76 μM SiO ₃ 8.85 ± 1.60 μM N:P 1.6 - 3.2 DO 6.9 ± 0.3 mg L ⁻¹ NW winds during colder months promoted HABs	Hernández-Sandoval et al., 2009
<i>Gymnodinium catenatum</i>	Mexico/ N East Pacific	Bahía Bacoichibampo, Son 1970–1994 43 events	Maximum 9.6 × 10 ⁴	16.5–17.2		Early Spring	Cortés-Altamirano et al., 1999a,b
		BAMAZ Apr 1979, apr 1980, may 1981, 1984, 1987, Apr–may 1988, Apr–may 1997, Sept–Oct 1997	18 × 10 ³ –5.15 × 10 ⁶	20–21 Maximum abundances		Upwelling conditions ENSO influence 1997 year with higher frequencies of HABs attributed to nutrients from water plant treatment	Morey-Gaines, 1982; Mee et al., 1986; Cortés-Altamirano et al., 1995, 1999a,b; Cortés-Altamirano and Alonso-Rodríguez, 1997
		Nayarit Dec 2005	1.01 × 10 ⁶	20			Castillo-Barrera and García-Murillo, 2007
		Bahía Banderas, Nay–Jal 2000–2001	450–2134 × 10 ³	23			Gómez-Villarreal et al., 2008
		BMANZ winter and spring 1999 Mar–May 2007 May 2010	35 × 10 ² –1.02 × 10 ⁷	20.5–27.5	31.8–34.4	N-NO ₃ 1 μg at L ⁻¹ DIN 6.16–6.45 μM PO ₄ 0.37–0.78 μM SiO ₃ 7.49–21.07 μM DO 5.09–6.08 pH 8.59–8.78 upwelling events	Blanco-Blanco et al., 1999; Morales-Blake et al., 2000; González-Chan et al., 2007; Quijano-Scheggia et al., 2012
		BACA Mar 1999 Dec 2005–Feb 2006 Dec 2007	78 × 10 ³ –10 × 10 ⁶	26–27			Licea-Durán et al., 1999; Gárate-Lizárraga et al., 2009
		Costa Grande, Guerrero Dec 2010	Maximum 129 × 10 ³			Multispecies bloom	Gárate-Lizárraga et al., 2011
		Oaxaca coast (Santiago Astata and Puerto Escondido) Apr 2010	Maximum 4 × 10 ³	28–29	32–33		Alonso-Rodríguez et al., 2015

(Continued)

TABLE 7 | Continued

Species	Country/ocean	Location/date	Abundance (cells L ⁻¹)	Temp (°C)	Salinity	Hydrographic conditions	References
	Ecuador/ S East Pacific	Península of Santa Elena* Feb 1993		25	Wind speed 8 kn		Torres, 2000
		Isia del Muerto (Santa Clara)* Jun, Aug 1997 Jan 1998*	<5 × 10 ⁴	25–29.7		ENSO	
		GGUAY* Feb-Mar 1999	3.5 × 10 ⁵			PO ₄ 10.1 µg-at L ⁻¹ SiO ₃ 170.69 µg-at L ⁻¹	
	Chile/ S East Pacific	MAGR* Mar-Apr 1999	4–8 × 10 ⁶	15 (1.5 higher than normal conditions)		Unusual climatic conditions, high irradiance, reduced rainfall. <i>A. catenella</i> also present	Clément et al., 2001
	Mexico/ Gulf of Mexico	S Gulf of Mexico 2006–2010	16–2.0 × 10 ³				Zamudio et al., 2013
		S Gulf of Mexico Campeche Laguna de Términos** Jun-sept 2013 (rainy season)	Maximum 9.5 × 10 ⁴	29.7–30.6	11.6–14.3	NO ₂ 0.3–3.4 µmol L ⁻¹ NO ₃ 1.31–3.42 µmol L ⁻¹ PO ₄ 0.14–0.60 µmol L ⁻¹ SiO ₃ 29.5–51.52 µmol L ⁻¹ OD 88.4–96.3 pH 7.4–7.8	Poot-Delgado et al., 2015
	Cuba/Caribbean Sea	Sabana-Camaguey May 1999		26.4–28.2	33.3–36.5	pH 7.95–8.08	Leal et al., 2001
		Bahía de Cienfuegos Jun 1999-rainy season	7.2 × 10 ³ -3.3 × 10 ⁴	30.6	31.4	OD 7.06 mgL ⁻¹ chl a 3.12 µg L ⁻¹	Moreira-González, 2009
		Laguna Guanaroca Nov 2004	2.3 × 10 ³	23.6	24.9	NO ₂ 0.007 mgL ⁻¹ SO ₄ 1870 mgL ⁻¹ OD 6.4 mgL ⁻¹ pH 7.94	Moreira-González et al., 2013
	Uruguay/S West Atlantic	1991 to 2004		21.8–24.0	18.4–32		Méndez, 2006
	Brasil/ S West Atlantic	Paranaguá Feb-Mar 2003	6.4 × 10 ³	29		High temperatures and high nutrient concentration	Mafra-Junior et al., 2006
	Argentina/S West Atlantic	MPlat Mar-Apr 1997 Mar 2003	0.8 × 10 ³ -8.9 × 10 ⁴			Rainy season Chl a 171 µg L ⁻¹ SW winds High rainfall	Akselman et al., 1998; Montoya et al., 2006
	Mexico/N East Pacific (Gulf of California)	S peninsula of Baja California Jul-Nov 2010	800–1110	28–28.5	35.2	ENSO event	Gárate-Lizárraga and González-Armas, 2011
		Costa Chica, Guerrero Jul-dec 2010	<1–194 × 10 ³	28.5–30.5			Gárate-Lizárraga et al., 2013
		Oaxaca Dec 1989	3.25 × 10 ⁴ -3.0 × 10 ⁶	27.4–31.3			Cortés-Altamirano et al., 1993; Ramírez-Camarena et al., 1999; Rojas-Crisóstomo et al., 2007; Gárate-Lizárraga et al., 2008; Alonso-Rodríguez et al., 2015

