4 Effects of Harmful Algal Bloom Toxins on Marine Organisms

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INTRODUCTION

Phytoplanktonic communities are vital to marine ecosystems. These communities constitute the basis of marine food webs throughout the planet, providing food for filter-feeding organisms, such as bivalves and planktivorous fish and also a number of vertebrate and invertebrate larval stages. Algal blooms are natural occurrences, defined as the sudden overgrowth of microscopic algae under optimal environmental conditions, reaching up to millions of cells per litre (Hallegraeff 1993). These blooms are typically beneficial for the ecosystem, increasing feeding opportunities for countless organisms. However, if toxin-producing microalgae undergo this sudden overgrowth, it can lead to harmful algal blooms (HABs). Despite the fact that approximately 2 percent of microalgae species produce toxins (Hallegraeff 2014, Smayda 1997), HABs can significantly impact marine communities.

In the marine realm, the majority of HAB-toxins are produced by dinoflagellates and diatoms (Table 1). Biochemically, phycotoxins are secondary metabolites that can have a wide range of effects. They can act on the nervous system (brevetoxins), which can induce permanent short-term memory loss (domoic acid) or cause sensorimotor impairment, leading to death (paralytic shellfish toxins) and act on the digestive tract, inducing gastrointestinal distress (diarrhetic shellfish toxins). During the last decades, several new toxins and new toxin derivatives, such as gymnodimines, azaspiracids, pterotoxins, pinnatoxins and hydroxybenzoate saxitoxin, okadaic and domoic acid

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Table 1. The most common toxins produced by marine phytoplankton.

Toxin	Toxic phytoplankton species	Mode of action	Toxin family
Saxitoxins	*Alexandrium* sp., *Gymnodinium catenatum*, *Pyrodinium bahamense*	Inhibition of voltage-gated sodium channels in neural cells	Paralytic shellfish toxins
Domoic acid	*Pseudo-nitzschia* spp., *Amphora coffaeaiformis*, *Nitzschia* sp.,	Binding to glutamate receptors in neural cells causing constant influx of Ca^{2+}	Amnesic shellfish toxins
Brevetoxins	*Karenia brevis*, *Karenia* sp., *Chatonella* cf. *verrucosa*, *C. antiqua*, *C. marina*, *Fibrocapsa japonica*, *Heterosigma akashiwo*	Binding to voltage-sensitive sodium channels causing membrane depolarization	Neurotoxic shellfish toxins
Okadaic acid and dinophysistoxins	*Dinophysis* sp., *Prorocentrum* sp.	Inhibition of activity of protein phosphatase 1 and 2	Diarrhetic shellfish toxins

analogues have been described, mostly due to scientific and technological advances (Cruz et al. 2006, Miles et al. 2000, Negri et al. 2003, Satake et al. 1998, Takada et al. 2000, Zaman et al. 1997). In addition, changes on global climate conditions and anthropogenic pressures have been conducting several tropical and subtropical endemic HAB-toxins, namely ciguatoxins, palytoxins and brevetoxins to expand their geographical range into temperate waters (Botana et al. 2015, Villareal et al. 2007).

There is a great body of available information regarding the effects of these toxins in marine organisms, although, the information is much dispersed. Therefore, and with recent increases in HAB frequency and intensity, this chapter aims to update and summarize the available information on the effects of different phycotoxins in marine organisms.

Routes of Toxin Exposure

Toxin transfer can be foodborne or waterborne, that is via food web transfer or through exposure to toxins dissolved in the water after their excretion or cell release (Fig. 1). The most likely pathway of toxin transfer is when toxin-producing species bloom, thus achieving massive concentrations in the water column. However, there are many potential toxin vectors (Fig. 2), depending mostly on the ecology of the toxin-producer (pelagic or epibenthic) and the organism's likelihood of exposure to the toxin.

If an organism is exposed to a sudden bloom of toxin-producing microalgae, the toxin concentrations will certainly trigger immediate physiological and behavioural alterations and ultimately cause the death of the organism. In addition, the continuous exposure to low HAB-toxin concentrations can lead to chronic effects.

Here, the pathways of exposure will be divided into direct and indirect contact with the toxin-producer. Through ingestion of toxic phytoplanktonic cells by filter-feeding organisms, such as bivalve molluscs, zooplankton and planktivorous fish, the toxins present inside the cell can accumulate in the predator's viscera. This can create

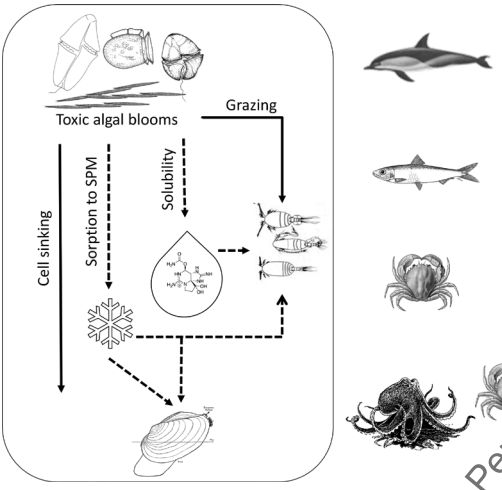

Fig. 1. Foodborne and waterborne exposure to HAB-toxins. Solid lines illustrate the well documented route of dietary exposure; dashed lines illustrate the less studied routes of dissolved toxins exposure.

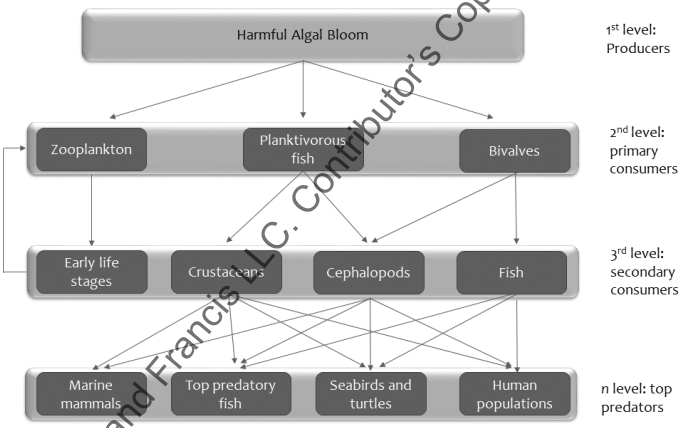

Fig. 2. Schematic view of HAB-toxins food web transfer.

a chain of vectors throughout the food web, potentially eliciting adverse effects in marine communities. Depending on the vector, these toxins can be transferred to humans and cause a variety of shellfish poisonings, due to the ingestion of contaminated shellfish, such as Amnesic Shellfish Poisoning (ASP), Paralytic Shellfish Poisoning (PSP), Neurotoxic Shellfish Poisoning (NSP), Diarrhetic Shellfish Poisoning (DSP) and other syndromes (Table 1).

Some microalgae species produce exotoxins, or exudates, that are released into the water column, causing other organisms to come inadvertently in contact with these compounds. Similarly, when the bloom becomes senescent, the cells lyse and release the toxins to the surrounding environment (Lefebvre et al. 2008), opening another possible pathway to the organisms' direct contact with the toxins. Lastly, there are other HAB-species which segregate the toxin on the outer surface of their

cells, potentially inducing damage upon contact. These toxins' effects on marine organisms will be discussed in detail in the following sections.

HAB-toxin Effects on Marine Organisms

Paralytic shellfish toxins

Paralytic shellfish toxins (PSTs) are one example of phycotoxins produced by dinoflagellates, and one of the most abundant and toxic phycotoxins in oceans worldwide. Dinoflagellates from three genera, *Alexandrium, Gymnodinium* and *Pyrodinium*, produce saxitoxin or a suite of over 50 derivatives (Anderson et al. 2012), which the most frequent can be divided according to their chemical structure into carbamoyl, decarbamoyl and sulfamate toxins. These compounds block the conduction of electrical impulses in neural cells through the inhibition of voltage-gated sodium channels on these cell's membranes. This leads to membrane hyperpolarization and results in paralysis in muscle cells as determined in laboratory animals (Kao and Nishiyama 1965, Ritchie and Rogart 1977). PSTs have shown to elicit a wide range of effects on marine organisms, from sublethal and recoverable effects to events of mass mortality in fish, marine mammals and seabirds (Tables 2a and 2b).