(Continued)

TABLE 7 | Continued

Species	Country/ ocean	Location/date	Abundance (cells L ⁻¹)	Temp (°C)	Salinity	Hydrographic conditions	References
	Mexico/ Gulf of Mexico	Several areas Gulf of Mexico 1966 to 1989 Campeche Laguna de Términos** Jun–sept 2013 (rainy season)	<0.1–3 × 10 ⁶ Maximum 6 × 10 ⁴	29.7–30.6	3–38 11.6–14.3	Northern winds Summer pH 7.4–7.8 OD 88.4–96.3 nitrites 0.3–3.4 μmol L ⁻¹ nitrates 1.31–3.42 μmol L ⁻¹ phosphates 0.14–0.60 μmol L ⁻¹ silicates 29.5–51.52 μmol L ⁻¹ Associated with seawater fluxes and northern winds	Reviewed by Gómez-Aguirre, 1998; Licea et al., 2004 Poot-Delgado et al., 2015
	Mexico/Caribbean Sea	Sian Kaan C. Roo 1996	1.5 × 10 ⁶		7–30		Gómez-Aguirre, 1998
	El Salvador/ S East Pacific	Nov 2005–Mar 2006 Nov 2009 Apr–Jun 2010 Aug 2011 Sept 2012	15 × 10 ³ –48.9 × 10 ⁶			1.5°C positive thermal anomaly Chl a 0.5–1 mg m ⁻³	Licea et al., 2008, 2012; Chow et al., 2010; Alvarado et al., 2014
<i>Alexandrium catenella</i>	Chile/South West Atlantic	Coast of Valdivia (región de Los Lagos) Late Summer 2016	2.5 × 10 ⁵			Extreme hydroclimatic conditions. ENSO, decrease wind force, higher SST, negative rainfall anomalies	Hernández et al., 2016
		Coast of Chile Diverse events 1972–1993	100–6 × 10 ⁵	4.88–10.3	8.14–31.51	Thermohaline stratification, precipitation, low salinity, upwelling, high nutrients, ENSO	Guzmán et al., 2002
		Patagonia X-XI region (Los Lagos-AYSF) 1994–2002 2005, 2006 Feb-mar 2009 S Austral Ecosystem	1.1–6 × 10 ⁶	11–14		Jan-Mar Germination of cyst banks, biannual variation, northern expansion, water circulation patterns stratification	Cassis et al., 2002; Molinet et al., 2003; Fuentes et al., 2008; Mardones et al., 2010; Díaz et al., 2014
				9–13	28–33	Ocean currents, and natural dispersion	Cruzat et al., 2018

Gymnodinium* sp., *Gymnodinium cf. catenatum*.

represented more than 85 mol% of the toxin content in all strains and culture conditions. B1 was detected only in one isolate from the AYSR, and this analog was detected only when cultured at 10°C. Interestingly, the highest toxin contents were reached at this temperature (in agreement with Navarro et al., 2006) and a salinity of 35. This isolate also presented the lowest (non-detectable) and the highest toxin content (239 fmol cell⁻¹) at those culture parameters, being the culture age the only difference (exponential and stationary, respectively) (Aguilera-Belmonte et al., 2013). The scale of the combined effects of temperature and salinity was not clear, and differences were found among strains during all the experimental process, even though, two of the isolates were apparently genetically identical at least in their nuclear ribosomal ITS sequences (Aguilera-Belmonte et al., 2011). Results showed differential effects of temperature and salinity on growth parameters and toxin content, being the first more affected by salinity and the second by temperature.

Toxin profiles research continued, and toxin profiles from cultures originated from cysts and vegetative cells from different Chilean zones (Los Lagos, AYSR, and MAGR) and different years of isolation were compared. Analyses were carried out in 0.05 M acetic acid extracts and separated by LC, but the detector is not reported. Identified toxins were STX, dcSTX, NEO, GTX1/4, GTX2/3, B1, B2, C1-3, though STX and dcSTX were reported only in trace amounts and not in all isolates (Varela et al., 2012). The authors recognized two toxin production patterns in the strains, according to their toxin profile: one constituted by a group where analogs C1/2 accounted for most of the toxin content (47–74%), and a second one, where GTX1/4 accounted for the main analogs (54–87%). This second group was also conspicuous because of the absolute absence of B1, previously reported as distinctive for Chilean isolates (Montoya et al., 2010). They also reported morphological, toxinological and genetic differences among strains of this species, in accordance to other studies that have also characterized the diversity of the species in other regions (MacKenzie et al., 2004; Orlova et al., 2007).

A recent work from an oceanographic expedition in 2015, reports the isolation of four *Alexandrium* strains from offshore the Argentine coasts, near Bahía Blanca Estuary, south Mar del Plata. The cells were isolated in 1/10 K medium, later transferred to 1/2 K medium flasks, and incubated at 15°C and 50 μmol photons m⁻²s⁻¹ on a 16:8 LD photocycle. One of the four isolates was identified as *A. catenella/tamarensis* morphotype, but further morphological and phylogenetic analysis conformed to the description of *A. catenella*. Toxin profile from this one culture was dominated by C1/2 (72%), GTX1/4 (15%), NEO (9%), GTX2/3 (2%), and STX (2%) (Guinder et al., 2018).

These studies confirm that the only way to differentiate species from the *Alexandrium tamarensis/fundyense/catenella* complex is by the use of molecular tools, and also, that more studies on toxin production are needed in the area. The presence of toxigenic planktonic species has been reported, and this indicates a hazard for fisheries, shellfish production and harvest and for human and animal health.

Alexandrium tamarensis

Carreto et al. (1996) isolated vegetative cells from MPlat and compared their toxin profile with the toxin profile of mussels

(*M. edulis*) and marine snails [*Zidona angulata* and *Adelomedon (Pachycymbiola) brasiliensis*]. Toxin profiles were analyzed in 0.1 M acetic acid extracts from dinoflagellate cells by LC-FLD with post column derivatization. They reported C1/2 toxins as the most abundant, followed by GTX1/4, NEO, GTX2/3, and dcGTX2/3; STX was also reported, but as a small fraction. Toxin profiles in gastropods were highly dissimilar to those from the dinoflagellate, confirming metabolic changes upon the ingested toxin cell content, though all presented high toxin levels, but mainly from STX with the exception of *M. edulis* that presented mostly GTX analogs (Carreto et al., 1996). This study evidenced the importance of toxin analysis in gastropods.

In Brazil, toxin content of isolates were determined. Five strains were cultured from cysts and one from vegetative cells, in f/2 medium at 20°C. Toxins were extracted with 0.05 M acetic acid and analyzed by LC-FLD with post-column derivatization. Toxin content ranged from 42 to 199 fmol cell⁻¹ and toxicity varied between 7.1 to 65.9 pg STXeq cell⁻¹, except for the culture originated from vegetative cells, which showed higher toxicity, mainly due to the higher GTX4 content (Persich et al., 2006).

In 2010, a comparative toxin profile study from cultured strains and natural populations was performed. Cultures were established from vegetative cells isolated from MPlat, GNVO, Golfo de San José and off Península Valdés (PVAL), and maintained in f/2 medium at 15°C and 12:12 L:D. At the same time, they sampled in MPlat, close to PVAL, Bahía Camarones and Bahía Grande. They found toxins in all isolates and in natural samples, though those from natural samples were significantly more toxic, and the highest toxicity was found in natural samples from open coastal waters in comparison with semi-enclosed water bodies such as bays or gulfs (Montoya et al., 2010). In general, natural samples produced more carbamoyl analogs whereas cultures produced more of the less potent *N*-sulfocarbamoyl toxins C1/2. A clear correlation ($r^2 = 0.993$) between nitrate concentration and GTX1/4 in natural samples was found, while GTX2/3 decreased significantly ($r^2 = 0.987$). Nevertheless, in culture, where nitrate concentration is higher than in natural conditions, the production of GTXs was considerably lower. When temperature and toxin content was compared, an inverse linear correlation ($r^2 = 0.989$) was found, in agreement with previous studies on the genus.