PSTs producers inhabit the pelagic realm, the same habitat as many planktonic species. Therefore, plankton species come in contact with PSTs through contact with PST-producing cells or their exudates. It has been shown that many planktonic organisms can be affected by these toxins. In some cases, PSTs inhibit the growth of diatoms, haptophytes and heliozoans, and induce disruptions in swimming behaviour leading to death in ciliates (Table 2a). Diatoms and haptophytes had reduced growth rates after being placed in water previously conditioned by the PSTs producer *A. lusitanicum*, presumably releasing the watersoluble toxins into the culture medium (Blanco and Campos 1988).

Regarding the effects of PSTs on planktonic grazers, there are several studies indicating that some species can selectively avoid ingestion of toxic dinoflagellates, while others do not (Turner and Tester 1997). The latter group can present different effects, with some species being less affected by the toxins, namely *Euterpina acutifrons*, and other species, such as *Acartia grani*, presenting high mortality rates (Costa et al. 2008, 2012).

Direct exposure of bivalve molluscs to PST-producers has been shown to elicit negative effects, as summarized in Table 2a. Exposure to dinoflagellate cells increased shell valve closure in many bivalve species (e.g., *Crassostrea virginica*, *Mytilus edulis*), leading to decreased filtration rates, potentially impacting the animal's normal feeding behaviour. *A. minutum* and purified STX exposure in *C. gigas* resulted in decreased phagocytic activity and ROS production in oyster hemocytes (Mello et al. 2013), leading to higher susceptibility of contracting an infection. Also, the presence of the toxic dinoflagellates decreased byssus production in *M. edulis* and *Geukensia demissa*. However, byssus production in mussels (*M. edulis*) that have been previously exposed to these toxins was less affected.

Table 2a. Documented cases of marine invertebrates exposed to and affected by paralytic shellfish toxins (PSTs).

	Target species	PST source	Route of exposure	Levels of exposure	Tissues analysed	Effects	Observations	References
Phytoplankton	*Isochrysis galbana*	*A. lusitanicum*	Exposure in pre-conditioned seawater with *A. lusitanicum*	-	-	Reduced growth rates	Seawater previously containing *A. lusitanicum* cultures	(Blanco and Campos 1988)
	Pavlova lutheri	*A. lusitanicum*	Exposure in pre-conditioned seawater with *A. lusitanicum*	-	-	Reduced growth rates	-	(Blanco and Campos 1988)
	Skeletonema costatum	*A. lusitanicum*	Exposure in pre-conditioned seawater with *A. lusitanicum*	-	-	Reduced growth rates	-	(Blanco and Campos 1988)
Ciliates	*Favella ehrenbergii*	*A. tamarense*	Exposure to *A. tamarense* cells	4×10^6 cells L^{-1}	-	Disruption of swimming patterns, immobilization, swelling and death	-	(Hansen 1989)
		A. ostenfeldii	Exposure to *A. ostenfeldii* cells	Higher than 2×10^6 cells L^{-1}	-	Backward swimming, swelling and death	-	(Hansen et al. 1992)
Crustaceans	*Acartia clausi*	*A. lusitanicum*	Exposure to *A. lusitanicum* cells	Up to 1600 µg C L^{-1}		Egg production limited	-	(Dutz 1998)

		A. minutum	Exposure to *A. minutum* cells	Up to 0.7 µg C ml^{-1}	*A. minutum* cultures	Increased feeding rates with increasing dinoflagellate densities, lower hatching success and nauplii production	-	(Frangopulos et al. 2000)
	A. hudsonica	*Alexandrium* spp.	Exposure to *Alexandrium* spp. cells	Up to 1×10^3 cells L^{-1}	-	Non-selectively fed on *Alexandrium* spp.	-	(Teegarden et al. 2001)
		A. fundyense	Exposure to *A. fundyense* cells	-	-	Naïve populations had decreased somatic growth, size at maturity, egg production and survival	-	(Colin and Dam 2004)
		Protogonyaulax tamarensis (now A. tamarense)	Exposure to *A. tamarense* cells	25×10^4–30×10^4 cells L^{-1}	-	Lower activity, reduced feeding rates	-	(Ives 1987)
	A. tonsa	*Alexandrium* spp.	Exposure to *Alexandrium* spp. cells	Up to 25 pg STX eq $cell^{-1}$	Dinoflagellate cultures	Avoided feeding on toxic *Alexandrium* spp.	-	(Teegarden 1999)
	Calanus helgolandicus	*G. tamarensis* (now *A. tamarense*)	Exposure to *A. tamarense* cells	-	-	Reduced fecundity	-	(Gill and Harris 1987)

Table 2a contd. ...

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	Target species	PST source	Route of exposure	Levels of exposure	Tissues analysed	Effects	Observations	References
	Calanus finmarchicus	*A. excavatum*	Exposure to *A. excavatum* cells	45 µg STX kg^{-1}	Copepods	Avoided feeding on toxic *A. excavatum*	-	(Turriff et al. 1995)
	Centropages hamatus	*Alexandrium* spp.	Exposure to *Alexandrium* spp. cells	Up to 31 pg STX eq $cell^{-1}$	Dinoflagellate cultures	Avoided feeding on toxic *Alexandrium* spp.	-	(Teegarden 1999)
	Eurytemora herdmani	*Alexandrium* spp.	Exposure to *Alexandrium* spp. cells	Up to 31 pg STX eq $cell^{-1}$	Dinoflagellate cultures	Non-selectively fed on *Alexandrium* spp.	-	(Teegarden 1999)
	Euterpina acutifrons	*A. minutum* and *G. catenatum*	Exposure to *A. minutum* and *G. catenatum* cells	Up to 10^6 cells L^{-1} (*A. minutum*) and 17.5×10^4 cells L^{-1} (*G. catenatum*)	-	Reduced naupliar activity at low cell densities, immobility at higher cell densities	-	(Bagøein et al. 1996)
	Palaemonetes pugio	*Gonyaulax monilata* (now *A. monilatum*)	Exposure to *A. monilatum* cells	Up to 1.2×10^6 cells L^{-1}	-	High mortality rates following molting	-	(Sievers 1969)
	Pseudocalanus sp.	*P. tamarensis (now A. tamarense)*	Exposure to *A. tamarense* cells	Up to 6×10^5 cells ml^{-1}		Lower activity, reduced feeding rates	-	(Ives 1987)
	Nauplii of *Semibalanus balanoides*	*Alexandrium* spp.	Exposure to *Alexandrium* spp. cells	Up to 1×10^3 cells L^{-1}	-	Avoided feeding on toxic *Alexandrium* spp.	-	(Teegarden et al. 2001)
	Temora longicornis	*G. tamarensis* (now *A. tamarense*)	Exposure to *A. tamarense* cells	-	-	Reduced fecundity	-	(Gill and Harris 1987)

Annelids	*Neanthes succinea*	*Gonyaulax monilata* (now *A. monilatum*)	Exposure to *A. monilatum* cells	Up to 1.2 × 10^6 cells L^{-1}	-	High mortality rates following spawning	-	(Sievers 1969)
	Polydora websteri	*Gonyaulax monilata* (now *A. monilatum*)	Exposure to *A. monilatum* cells	Up to 1.2 × 10^6 cells L^{-1}	-	High mortality rates following spawning	-	(Sievers 1969)
Molluscs	Larvae of *Argopecten irradians concentricus*	*A. tamarense*	Exposure to *A. tamarense* cells	Up to 11 pg STX eq $cell^{-1}$	*A. tamarense* cultures	Activity and growth inhibition, lower attachment rates and reduced climbing rates	-	(Yan et al. 2003)
	A. ventricosus	*G. catenatum*	Exposure to *G. catenatum* cells	Up to 4 × 10^6 cells L^{-1}	-	Lower feeding activity, paralysis, increase in hemocytes, epithelial melanisation, increase in pseudofaeces production	Paralysis was found to be reversible	(Escobedo-Lozano et al. 2012)
	Larvae of *Chlamys farreri*	*A. tamarense*	Exposure to *A. tamarense* cells	Up to 5.9 × 10^9 g STX L^{-1}	*A. tamarense* cultures	High mortality rates, lower hatching rates	-	(Yan et al. 2001)
	Crassostrea gigas	*G. washingtonensis* (now *A. catenella*)	Exposure to *A. catenella* cells	5 × 10^4 cells L^{-1}	-	Reduced pumping activity, increased valve activity	-	(Dupuy and Sparks1967)
		A. minutum	Exposure to *A. minutum* cells	Up to 12 × 10^4 cells L^{-1}	-	Decreased valve activity, clearance and filtration rates		(Lassus et al. 1999)

Table 2a contd. ...