The fact that natural populations were notably more toxic than those in culture raises the question about the natural factors involved, and one could be associated to bacteria (Uribe and Espejo, 2003), and that natural conditions are far from being imitated in culture. Also, the fact that populations from open waters (e.g., out from PVAL) were more toxic than those from enclosed water habitats remains enigmatic, and is probably related to specific responses to environmental conditions (Montoya et al., 2010). In many cases, cultured *Alexandrium* cells are less toxic than those from natural environments, and they can lose toxin production during routine culture maintenance, which has been stated previously, and this has led to the hypothesis that some aspects on toxin production might not be genetically determined (Ogata et al., 1987). Nevertheless, field samples displayed important variability just as in other *Alexandrium* species and other toxin-producing dinoflagellates, like *G. catenatum*. Authors stated a clear need of further research

on toxin-producing species to reach a better understanding on toxin metabolism, changes within culture conditions, and significance of environmental conditions and associated bacteria (Uribe and Espejo, 2003).

In 2012, during a research cruise, Krock et al. (2007) sampled 48 stations along the Argentinian coast. From one station, outside Golfo de San Jorge, they isolated *A. tamarensis* and established two clonal cultures using half strength K medium, 15°C and 16:08 L:D. PSTs were analyzed from 0.03 M acetic acid extraction by LC-FLD, according to previous methodology. Toxin profiles of the cultures were almost identical, and consisted of GTX1/4, C1/2 and minor proportions of NEO, GTX2/3, and STX (Krock et al., 2015). This profile has been previously reported for Argentinian strains in culture and natural populations (Carreto et al., 1996; Montoya et al., 2010). In comparison, toxin profiles in field samples consisted only of GTX2/3, while this toxin accounted for minor proportion in cultures. One possible explanation for these results could be that a chemical conversion due to storage conditions, since field samples were analyzed 3 months after the sampling and were transported from Argentina to Germany, where the analysis was performed. Nevertheless, it is interesting that not only the lateral chain was lost in toxins C1/2 to be converted into GTX2/3, but a dehydroxylation implying the loss of the N-1 hydroxyl group on GTX1/4 and NEO happened, and were converted into GTX2/3 and STX, respectively. Undeniably, further studies are needed under controlled conditions to clarify these processes (Krock et al., 2015).

Alexandrium ostenfeldii

During the expedition carried out in 2015 by Guinder et al. (2018), three of the isolates were identified as *A. ostenfeldii*. Cells from this species were isolated as mentioned (in 1/10 K medium and transferred to 1/2 K medium flasks and incubated at 15°C and 50 $\mu\text{mol photons m}^{-2}\text{s}^{-1}$ on a 16:8 LD photocycle). These cultures were specifically analyzed for spiroimines and also for PSTs (Guinder et al., 2018).

Toxin analysis from these cultured strains showed GTX2/3, C1/2 and STX as the most abundant toxins (no percentages reported). The three isolates produced six spiroolides, being SPX-1 the most abundant (83–93% of the total). The authors reported a novel analog, and named it spirolide M. The other four are still uncharacterized (named “compounds 1–4”) (Guinder et al., 2018). The novel spiroolides produced by the *A. ostenfeldii* isolates highlight the richness and structure variability of these toxins, and there are probably more analogs than previously thought, as often seen in toxin-producing plankton. This is the first toxinological research on *A. ostenfeldii* at higher latitudes of the Patagonian shelf, and the other isolated strain from a southern geographical area (Beagle Channel) did not produce PSTs, but only spiroolides (Almandoz et al., 2014).

Nevertheless, during this expedition the PST profiles from field plankton samples and those from the isolates did not match. The dominant toxins in field samples were GTX1/4, while the dominant toxins in cultures, including *A. catenella* and *A. ostenfeldii*, were C1/2 and GTX2/3, respectively. According to the authors, this discrepancy could be the result of a lack of detection of GTX1/4 due to the high limit of detection (LOD) for

this epimeric pair. Other possibilities are that the profile changed due to the growth conditions in culture or due to other PSTs producing organisms that have not been reported in the SW Atlantic (Guinder et al., 2018), which highlights the importance of enhanced research in the area.