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	Target species	PST source	Route of exposure	Levels of exposure	Tissues analysed	Effects	Observations	References
		A. tamarense and *A. minutum*	Exposure to dinoflagellate cells	Up to 12 × 10^8 cells L^{-1}	-	Reduced clearance rates		(Laabir and Gentien 1999)
		A. minutum	Exposure to *A. minutum* cells	5 × 10^6 cells L^{-1}	-	Mono and diacylglycerols reduced in digestive gland, inflammation of gastrointestinal tract, modified spermatozoa and mitochondria	-	(Haberkorn et al. 2010)
		A. minutum	Exposure to *A. minutum* cells	15 × 10^6 cells L^{-1}	-	Altered circadian rhythm	-	(Tran et al. 2015)
		A. minutum	Exposure to *A. minutum* cells and purified STX	2 × 10^4 cells L^{-1} and 0.05 µg STX L^{-1}	-	Reduced hemocyte phagocytic activity, decreased ROS production	Results obtained in both treatments	(Mello et al. 2013)
	Larvae of *C. gigas*	*A. tamarense*	Exposure to *A. tamarense* cells	Up to 10^8 $cells^{-1}$	-	High mortality rates	-	(Matsuyama et al. 2001)
		A. taylori	Exposure to *A. taylori* cells	Up to 10^8 $cells^{-1}$	-	High mortality rates	-	(Matsuyama et al. 2001)
	C. virginica	*G. monilata* (now *A. monilatum*)	Exposure to *A. monilatum* cells	Up to 1.2 × 10^6 cells L^{-1}	-	Inhibition of byssus production and shell closure	-	(Sievers 1969)
	Brachiodontes recurvus	*G. monilata* (now *A. monilatum*)	Exposure to *A. monilatum* cells	Up to 1.2 × 10^6 cells L^{-1}	-	Inhibition of byssus production and shell closure	-	(Sievers 1969)

	Geukensia demissa	*P. tamarensis* (now *A. tamarense*)	Exposure to *A. tamarense* cells	2.5–5.5 × 10^5 cells L^{-1}	-	Inhibited cardiac activity	-	(Gainey and Shumway 1988)
		A. tamarense	Exposure to *A. tamarense* cells	10^5 cells L^{-1}	-	Reduced clearance rates	-	(Lesser and Shumway 1993)
		P. tamarensis (now *A. tamarense*)	Exposure to *A. tamarense* cells	5 x 10^5 cells L^{-1}	-	Reduced clearance rates, increased mucus production	-	(Shumway and Cucci 1987)
		P. tamarensis (now *A. tamarense*)	Exposure to *A. tamarense* cells	10^6 cells L^{-1}	-	Inhibition of byssus production	-	(Shumway et al. 1987)
	Mercenaria mercenaria	*A. tamarense*	Exposure to *A. tamarense* cells	10^5 cells L^{-1}	-	Reduced clearance rates	-	(Lesser and Shumway 1993)
	Mya arenaria	*P. tamarensis* (now *A. tamarense*)	Exposure to *A. tamarense* cells	2.5–5.5 × 10^5 cells L^{-1}	-	Inhibited cardiac activity	-	(Gainey and Shumway 1988)
		A. tamarense	Exposure to *A. tamarense* cells	Up to 77 × 10^4 µg STX eq kg^{-1} in viscera	Viscera and other tissues	Naïve populations had higher toxicity and mortality, reduced clearance rates, oxygen consumption rates and burrowing capacity	-	(MacQuarrie and Bricelj 2008)
		A. tamarense	Exposure to *A. tamarense* cells	10^5 cells L^{-1}	-	Reduced clearance rates	-	(Lesser and Shumway 1993)

Table 2a contd. ...

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	Target species	PST source	Route of exposure	Levels of exposure	Tissues analysed	Effects	Observations	References
		P. tamarensis (now *A. tamarense*)	Exposure to *A. tamarense* cells	5×10^5 cells L^{-1}	-	Reduced clearance rates	-	(Shumway and Cucci 1987)
		A. excavata and *A. tamarense*	Exposure to *Alexandrium* spp. cells	Up to 30.4×10^4 µg STX eq kg^{-1}	Soft tissue	Burrowing incapacity	-	(Bricelj et al. 1996)
	Larvae and post-larvae *M. arenaria*	*A. tamarense*	Exposure to *A. tamarense* cells	Up to 64–69 pg STX eq $cell^{-1}$	Soft tissue	Larvae not affected, post larvae exhibited high mortalities, paralysis, burrowing incapacity	Naïve populations were more severely affected	(Bricelj et al. 2010)
	Mytilus edulis	*P. tamarensis* (now *A. tamarense*)	Exposure to *A. tamarense* cells	$2.5–5.5 \times 10^5$ cells L^{-1}	-	Inhibited cardiac activity	Transient inhibition, long term inhibition and long-term excitation	(Gainey and Shumway 1988)
		Dissolved STX	Intramuscular injection	3330 µg STX kg^{-1}	Digestive glands	Higher GST activity	-	(Gubbins et al. 2001)
		A. tamarense	Exposure to *A. tamarense* cells	10^5 cells L^{-1}	-	Reduced clearance rates	-	(Lesser and Shumway 1993)
		P. tamarensis (now *A. tamarense*)	Exposure to *A. tamarense* cells	5×10^5 cells L^{-1}	-	Increased mucus production	-	(Shumway and Cucci 1987)
		P. tamarensis (now *A. tamarense*)	Exposure to *A. tamarense* cells	10^6 cells L^{-1}	-	Inhibition of byssus production	-	(Shumway et al. 1987)

	M. chilensis	*A. catenella*	Exposure to *A. catenella* cells	Up to 7240 µg STX eq kg^{-1}	Soft tissue	Clearance rates, ingestion of organic matter, and absorption efficiency decreased at the start of the experiment.	Effects reversible after three days	(Navarro and Contreras 2010)
	Nodipecten subnodosus	*G. catenatum*	Intramuscular injection of GTX 2/3	Up to 0.18 µg STX	-	Paralysis, mantle retraction, inhibition of shell closure, hemocyte reduction		(Estrada et al. 2010)
	N. subnodosus	*G. catenatum*	Exposure to *G. catenatum* cells	2×10^6 cells $individual^{-1}$	-	Production of pseudofaeces, partial shell closure, increase in melanisation, increased activity of GPx and lipid peroxidation in gills, decrease in SOD activity in gills	-	(Estrada et al. 2007)
	Ostrea edulis	*P. tamarensis* (now *A. tamarense*)	Exposure to *A. tamarense* cells	$2.5–5.5 \times 10^5$ cells L^{-1}	-	Decreased in heart rate	Effects reversible	(Gainey and Shumway 1988)
	Perna canaliculus	*A. tamarense*	Exposure to *A. tamarense* cells	12950 µg STX eq kg^{-1}	Soft tissue	No mortalities, normal byssus production and oxygen consumption rates	Oxygen consumption rate increased after 1 h of exposure but normalized after 24 h recovery	(Marsden and Shumway 1992)

Table 2a contd. ...

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	Target species	PST source	Route of exposure	Levels of exposure	Tissues analysed	Effects	Observations	References
	P. viridis	*A. tamarense*	Exposure to *A. tamarense* cells	10^5 cells L^{-1}	-	Reduced clearance rates	-	(Lesser and Shumway 1993)
	Placopecten magellanicus	*P. tamarensis* (now *A. tamarense*)	Exposure to *A. tamarense* cells	5×10^5 cells L^{-1}	-	Increased clearance rates	-	(Shumway and Cucci 1987)
	Ruditapes phillipinarum	*A. tamarense*	Exposure to *A. tamarense* cells	Up to 170 µg STX eq kg^{-1}	Soft tissue	Decreased absorption efficiency and reduced scope for growth with higher toxin concentration, decreased clearance and growth rates	-	(Li et al. 2002)
		A. tamarense	Exposure to *A. tamarense* cells	2×10^5 cells L^{-1}	-	Hepatic GPx, gill LPO were positively correlated with PSP concentrations, GST presented negative correlation	-	(Choi et al. 2006)
	Spisula solidissima	*A. tamarense*	Exposure to *A. tamarense* cells	10^5 cells L^{-1}	-	Reduced clearance rates	-	(Lesser and Shumway 1993)

Table 2b. Documented cases of marine vertebrates exposed to and affected by paralytic shellfish toxins (PSTs). IP – Intraperitoneal; IC – Intracoelomic.

	Target species	PST source	Route of exposure	Levels of exposure	Tissues analysed	Effects	Observations	References
Fish	*Chanos chanos* fingerlings	*A. minutum*	Dinoflagellate cells and extracts	-	-	Damage to the gills (hyperplasia, edema and necrosis)	Exposure to different cell densities	(Chen and Chou 2001)
	Clupea harengus harengus	PSTs extracted from *G. excavata* (now *A. tamarense*)	Oral and IP (intraperitoneal injection)	Up to 5240 µg STX eq kg^{-1}	Viscera	Irregular swimming behaviour, loss of balance, shallow and arrhythmic breathing	Death occurred after 20–60 min of exposure in both routes	(White 1981)
	Larval *Clupea harengus harengus*	*P. tamarensis* (now *A. tamarense*)	Dinoflagellate cells and extracts, via prey	Exposure up to 15×10^5 cells L^{-1}	-	Paralysis and erratic swimming, increased mortality	Heart stopped 20 min after complete immobilization	(Gosselin et al. 1989)
	Larval *Clupea harengus pallasi*	Dissolved STX	Uptake from surrounding seawater	4000 µg STX eq kg^{-1}/day for 7 days	-	Reduced spontaneous and touch-activated swimming	Effects reversible	(Lefebvre et al. 2005)
	Cyprinodon variegatus	*G. monilata* (now *A. monilatum*)	Exposure to *A. monilatum* cells	Up to 1.2×10^6 cells L^{-1}	-	100 percent mortality rate	-	(Sievers1969)
	Larval *C. variegatus*	*A. fundyense*	Prey (copepod *Coullana canadensis*)	9–12 µg STX eq kg^{-1}	Whole body	Death after consuming 6–12 contaminated copepods	Reduced prey capture and predator avoidance	(Samson et al. 2008)
	Diplodus sargus	PSTs extracted from *G. catenatum*	Intracoelomic injection (IC)	15.2 µg STXeq kg^{-1}	Liver	Increased GST activity and erythrocyte nuclear abnormalities	-	(Costa et al. 2012)

Table 2b contd. ...

Table 2b contd. ...

	Target species	PST source	Route of exposure	Levels of exposure	Tissues analysed	Effects	Observations	References
	Fundulus heteroclitus	Dissolved STX	Uptake from surrounding seawater	0, 75, and 150 ppb, nominal concentrations	-	Decreased c-Fos expression, paralysis, decreased activity, floating	-	(Salierno et al. 2006)
	Larval *Fundulus heteroclitus*	*A. fundyense*	Prey (copepod *Coullana canadensis*) and *A. fundyense*	17–25 µg STX eq kg^{-1}	Whole body	Death after consuming 6–12 copepods and following direct ingestion of dinoflagellate cells	Reduction in prey capture, swimming performance	(Samson et al. 2008)
	Larval *Mallotus villosus*	*P. tamarensis* (now *A. tamarense*)	Exposure to *A. tamarense* cells	Up to 15×10^5 cells L^{-1}	-	Paralysis and erratic swimming, increased mortality	Heart stopped 20 min after complete immobilization	(Gosselin et al. 1989)
	Pollachius virens	PSTs extracted from *G. excavata* (now *A. tamarense*)	Oral and IP	Up to 3430 µg STX eq kg^{-1}	Viscera	Irregular swimming behaviour, loss of balance, shallow and arrhythmic breathing	Death occurred after 20–60 min of exposure in both routes	(White 1981)
	Pseudopleuronectes americanus	PSTs extracted from *G. excavata* (now *A. tamarense*)	Oral and IP	Up to 8370 µg STX eq kg^{-1}	Viscera	Irregular swimming behaviour, loss of balance, shallow and arrhythmic breathing	Death occurred after 20–60 min of exposure in both routes	(White 1981)
	Recently-settled *P. americanus*	*A. fundyense*	Prey (copepod *Coullana canadensis*)	41–58 µg STX eq kg^{-1}	Whole body	Death after consuming 6–12 contaminated copepods	Reduced swimming abilities	(Samson et al. 2008)

	Onchorhynchus mykiss	Dissolved STX	IP injection	1.752 µg kg^{-1}	-	Elevated levels of cortisol, decreased attack latency times	-	(Bakke et al. 2010)
	Salmo salar	Dissolved STX	IP injection	10 µg STX kg^{-1}	-	Loss of balance, decreased respiration rate, muscle bursts and twitching	-	(Bakke et al. 2010)
		PSTs extracted from *G. excavata* (now *A. tamarense*)	Oral and IP	Up to 9410 µg STX eq kg^{-1}	Viscera	Irregular swimming behaviour, loss of balance, shallow and arrhythmic breathing	Death occurred after 20–60 min of exposure in both routes	(White 1981)
Seabirds	*Uria aalge californica, Gavia arctica pacifica, Melanitta fusca deglandi, Lunda cirrhata, Puffinus griseus, Fulmarus glacialis, Diomedea nigripes*	*Gonyaulax catenella* (now *A. catenella*)	Prey (small fish and crustaceans)	-	-	Death	-	(Mckernan and Scheffer 1942)
	Larus argentatus	*G. catenella* (now *A. catenella*)	Prey (small fish and crustaceans)	-		Death	-	(Mckernan and Scheffer 1942)
		A. tamarense	Likely *Ammodytes hexapterus*	1100 (intestine) and 480 (brain) µg STX eq kg^{-1}	Intestine and brain of dead birds	Death	-	(Levasseur et al. 1996)
		G. excavata (now *A. tamarense*)	Likely *A. hexapterus*	970 µg STX eq kg^{-1} in *A. hexapterus*	Prey	Death	-	(Nisbet 1983)

Table 2b contd. ...

Table 2b contd. ...

	Target species	PST source	Route of exposure	Levels of exposure	Tissues analysed	Effects	Observations	References
	L. dominicus	*G. catenella* (now *A. catenella*), *G. grindleyi* (now *Protoceratium reticulatum*)	Prey (mussels)	-	-	Death	Some bird populations decreased drastically following dinoflagellate outbreak	(Shumway et al. 2003)
	L. hartlaubii	*G. catenella* (now *A. catenella*), *G. grindleyi* (now *Protoceratium reticulatum*)	Prey (mussels)	-	-	Death	Some bird populations decreased drastically following dinoflagellate outbreak	(Shumway et al. 2003)
	L. occidentalis	*G. catenella* (now *A. catenella*)	Prey (small fish and crustaceans)		-	Death	-	(Mckernan and Scheffer 1942)
	Haematopus moquini	*G. catenella* (now *A. catenella*), *G. grindleyi* (now *Protoceratium reticulatum*)	Prey (mussels)	-	-	Death	Some bird populations decreased drastically following dinoflagellate outbreak	(Shumway et al. 2003)
	L. atricila	*G. excavata* (now *A. tamarense*)	Likely *A. hexapterus*	970 µg STX eq kg^{-1} in *A. hexapterus*	-	Death	-	(Nisbet 1983)

	Phalacrocorax aristotelis	*G. tamarensis* (now *A. tamarense*)	-	Not determined in birds. Up to 6000 MU (mouse units) 100 g^{-1} in mussel meat	-	Intestinal hemorrhaging; loss of balance and stagger, vomiting, death	Drastic population decline	(Armstrong et al. 1978)
	Anas rubripes	*G. tamarensis* (now *A. tamarense*)	Prey (mussels)	20000–40000 µg STX eq kg^{-1}	-	Death	Other bird species affected nearby	(Shumway et al. 2003)
	Sterna hirundo, S. paradisaea, S. dougallii	*G. excavata* (now *A. tamarense*)	Likely *A. hexapterus*	970 µg STX eq kg^{-1} in *A. hexapterus*	-	Death	-	(Nisbet 1983)
Marine Mammals	*Monachus monachus*	*A. minutum*		3030–3390 µg STX eq kg^{-1}	Liver	Death	Analysis on stranded animals	(Costas and Lopez-Rodas 1998)
		G. catenatum or *Pyrodinium bahamense* var. *compressa*	Prey	6–900 µg dcSTX kg^{-1}	Liver, kidney, muscle, brain	Death	PST producer uncertain, analysis on stranded animals	(Reyero et al. 2000)
		A. minutum, G. catenatum, D. acuta	Prey	2–280 µg dcSTX kg^{-1} liver 8–64 µg dcSTX kg^{-1} brain	Liver, kidney, muscle, brain	Lethargy, sensorimotor impairments, paralysis, death	PST producer uncertain	(Hernández et al. 1998)
	Megaptera novaeangliae	-	Horse mackerel (*Scomber scombrus*)	-	-	Death	PST producer uncertain, analysis on stranded animals	(Geraci et al. 1989)

Similar experiments performed on greenshell mussels (*Perna canaliculus*) showed that mussels presented oxygen consumption and clearance rates similar to the control group after 24 h exposure to *A. tamarense* (Marsden and Shumway 1992).