Salgado et al. (2015) studied a Chilean strain of *A. ostenfeldii*. The authors analyzed and compared morphology and toxin production of three strains from the Baltic Sea (Finland), the Mediterranean Sea (Spain) and the Chilean coast. Strains were cultured L1 medium with a photoperiod of 12:12 L:D and different temperatures and salinities were tested, in a total of nine treatments for each isolate. Paralytic shellfish toxins were extracted with 0.05 M acetic acid, and analyzed by LC-FLD. For detection of *N*-sulfocarbamoyl toxins, a fraction of the acid extract was hydrolyzed. Less polar toxins SPX and GYM, were extracted with 100% methanol and LC coupled to high resolution mass spectrometry (LC-HRMS) was used. Analysis showed PSP toxins in Chilean and Baltic isolates, but no detectable amounts in the Mediterranean strain; PSP toxin profiles were similar in both strains but the Chilean isolate had a greater toxin content than the Baltic strain ($4.0 \pm 1.9 \text{ pg cell}^{-1}$). These results showed a significant correlation of toxin content and cell biovolume; as stated in previous studies with *A. catenella* from Chile, *A. ostenfeldii* showed higher toxin values when cultured at lower temperature (10°C), also at this temperature the cell volume was larger. In both isolates, detected toxins were GTX2/3 and STX. Trace amounts of dcSTX were found in all treatments except at 10°C and at a salinity of 32, where toxin content and cell biovolume were highest. Toxin profile and proportions did not change significantly among treatments (Salgado et al., 2015). Only the Mediterranean isolate produced detectable amounts of SPX, and only the Baltic isolate produced GYM toxins. Treatments affected mostly cell growth and toxin content, but no changes in the toxin profile were observed. The significantly high PSP toxin content detected in the Chilean isolate (max. 279.8 pg cell^{-1}) suggested that this species could be more toxic than isolates previously reported, and should be further analyzed given the natural conditions of the region, where water temperatures of 10°C and salinity of 32 are common (Almandoz et al., 2014). However, the three isolates showed great variations in toxin profiles in all treatments, suggesting this species has a great capability of adaptation, as reported for *A. catenella*. So far, information on this species complex in LAM is still scarce and there is a great need for more studies (Salgado et al., 2015).

Alexandrium tamiyavanichi

Only one study on *A. tamiyavanichi* toxin analysis has been reported in LAM. Toxins were extracted with 0.03 M acetic acid, and analyzed with LC-FLD. Analogs STX, NEO, GTX1-5, and dcGTX2/3 were searched for, but *N*-sulfocarbamoyl toxins were not analyzed. Reported toxins were STX, NEO, and GTX4 as the main components, followed by GTX3 and dcGTX2/3 (Menezes et al., 2010). In their study, despite general morphological characters agreed with those reported for *A. tamiyavanichi*, they detected important variability that could also match with the morphology of *A. cohorticula*, suggesting the possibility of being a conspecific species, pointing out the need

of genetic studies on wild and cultured populations to confirm their taxonomic identity, given that the use of morphological characters as the only tool for identification has caused previous misidentifications. Their phylogenetic analysis supported their identification as *A. tamiyavanichi*, even when the species has not been reported in the Atlantic coasts of South America. Previously *A. tamiyavanichi* has been reported in Asian countries (see Menezes et al., 2010 and references therein), and the possible explanation for this finding, given the lack of previous records of the species, could be that it has been part of the cryptic flora and that this zone has been part of their natural biogeography. The report of this toxin-producing species account to four PSTs producing dinoflagellates in the Brazilian coasts, where more studies are needed (Menezes et al., 2010).

Molecular Studies

Molecular markers have been particularly useful for discerning *Alexandrium* species when morphological traits are not sufficient, to know the genetic diversity among populations, or to determine phylogenetic relationships among species geographically distant. In LAm the few genetic studies in *Alexandrium* species have allowed to corroborate taxonomic questions, biogeographic history, and changes in distribution patterns. A classic study related with molecular phylogeny of *Alexandrium* genus in North America was published by Scholin et al. (1995). *Alexandrium catenella* and *A. tamarensis* belong to the species complex *A. catenella/tamarensis/fundyensis*; this group has reached relevance in South America due to its impact on fishing and aquaculture activities. The molecular markers developed by these authors are still used to answer current taxonomic and phylogenetic issues (Scholin et al., 1995).

The first attempt to obtain sequences of LSUrDNA of *A. catenella* was carried out in Chile. Sequences showed at least two different strains of the species that bloom in this region, with a proximity to the North American ribotype and distant proximity from the Asian ribotype (Córdova and Müller, 2002). Six years later, Uribe et al. (2008), constructed cDNA libraries from axenic strains from the AYSR in Chile, obtaining 10,850 expressed sequence tags (ESTs), where the most expressed genes corresponded to proteins coding for bioluminescence, carbohydrates, and those associated with photosynthesis (Uribe et al., 2008). They also carried out a detailed analysis of bioluminescent proteins: luciferin-binding protein and luciferase, additionally two unigenes presented 100% identity with a toxic strain-specific sequence of *A. tamarensis*. Moreover, ESTs of *A. catenella* were closely related to *A. tamarensis*. Taking into account that bioluminescence proteins were among the most expressed genes in *A. catenella*, the authors suggested that probably bioluminescence could be related with physiological responses such as predation avoidance and cell communication (Uribe et al., 2008).

Aguilera-Belmonte et al. (2011) compared physiological and genetic variability in populations of *A. catenella* from southern Chile isolated from the same toxic event. A remarkable variability at the genetic and physiological level among strains was observed. Chilean strains showed a higher genetic diversity (3%) than other strains of the world, and differences on PSTs

analogs were detected between strains. Intra-regional diversity of this species, partial sequences of the LSU gene, and ITS regions of rDNA, as well as toxicological and morphological analysis, have been evaluated. The analysis of rDNA sequences of Chilean strains were separated as part of the Clade I (North American) of the *A. tamarensis* species complex (Varela et al., 2012). However, a significant genetic diversity was observed between Chilean strains with ITS sequences. Although morphological variations within and between strains were observed, some features were absent, such as a ventral pore in the 1' plate, which was a distinctive characteristic in Chilean strains. These approaches indicate a significant intra-regional variability, however this genetic diversity does not agree with the supposed northward expansion along the west coast of South America.

Sequences from the ITS1, 5.8S rDNA, ITS2, and D1-D5 LSUrDNA regions, were used to identify strains of the morphospecies *A. catenella* as *A. tamarensis*. Species-specific primers designed for real time PCR were a good molecular tool to detect this dinoflagellate in bivalves such as *M. edulis* (Jedlicki et al., 2012).

Persich et al. (2006) investigated the probable origin of *A. tamarensis* in Brazil, and found a close relationship between this species with *A. tamarensis*, *A. fundyensis* and *A. catenella* from North America, northern Europe and northern Asia (Scholin et al., 1994; Medlin et al., 1998). Interestingly, they did not find any close relationship to any of the *A. tamarensis* complex from the southern hemisphere. According to the molecular information, they proposed that the isolates used for this study were probably transported from Uruguayan waters during coastal fronts in Argentina and Uruguay; they considered the possibility of further outbreaks from transported cells or resting cysts in Brazilian coasts (Persich et al., 2006). Even though the origin of the so-called "North American type" *Alexandrium* is not clear, DNA results in this study support the hypothesis of an early establishment of these populations during a period of cooler global oceans, when natural boundaries did not exist and transport across hemispheres was possible. This hypothesis was proposed since the LSUrDNA sequences from South American isolates have enough differences from the North American modern populations that may indicate that these populations have been separated for a long time, and evolutionary processes have occurred (Persich et al., 2006).

Recently, Fabro et al. (2017) carried out morphological and genetic analyses of three morphospecies of *Alexandrium* from the Argentinean Sea. Their results showed some variations in morphological characteristics, but were consistent with classical descriptions of *A. tamarensis* and *A. ostenfeldii*, however cells of *A. minutum* had morphological traits that did not agree completely with the description from Balech (Balech, 1995; Fabro et al., 2017). Using qPCR method, it was possible to corroborate the presence of *A. minutum* and *A. ostenfeldii* in NT samples. While partial sequences of the LSUrRNA of the *A. tamarensis* complex clustered within the *Alexandrium* ribotype Group I, and were consistent with *A. catenella*. This was the first report of *A. minutum* and *A. ostenfeldii* on this area of Argentinean Sea (Fabro et al., 2017).

Cruzat et al. (2018) determined genetic variability of *A. catenella* analyzing ITS1-5.8S-ITS2 sequences of ribosomal DNA of environmental samples from the Southern Austral ecosystem. The authors found 33 haplotypes, three of these highly frequent, increasing the genetic diversity from 2.8 to 3.1%, for this species in the study area. All sequences agreed with the morphological identification for *A. catenella*, with sub-clades that correspond to haplotypes from distinct geographic regions (Cruzat et al., 2018).

Toxin profiles, morphology and phylogeny were also investigated by Salgado et al. (2015) in three strains of *A. ostenfeldii* from the Baltic, Mediterranean, and southern Chile. The phylogenetic reconstruction was performed with LSU rRNA sequences, showing a geographic distribution congruent with the selected strains. Strain AOA32 from Chile only produced PSTs, and had a close phylogenetic relationship with a strain from Callao, Peru (Salgado et al., 2015).