Exposure of *M. chilensis* to *A. catenella* for 21 days (Navarro and Contreras 2010) resulted in lowered clearance rates, organic matter intake and absorption efficiency at the start of the experiment, followed by an increase to levels similar to the ones presented in the control group. The STX uptake steadily increased throughout the experiment, similarly to the mussels' excretion rates. Oxygen consumption rates seemed unaffected by the ingestion of this toxic species, revealing that this species may possess defence mechanisms that allow them to feed safely on this dinoflagellate.

On the other hand, some scallop and clam species presented negative effects when exposed to this toxin. The scallop *Nodipecten subnodosus* presented paralysis of the adductor muscle while maintaining the digestive tract functioning after receiving intramuscular injections of GTX 2/3. Also, the hemocyte number decreased and they presented mantle retraction and their shells remained open up to 40 days after the exposure (Estrada et al. 2010). In a different study on the same species (Estrada et al. 2007), exposure to *G. catenatum* cells resulted in the increased production of mucus, pseudo-faeces, melanisation and hemocyte aggregation in gill tissue. Biochemically, an antioxidative stress response to the toxin was shown in gill tissue, this tissue being the first to come in contact with the toxin. There was an increase in glutathione peroxidase (GPx) activity and lipid peroxidation, along with a decrease in superoxide dismutase activity, indicating oxidative and cellular damage. Similar results were obtained when feeding *G. catenatum* cultures to scallops (*Argopecten ventricosus*) (Escobedo-Lozano et al. 2012). The scallops presented paralysis of the adductor muscle, lower feeding activity, increased pseudo-faeces production, increased number of hemocytes in gill, mantle and adductor muscle tissue and epithelial melanisation in gill and mantle tissue. These results indicate that scallops have efficient mechanisms that protect them against lethal effects from external toxicants. Studies conducted in *Ruditapes phillipinarum* feeding on *A. tamarense* cultures for 6 (Li et al. 2002) and 15 days (Choi et al. 2006) showed reduced scope for growth, decreased absorption efficiency, clearance and growth rates after six days of exposure, and increased activity of GPx in hepatopancreas and gill lipid peroxidation with increasing toxin burden after 15 days of exposure.

PST effects on bivalve early stages are comparatively less understood. Bricelj et al. (2010) addressed this issue by exposing larvae, post-larvae and juveniles of *Mya arenaria* to *A. tamarense*. They showed that larvae were not significantly affected by the dinoflagellate due to the fact that the cells were too large for prey capture; thus, the larvae did not accumulate the toxin or displayed any intoxication symptoms. On the other hand, the post-larvae presented decreased burrowing capacity, here used as proxy of sensitivity to PSTs. Also, the post-larvae had increased mortality rates, especially in populations that are not usually exposed to *A. tamarense* blooms, while juvenile were less susceptible.

PST effects on bivalves are species-specific and seem to differ geographically within the same species and life stages. Species that are usually exposed to toxic dinoflagellate blooms seem to be more resistant, and appear to have developed

defence mechanisms that allow them to cope with high PST levels, unlike other species in areas less affected by blooms.

These studies reveal that bivalves are not immune to the effects of PST contamination, and there are some species with higher sensitivity to these toxins. This may pose additional concerns over the ecosystem's health and elicit negative economic impacts, since some of these species are commercially farmed in shellfish aquacultures, and blooms may occur in farmed areas.

PSTs have long been associated with fish kills. Fish can be directly exposed to the toxins, as is the case of planktivorous fish such as sardines, herring and anchovies, or indirectly through feeding on vectors, affecting many levels of the marine food web, from groupers and hake to sturgeons and artificially fed fish, such as farmed salmon.

Only a few events have been directly linked to PST contamination, since these events are unpredictable and sporadic, many times leading to inconclusive data. For a complete list of fish kills associated with PSTs refer to Costa (2016, Table 1).

When studying PST's effect on fish, it is procedurally simpler to inject the toxin intracoelomically (IC), in order to closely control the given concentration. Standard STX is the toxin most commonly administered. However, despite the benefits, these methods are less ecologically relevant, since the toxins do not enter directly in the coelom, and STX is but a fraction of the toxins produced by the dinoflagellate species. Nevertheless, these studies provide windows into the symptoms presented by fish and insight into the effects of these neurotoxins.

STX's effects on killifish (*Fundulus heteroclitus*) were quantified regarding the expression of c-Fos protein (Salierno et al. 2006), responsible for regulating neural cells' survival, and is associated with long term memory (Sadananda and Bischof 2002). It was shown that the expression of this protein decreased, and the fish presented behavioural alterations including paralysis, lethargy and loss of balance. STX most likely affects the neural pathways responsible for swimming. In Atlantic salmon (*Salmo salar*), it was shown that STX crosses the blood-brain barrier and that sublethal doses of this toxin affect the activity of brain subregions in the central nervous system (CNS), possibly affecting the organism's cognitive abilities (Bakke and Horsberg 2007). Intracoelomic injections of STX in white seabream (*Diplodus sargus*) resulted in an increase of glutathione-S-transferase (GST) activity, an enzyme responsible for removing xenobiotics, among many other roles. STX also induced DNA damage (chromosome breaks or loss) and increased erythrocyte nuclear abnormalities (Costa et al. 2012).

In order to simulate bloom conditions, milkfish (*Chanus chanus*) fingerlings were exposed to STX extract and *A. minutum* cells in increasing concentrations and cell density, respectively (Chen and Chou 2001). After 24 h, the fish presented oedema, hyperplasia and necrosis in gill lamellae. The exposure also resulted in increased mortality rates in the treatments with higher cell density and STX concentrations, due to increasing oxygen demand following gill damage. Similar results reporting gill damage following fish exposure to PST-producing dinoflagellate cells were found in salmon and trout (Mortensen 1985). White (1981) reported high mortality rates after 20 to 60 minutes in Atlantic herring (*Clupea harengus harengus*), American pollock (*Pollachius virens*), winter flounder (*Pleuronectes americanus*), Atlantic salmon (*S. salar*) and cod (*Gadus morhua*) when dosed intraperitonially (IP) or orally with

toxin extracts from *A. tamarense* cultures. Prior to death, the fish presented loss of balance, immobilization and arrhythmic breathing, consistent with the symptoms described here in adult fish.

In early stages of development, some fish species present different ecologies than the adults, starting out as planktonic larvae, and thus occupying the same niche as the pelagic dinoflagellate PST-producers. Also, earlier stages of development are likely more vulnerable to the effects of these toxins as they possess higher mass-specific metabolic rates and they lack fully developed detoxification systems (Vasconcelos et al. 2010).

Overall, when fish early stages are exposed to bloom simulations in experimental conditions, it resulted in extremely high mortality rates, nearing the totality of the experimental population, besides the sublethal effects displayed by the young (Table 2b). Fish early stages can be exposed to the toxin through feeding on zooplanktonic vectors, such as copepods, or through direct exposure to the dissolved toxins. Recently settled flounders (*P. americanus*), sheepshead minnow (*Cyprinodon variegatus*) and mummichog larvae (*F. heteroclitus*) were fed with contaminated copepods, acting as vectors of *A. fundyense* (Samson et al. 2008). After consuming 6–12 contaminated copepods, the fish died. In this study, the fish were also fed with fewer copepods, resulting in a variety of effects, such as reduced swimming abilities, prey capture success, predator avoidance and overall activity (Table 2b).