Using morphological traits and LSU and ITS sequences Menezes et al. (2010), identified *A. tamiyavanichi* and general morphological characters agreed with those reported previously; however, they detected important variability that could also match with the morphology of *A. cohorticula*. The most important feature to identify cells of this species is the anterior sulcal plate, while less than 10% of the analyzed specimens did not agree with the morphology of *A. tamiyavanichi*. Therefore, they suggested the possibility of them being conspecific species, and pointed out the need of genetic studies on wild and cultured populations to confirm their taxonomic identity, given that the use of morphological characters as an only tool for identification has caused misidentifications. Phylogenetic reconstruction showed a monophyletic clade, which included Brazilian and Asiatic strains, with enough genetic distance between them. Moreover, based on their results they propose a *fraterculus* group (*A. tamiyavanichi/tropicale/fraterculus*) as a sister group of *A. tamarensis* species complex (Menezes et al., 2010). New morphological and molecular data (28S and ITS rDNA) for *Alexandrium* species from Brazil, confirm a close phylogenetic relationship among *A. tamiyavanichi* and *A. fraterculus* (Menezes et al., 2018), while *A. catenella* sequences were grouped with con-specifics from North America, Chile and Japan, moreover a genetic variability within *A. tamutum* clade was found, including a new record of this species for Brazil. Two strains isolated from Guanabara Bay formed a monophyletic clade with both molecular markers; suggesting it could be a new species of *Alexandrium* closely related to *A. minutum* and *A. tamutum*.

In the Mexican Pacific coast *A. tamiyavanichii* was found and described less than a decade ago (Esqueda-Lara and Hernández-Becerril, 2010), due to the difficulty for identifying and quantify this species Hernández-Becerril et al. (2018) analyzed ITS2 rDNA sequences obtained by real-time quantitative PCR (qPCR), managing to detect cell abundances of <30 cells L^{-1} in field samples. Differences in cell densities and their distribution in water column were observed, and two explanations were proposed: *A. tamiyavanichii* could be transported off the coast due to physical forces such as winds and upwelling, or when environmental conditions are favorable, the physiological

characteristics of this species allows it to maintain high cell abundances.

Associations With Bacteria

Dinoflagellates are characterized by different ecological relationships. A relationship that has acquired a great interest is the one established between bacteria and dinoflagellates. This interest relies since bacteria are capable of regulating the different HAB phases, in addition that they are considered to have a role in cell toxicity, growth, and other physiological aspects of dinoflagellates (Hold et al., 2001; Uribe and Espejo, 2003; Croft et al., 2005; Maas et al., 2007).

Alexandrium strains from the southern coast of Chile grow in association with heterotrophic bacteria that mostly affect its growth by the synthesis of algicidal substances that promote cell lysis (Vasquez et al., 2001; Córdova et al., 2002; Uribe and Espejo, 2003). The proliferation of *A. catenella* in the decade of 1980 in Chile, allowed to report the presence of intracellular bacteria in vegetative cells, and to describe the process of bacterial phagocytosis (Córdova et al., 2002). Also, this was the first time that bacteria of the genus *Moraxella* sp. were isolated from the cell surface of the dinoflagellate, and related with the production of small amounts of STX (Guzmán et al., 1975; Silva, 1982; Kodama et al., 1990; Orr et al., 2013).

The genera *Cytophaga*, *Pseudoalteromonas*, and *Ruegeria* released alga-lytic compounds among other compounds when grown in absence of phytoplankton cells, causing high mortality ($>50\%$) in *A. catenella*. When the same bacteria, free of organic nutrients, were returned to the algal culture they displayed no detrimental effects on the dinoflagellate and recovered their symbiotic characteristics. Thus, bacterial-derived lytic activities are expressed only in the presence of high-nutrient media and it is likely that *in situ* environmental conditions modulate their expression (Amaro et al., 2005). Another aspect to consider is the geographical distribution of strains, since despite isolating the bacteria from different regions, the associated bacteria community is similar, recording the presence of the genera *Psychrobacter*, *Sulfitobacter*, *Aeromonas*, *Flavobacterium*, *Pseudomonas*, *Proteus* and *Moraxella* in isolates of *A. catenella* and *A. fundyense* from different regions of Chile and the Bay of Fundy, respectively (Ferrier et al., 2002).

Bacterial phagocytosis by *Alexandrium* has also been documented (Silva, 1982). In total absence of bacteria, cell toxicity of *A. catenella* decreased five times as the majority of the STX analogs decreased significantly, with the exception of NEO. Also, as the culture of the dinoflagellate reached the stationary phase, the cell abundance proportion of bacteria:dinoflagellate remained constant (3,000 bacteria cell⁻¹ of *Alexandrium*), however, bacterial size tended to increase, suggesting they could be saprophytic bacteria that feed on dinoflagellate by-products (Schut et al., 1993; Dantzer and Levin, 1997; Uribe and Espejo, 2003).

CONCLUSION

In LAM, the three main marine dinoflagellate genera that produce PSTs are widely distributed and represent an important

risk for human health, economic and ecological reasons. PSTs have been also related to epizootic events, fish and aquaculture losses, though most of the times the impacts have not been calculated in economic terms. Despite these problems and risks, few countries have established and maintained monitoring programs, and losses due to PSTs are becoming an important public concern. HABs research efforts have been concentrated in North America (*G. catenatum* in Mexico) and in South America (*A. catenella*, *A. tamarensis* mainly in Chile and Argentina). Few studies regarding *P. bahamense* exist, probably because this species is found mainly in regions with low resources for research, which could explain partially why this is the PST species that has caused greater human impacts.

Studies related to bloom dynamics, autoecology and toxins of *G. catenatum* are mostly from Mexico, however, this species has been reported in several countries, but in some regions, the species identification remains to be confirmed. Blooms have been associated with a narrow temperature window (18–25°C), high irradiance, transitional hydrographic conditions, El Niño events, and nutrient increase, mostly from river runoffs and coastal upwelling (Table 7). Even though natural plankton samples have a low toxicity, and a profile dominated by the less toxic sulfocarbamoyl analogs, this profile can change in mollusk tissues due to their digestive metabolism and become highly toxic for consumers. Interestingly, autoecology studies have demonstrated that the cell toxin content is higher under *in vitro* conditions than in the natural environment, which can be partly explained by the higher nutrient concentrations used in culture media. It has also been proposed that the toxin composition is not a conservative feature in *G. catenatum*, however some populations appear to be pretty consistent in their toxin profile, such as strains from LAm, but strain studies from other regions of LAm need to be carried out to confirm this. It has also been demonstrated that under culture conditions, *G. catenatum* tolerates a wide range of temperature, salinity, irradiance and N:P ratios, which probably explains its wide distribution along the Mexican Pacific coast. Nevertheless, some variations exist, which have been related to strain origin, temperature, and culture age.

The distribution of *P. bahamense* is restricted to tropical latitudes. Blooms have been related to warm waters (27–31°C), heavy rains, strong winds, and to El Niño events (Table 7). This species is found in a broad salinity range from 7 to 35. It has been suggested that it could be an invasive species in the northern boundary of its distribution (GOLCA region). Data regarding toxicity and toxin profile of natural phytoplankton samples are scarce and contradictory, carbamoyl or sulfocarbamoyl analogs can dominate. Toxin profiles in mollusks is also quite variable. It is clear that more research and close monitoring is needed for the understanding of the bloom ecology on this species.

HABs of *Alexandrium* toxic species are mostly reported in South America, being the main responsible species *A. catenella* (Chile) and *A. tamarensis* (Uruguay-Argentina), which have had severe social impacts, and for this reason research has been concentrated on these two species. In general, *Alexandrium* species bloom at colder temperatures (5–14°C) than *G. catenatum* and *P. bahamense*. HABs of *A. catenella*

are related to high irradiances, water stratification, and extreme climatic conditions such as a higher SST, decreased salinity and precipitation, higher nutrients and El Niño events (Table 7). Deep water upwelling also trigger blooms and cyst beds play an important role in the initiation of blooms. Also, an important expansion in the northern limits of these species has been registered, but the reason for this remains to be understood. Seasonal differences in cell toxicity and in toxin analogs in *A. catenella* have been found in environmental samples, and contrary to *G. catenatum* cell toxin content is higher in environmental samples than cultured strains, indicating that toxin metabolism in both species is regulated by different factors.

Regarding toxin analysis in PSTs producers, an important factor to be considered is the different techniques used to extract and analyze toxins which have led to different and confusing results in some cases samples from the same species and region. Different studies have used two acids (hydrochloric acid or acetic acid) in various concentrations, sometimes even using thermic processing of samples. Post-column and pre-column oxidations methods are used, with different drawbacks such as lack of separation of some analogs or the inability to detect some others, and even the appearance of phantom peaks that could be mistaken for toxin analogs. Also, GC toxins are not yet considered in normal analysis and their presence is often neglected due to the longer retention times needed to elute them, and to the lack of commercial standards. It is clear that only a few countries in LAm have the sufficient technological and technical capacity to analyze paralytic toxins a factor that needs to be considered to support both research and monitoring programs in this region.

Other studies such as molecular biology, *in silico* analyses in order to assess toxicity, nutrient assimilation, trophic interactions, and bacterial community studies are still incipient in LAm, but given the great importance of PSTs producing species in LAm, undoubtedly they will continue to increase in the next few years.

This review evidences that studies have been concentrated in relatively few countries, species and topics. And in some regions studies are only supported for a few years by specific research groups. In general, there is equipment and technical limitation in the different regions of LAm. A regional HAB research program is needed in order to have a more complete understanding of the environmental conditions that favor the PST blooms in this region.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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