Gosselin et al. (1989) exposed capelin and herring larvae to three different treatments to ascertain the effects of PSTs through different routes of exposure, recurring to both direct exposure through feeding the larvae with *A. tamarense* cells in increasing densities, and placing toxin extracts in the experimental tanks. Indirect exposure was achieved by feeding the larvae with contaminated microzooplankton. Capelin and herring larvae fed on *A. tamarense* swam erratically, lost motility and sank to the bottom paralysed, dying after 20 minutes of exposure, contrary to the lack of effect when exposed directly to the toxin dissolved. Feeding these larvae with contaminated zooplankton elicited similar results as feeding directly on the dinoflagellate, resulting in paralysis and high mortality rates. However, exposure of herring larvae to dissolved STX resulted in a reversible dose-dependent suite of sensorimotor impairments (Lefebvre et al. 2005), such as spontaneous swimming and tactile response inhibition. Also, it was shown that older larvae were more susceptible to the dissolved toxin, likely due to the degree of gill and body maturation leading to higher toxin uptake.

Monk seal populations have been greatly impacted by PST outbreaks. In the late 1990s in Cape Blanc Peninsula over 100 monk seals died following PST intoxication. Tissue analysis revealed PSTs in brain tissue, suggesting that these toxins were present in the seal's nervous system (Costas and Lopez-Rodas 1998, Reyero et al. 2000). The cause has been attributed to PSTs since there were high levels of these toxins in many fish species that the seals prey upon (Reyero et al. 2000). Dying organisms presented many behavioural alterations, lethargy, paralysis and sensorimotor discoordination (Hernández et al. 1998).

Earlier, in 1987, over a dozen humpback whales washed ashore dead along Nantucket Sound. The cause of the stranding was ascertained by analysing fish and whale tissues. It was determined that one of the fish species analysed, Atlantic

mackerel (*Scomber scombrus*), presented high levels of STX and stomachal content analysis revealed that the whales were previously feeding on this species. It was worth noting that the time-lapse between the onset of the first symptoms and death (approximately 90 minutes, Geraci et al. 1989), suggesting a very quick process, characteristic of severe STX intoxication.

Seabird deaths due to HAB-toxins have been comparatively overlooked. However, there have been countless events where many seabird species died following the ingestion of contaminated fish and shellfish (Table 2b). Shumway et al. (2003) extensively reviewed all the registered seabird deaths that were linked with HAB-toxins, including PSTs. PSTs were reported to cause loss of motor coordination and paralysis, resulting in the bird's inability to feed and thus, causing death by starvation. Female terns presented an inability to lay eggs due to sublethal onset of paralysis, resulting in the egg breaking inside the body and causing fatal haemorrhages. Other species presented severe inflammation of the gastro-intestinal tract and haemorrhages in the intestines and brain.

Understanding the effects of PSTs, which are produced worldwide, is of vital importance, since, as reviewed here, the range of possible consequences is very wide. In some cases, the toxins directly affect the species, causing high mortalities, and in other cases the toxin accumulates and is transferred throughout many levels of the marine food web, causing indirect damage to the ocean's health, communities and human populations.

Amnesic shellfish toxins

Domoic acid (DA) is a potent neurotoxin produced by some species belonging to two genera of diatoms, *Pseudo-nitzschia* and *Nitzschia*. This toxin is known to cause Amnesic Shellfish Poisoning (ASP), and the attention on this toxin and its possible consequences was focused after an incident involving the death of three people in 1987 following the ingestion of mussels contaminated with DA. Afterwards, most coastal countries developed monitoring programs, regularly analysing bivalve tissue for DA and other phycotoxins in order to prevent foodborne illnesses. These monitoring programs have been successful at avoiding further human casualties. Nevertheless, there have been many events of DA intoxication in marine organisms.

DA acts in neural cells, competing for the same receptors as glutamate, an excitatory neurotransmitter. By having less affinity for these receptors, glutamate fails to bind normally, causing excessive concentrations of glutamate outside the synapses, triggering AMPA, kainate and NMDA receptors' activation, permanently opening the neural cell's membrane, leading to excessive influx of Ca^{2+} (Berman and Murray 1997). This causes membrane depolarization and subsequent degeneration of neural cells. The higher concentration of glutamatergic receptors in the hippocampus, the brain region responsible for memory acquisition and learning, is the cause for the memory loss.

In Table 3 we summarized the effects of DA in marine organisms. Bivalves are common vectors of this toxin and the effects of this toxin seem somewhat overlooked. DA seems to affect haemolymph chemistry, increase the number of hemocytes as well as increase cholinesterase activity and DNA damage. On the other

Table 3. Documented cases of marine organisms exposed to and affected by domoic acid (DA). IP – Intraperitoneal; IC – Intracoelomic.

	Target species	DA source	Route of exposure	Toxicity	Tissues analysed	Effects	Observations	References
Crustaceans	*Tigriopus californicus*	Dissolved DA	Uptake from seawater	8.62 µM	-	Death	-	(Shaw et al. 1997)
Molluscs	*C. gigas*	*P. pungens* f. *multiseries*	Exposure to diatom cells	Up to 0.86 µg DA g^{-1}	Soft tissue	Increased number and activity of hemocytes	Effects reversible	(Jones et al. 1995)
		P. pungens f. *multiseries*	Exposure to diatom cells	36.3 µg DA g^{-1}	Soft tissue	Respiratory acidosis, haemolymph hypercapnia and increased bicarbonate, low haemolymph PO_2 levels	Haemolymph PO_2 and pH returned to normal	(Jones et al. 1995)
	M. californianus	*P. pungens* f. *multiseries*	Exposure to diatom cells	3.6 µg DA g^{-1}	Soft tissue	Increased haemolymph pH, decreased PO_2, decreased PCO_2	Effects reversible	(Jones et al. 1995)
	M. edulis	Dissolved DA	Intramuscular injection	Up to 50 µg DA g^{-1}	-	Cholinesterase activity, DNA damage and number of hemocytes increased, phagocytic activity decreased	-	(Dizer et al. 2001)
	Larvae of *P. maximus*	Dissolved DA	Uptake from seawater	5.21 pg DA $individual^{-1}$	Whole body	Decreased growth, shell length and survival	Exposure of 25 days	(Liu et al. 2007)
	P. maximus	Dissolved DA	Feed incorporated with DA	Up to 302.5 ng DA g^{-1}	Whole body	Decreased growth and survival	-	(Liu et al. 2008)

Fish	*O. kisutch*	Dissolved DA	IC injections	Up to 34 µg DA g^{-1}	-	Circle, spiral and upside-down swimming	-	(Lefebvre et al. 2007)
	O. mykiss	Dissolved DA	IP injections	0.75 mg DA kg^{-1}	-	Increased cortisol levels, decreased attack latency time	-	(Bakke et al. 2010)
	Engraulis mordax	Dissolved DA	IC injections	Up to 14 µg DA g^{-1}	-	Spinning, disorientation, inability to school, death	-	(Lefebvre et al. 2001)
	S. salar	Dissolved DA	IP injections	6 mg DA kg^{-1}	-	Increase in metabolic activity	-	(Bakke and Horsberg 2007)
	F. heteroclitus	Dissolved DA	IP injections	5 mg DA kg^{-1}	-	Increased c-Fos activity expression in optic brain regions	-	(Salierno et al. 2006)
	Sparus aurata	Dissolved DA	IP injections	Up to 9 mg DA kg^{-1}	-	Death at higher concentrations, spiral, circle and upside-down swimming	Sublethal effects (swimming anomalies) reversible after 24 h	(Nogueira et al. 2010)
	Siganus oramin	Dissolved DA	IC injections	2 x 10^3 µg DA kg^{-1}	-	Increased CYP1A activity (protein involved in xenobiotic metabolism)	-	(Wang et al. 2008)

Table 3 contd. ...

...Table 3 contd.

	Target species	DA source	Route of exposure	Toxicity	Tissues analysed	Effects	Observations	References
Sea birds	*Callithrix jacchus*	Dissolved DA	IP injection	4 mg DA kg^{-1}	-	Epileptic seizures, death	-	(Perez-Mendes et al. 2005)
	Pelecanus occidentalis	*Pseudo-nitzschia* sp.	Prey (*S. scombrus*)	37.17 × 10^3 µg DA kg^{-1}	Digestive tract	Death	150 birds dead in 5 days	(Sierra-Beltrán et al. 1997)
		P. australis	Prey (*E. mordax*)	27.9 × 10^3 µg DA kg^{-1}	Pelican stomach	Hemorrhage, tissue necrosis, death	Death occurred after ~ 60 min of exposure	(Work et al. 1993)
		P. australis	Prey (*E. mordax*)	45–48 × 10^3 µg DA kg^{-1}	Pelican stomach	Death		(Fritz et al. 1992)
	Phalacrocorax penicillatus	*P. australis*	Prey (*E. mordax*)	27.9 × 10^3 µg DA kg^{-1}	Cormoran stomach	Hemorrhage, tissue necrosis, death	Death occurred after ~ 60 min of exposure	(Work et al. 1993)
		P. australis	Prey (*E. mordax*)	45-48 × 10^3 µg DA kg^{-1}	Cormoran stomach	Death		(Fritz et al. 1992)
Marine mammals	*Balaenoptera acutorostrata*	*P. australis*	Prey (*E. mordax*)	258 × 10^3 µg DA g^{-1}	Whale feces	Death	-	(Fire et al. 2010)
	Callorhinus ursinus	*Pseudo-nitzschia* sp.	Likely through prey	18600 × 10^3 ng DA kg^{-1}	Seal's feces	Ataxia, seizures, lesions in brain and heart, death	-	(Lefebvre et al. 2010)
	Kogia breviceps	*Pseudo-nitzschia* sp.	Likely through prey	13.56 × 10^3 ng DA kg^{-1}	Whale feces	Death	-	(Fire et al. 2009)

	K. sima	*Pseudo-nitzschia* sp.	Likely through prey	967 × 10^3 ng DA kg^{-1}	Whale feces	Death	-	(Fire et al. 2009)
	Zalophus californianus	*Pseudo-nitzschia* sp.	Likely through prey	96.8 × 10^3 µg DA kg^{-1}	Sea lion's feces	Ataxia, head weaving, disorientation, seizures and death	-	(Bargu et al. 2011)
		P. australis	Likely through prey	Up to 182.01 × 10^3 µg DA L^{-1}	Sea lion's feces	Ataxia, head weaving, disorientation, seizures and death	-	(Scholin et al. 2000)
		Pseudo-nitzschia sp.	Maternal transfer	44 × 10^3 ng DA L^{-1}	Stomach contents of premature pups	Premature births, abortions, reproductive failure and brain edema	-	(Goldstein et al. 2009)
		Pseudo-nitzschia sp.	Maternal transfer	261 × 10^3 ng DA L^{-1}	Maternal urine	Premature births, abortions and reproductive failure	-	(Brodie et al. 2006)
		P. australis	Prey (*E. mordax*)		-	Seizures, hippocampal atrophy, neural necrosis	-	(Silvagni et al. 2005)
		-	-	-	-	Heart and brain lesions, death	-	(Zabka et al. 2009)
		P. australis	Prey (*E. mordax*)	136.5 × 10^3 µg DA kg^{-1}	Sea lion's feces	Death	-	(Lefebvre et al. 1999)

hand, exposure to this toxin decreased phagocytic activity, growth and survival rates. In some cases, the effects of exposure to the DA-producing diatoms were reversible and the organisms recovered after a short period of time (up to 24 h), emphasizing the notion that bivalves are quite resilient to DA and other toxins.

Information regarding the effects of DA in wild animals is very scarce and limited to marine mammals and seabirds. Domoic acid's effects on fish have been studied through IC injection (Table 3). This technique allows the use of known DA concentrations without dispersal throughout the organism's body. However, this method does not always allow for ecologically relevant DA concentrations to be used or for natural DA uptake and transfer between body tissues to take place naturally. Regarding the effects of DA in fish, most studies concluded that it causes abnormal swimming behaviour, including spiral, circle and upside-down swimming, and ultimately death. Other effects that can escalate DA toxicosis are inability to school in *Engraulis mordax* (Lefebvre et al. 2001), possibly making the fish easier targets for predators, disrupting the balance of the food web during diatom blooms.

Killifish (*F. heteroclitus*) IC injected with up to 9 mg DA kg^{-1} showed that c-Fos activity, a protein associated with long term memory (Sadamanda and Bischof 2002), increased in several brain regions, indicating neuronal stress following exposure. Variations in c-Fos expression can lead to effects at the behavioural levels, as observed in Salierno et al. (2006), such as disorientation and loss of equilibrium.

One of the main groups affected by domoic acid are marine mammals, more specifically sea lions. There is an extensive record of sea lion deaths going back nearly two decades, when over 400 sea lions (*Zalophus caifornianus*) were found stranded or displayed neurological symptoms associated with DA intoxication, later confirmed by detecting DA in sea lions' tissues (Scholin et al. 2000). The cause of death was attributed to ingestion of contaminated anchovies, a common food source for these mammals. Behavioural tests and magnetic resonance imaging (MRI) performed on sea lions displaying intoxication symptoms revealed abnormal behaviours, such as head weaving, ataxia and severe disorientation. The MRIs showed hippocampal lesions damaging hippocampal-thalamic networks. Also, DA has been detected in the stomach contents of premature pups and shown to elicit premature births, abortions and death of pregnant sea lions (Brodie et al. 2006) due to the consumption of contaminated prey, possibly endangering this species' populations. Throughout the years, many other events of sea lion mortality have been attributed to DA intoxication (Table 3).

Studies regarding the interaction of HAB-toxins occurring simultaneously is very scarce. However, between February–April 2008, over 100 dolphins (*T. truncatus*) were found stranded along the coast of Texas, and their tissues were positive for DA, brevetoxins and okadaic acid (Fire et al. 2011), although in different proportions and only a small percentage was positive for more than one toxin. The mass stranding may be linked to an interaction of these three toxins, but without historical data and means of comparison, it may not be safe to conclude so.

DA, as mentioned above, acts on glutamatergic receptors, mainly present in organisms with developed brains, possibly explaining the discrepancy between the effects caused in vertebrates and invertebrates. Invertebrates are likely less affected by this toxin, since they mostly lack complex brains and possess effective

elimination systems, as in the case of bivalve molluscs. The fact that bivalves seem to be less affected and are efficient at eliminating DA does not exclude the sublethal effects that it may cause in other organisms higher up the food web, through chronic ingestion of contaminated prey.

Brevetoxins

Brevetoxins (BTXs—PbTx1-10, BTX 1-4) are produced by dinoflagellates and raphidophytes and can cause Neurotoxic Shellfish Poisoning (NSP). These toxins are a group of complex polycyclic polyether compounds that alter the properties of membranes in excitable cells by binding to voltage sensitive sodium channels in nerve cells, leading to membrane depolarization and disrupting normal processes in nerve cells (Landsberg 2002, Lopes et al. 2013). The term "red tides" is mainly associated with blooms of *Karenia brevis* (= *Gymnodinium breve*), which proliferate in great concentrations and their pigments discolour the surrounding seawater. This dinoflagellate is mainly responsible for causing many events of mass mortality in marine organisms, with reports dating back to the 19th century (Glennan 1887). Although no human deaths have been related to brevetoxins, human populations are affected at the sublethal level, mostly through consumption of contaminated shellfish or aerosol inhalation during red tide events (Landsberg 2002). Effects of brevetoxins in marine organisms, from copepods to marine mammals, are summarized in Table 4.

Brevetoxins can have allelopathic effects on other species of phytoplankton, as shown in Prince et al. (2008), where cultures of *Asterionellopsis glacialis*, *Prorocentrum minimum* and *Skeletonema costatum* presented decreased growth rates when their individual cultures were mixed with *K. brevis* cultures and exudates.

Studies on copepods revealed that these organisms are very sensitive to *K. brevis*, by presenting accelerated heart rates, loss of motor control, suppressed swimming behaviour, lethargy, paralysis, regurgitation and decreased survival and growth (Cohen et al. 2007, Huntley et al. 1987, Huntley et al. 1986, Sykes and Huntley 1987, Turner et al. 1996). Other BTXs producers have elicited negative impacts upon feeding in copepods (Uye 1986, Uye and Takamatsu 1990).

Bivalves, as one of the main vector of phycotoxins, also accumulate high concentrations of BTX, with very few studies regarding its effect. Leverone et al. (2007) showed that when exposed to *K. brevis* cells and extracts caused reduced clearance rates in *A. irradians, C. virginica, Mercenaria mercenaria* and *P. viridis*. Recruitment of bay scallop (*A. irradians concentricus*) in North Carolina was greatly affected by *K. brevis* blooms, jeopardizing the sustainability of scallop beds in the region (Summerson and Peterson 1990).

Red tides can also affect the species' abundance and richness of the impacted areas, in some cases nearly wiping out many important benthic infaunal species (Simon and Dauer 1972), decreasing richness in fish species by 50 percent and causing a decrease in invertebrate species' abundance in general (Dupont et al. 2010).

Knowledge on the effects of BTXs in fish is very scarce beside the numerous accounts of fish kills associated with BTXs (Gunter et al. 1948, 1947, Rounsefell and Nelson 1966, Thronson and Quigg 2008). Flaherty and Landsberg (2011) reported reduced annual recruitment in *Cynoscion nebulosus*, *C. arenarius*, and *Sciaenops*

Table 4. Documented cases of marine organisms exposed to and affected by okadaic acid (OA) and dinophysistoxins (DSTs).

	Target species	OA source	Route of exposure	Toxicity	Tissues analysed	Effects	Observations	References
Molluscs	*M. edulis*	Dissolved OA	Mixed with algal diet	2.5 nM OA	-	Increased DNA fragmentation	-	(McCarthy et al. 2014)
	M. galloprovincialis	Dissolved OA	*In vitro* exposure	Up to 500 nM OA	-	DNA damage leading to necrosis and apoptosis in gill tissue	-	(Prego-Faraldo et al. 2015)
		Dissolved OA	Mixed with mussel feed	Up to 6.5 µg OA	-	Up-regulation of gene transcripts associated with stress response	-	(Manfrin et al. 2010)
	C. gigas	Dissolved OA	Mixed with algal diet	2.5 nM OA	-	Increased DNA fragmentation	-	(McCarthy et al. 2014)
	C. virginica	*P. minimum*	Exposure to dinoflagellate cells	3.9×10^6 cells ml^{-1}	-	Larvae presented lower growth rates, and slower development	-	(Wikfors and Smolowitz 1995)
	P. perna	*P. lima*	Exposure to dinoflagellate cells	Up to 10000 cells $mussel^{-1}$	-	Higher incidence of micronuclei and nuclear lesions in hemocytes	-	(Carvalho Pinto-Silva et al. 2005)
		Dissolved OA	Uptake from seawater	0.3 µg OA	-	Higher incidence of micronuclei in hemocytes	-	(Carvalho Pinto-Silva et al. 2003)

	R. decussatus	*P. lima* extracts and cells	Exposure to extracts and dinoflagellate cells	Up to 100 nM OA and 20000 cells ml^{-1}	-	DNA damage in gill tissue	-	(Flórez-Barrós et al. 2011)
Fish	*Dicentrarchus labrax*	*P. lima* pre-conditioned seawater	Exposure to pre-conditioned sewater with *P. lima*	Previously with 9×10^3 cells ml^{-1}	-	Reduced feeding reflexes, abnormal swimming patterns	-	(Ajuzie 2007)
		P. lima	Exposure to dinoflagellate cells	4.5×10^3 cells ml^{-1}	-	Death	-	(Ajuzie 2007)

ocellatus and Riley et al. (1989) revealed that upon hatching, larvae of *S. ocellatus* were negatively affected by BTXs, developing deformities, swimming erratically and being paralysed before dying. Seabird deaths attributed to brevetoxicosis date back to the early 70's, when thousands of lesser scaup (*Athya affinis*) died concurrently in a red tide event (Forrester et al. 1977), along with many other seabird species throughout the years (Landsberg et al. 2009). Also, a number of sea turtles strandings have been positively linked to red tide events, as the number of strandings increases during red tides (Landsberg et al. 2009).

The highly endangered Florida manatees (*Trichechus manatus latirostris*) have suffered great impacts from red tides. In 1996, over a hundred manatees died following a red tide caused by *K. brevis* (Bossart et al. 1998), likely through prolonged exposure to BTX aerosols or ingestion of contaminated seawater. Recently, Flewelling et al. (2005) showed that seagrass (*Thalassia testudinum*) accumulates high concentrations of BTXs, the main manatee food source, opening a likely pathway for manatees' BTX uptake. Since 1996, many other events of marine mammal mortality have been attributed to BTXs intoxication (reviewed in Landsberg et al. 2009). What is worth noting is the death of 107 bottlenose dolphins (*Tursiops truncatus*), following a red tide in 2002. Again, Flewelling et al. (2005), analysed dolphin tissues and undigested fish remains, and concluded that both had very high levels of BTXs, enough to cause brevetoxicosis and death. Until then, fish were not considered likely vectors of this toxin, as it caused the fish to die in a very short period of time, limiting the toxin transfer higher up the food chain. Several mass fish kills followed red tides (Landsberg 2002, 2009, Steidinger et al. 1973), drawing attention to this toxin's ichthyotoxic potential. Many studies have revealed that fish are more sensitive to BTXs dissolved in seawater than ingestion of *K. brevis* cells. It was shown that fish survive direct exposure to the dinoflagellate cells, whereas exposure to the dissolved toxin leads to death (Landsberg et al. 2009).

The effects of BTXs are still poorly understood, especially in marine invertebrates, despite the great impact red tides have on ecosystems worldwide.

Diarrhetic shellfish toxins

Diarrhetic Shellfish Toxins (DSTs) are produced by many species of *Dinophysis* and *Prorocentrum*, both cosmopolitan genera occurring worldwide. *Dinophysis* are pelagic species, whereas *Prorocentrum* are typically epibenthic. DSTs are lipophilic toxins, comprising okadaic acid (OA) and dinophysistoxins (DTX).

OA was first isolated from the marine sponge *Halichondria melanodocia*. It was later discovered that this toxin was produced by a dinoflagellate that was accumulated in the sponge through filter-feeding. OA specifically inhibits the activity of protein phosphatase 1 and 2, two of the main protein phosphatases in mammals, increasing protein phosphorylation. Gastrointestinal distress symptoms may arise from the loss of balance in membrane transport and substance secretion, resulting in loss of fluids.

The effects of OA and dinophysistoxins on marine organisms are summarized in Table 5. DSP outbreaks are not caused any human fatalities (Hallegraeff et al. 2003), and of all the other shellfish poisonings, it can be considered the mildest, with patients fully recovering after few days. However, OA has been identified as a

tumour promoting compound (Suganuma et al. 1988), posing additional threats to human health and marine life alike.

OA has been documented to be actively accumulated in sponges, which increases the sponge's immune system against parasites and bacterial infections (Schröder et al. 2006, Wiens et al. 2003).

It is worth noting that, although greatly lacking supportive evidence, *P. lima* has been shown to elicit allelopathic effects when grown in culture with other microalgal species. OA and DTX-1 produced by *P. lima* inhibit the growth of the other species present, and, at lower concentrations it enhanced growth in *P. lima* cultures (Windust et al. 1996). Similarly, when exposed to OA, *Dunaliella tertiolecta* cultures decreased cell density and increased oxidative stress response. Additionally, OA inhibited the ability for electron transport in photosystem II, impairing photosynthesis (Perreault et al. 2012).

Regarding other marine organisms, OA has been found to accumulate in numerous shellfish species, the main vectors of this toxin. Blue mussels have been reported to accumulate high concentrations of OA for long periods of time (up to five months, Shumway 1990). Typically, bivalves are not directly affected by the toxins, most likely due to their rapid clearance rates and the fact that many species can convert the parent compound into less toxic derivatives (Suzuki et al. 1999). Most studies regarding OA toxicity beyond DSP symptoms have been performed in mice and human cell lines. The toxic effects of OA on marine organisms is still fairly unknown. Recently it was shown that OA induced genotoxic and cytotoxic effects on bivalves (McCarthy et al. 2014). OA has been shown to elicit the formation of micronuclei and nuclear lesions in mussel hematocytes (Carvalho Pinto-Silva et al. 2003, 2005) and up-regulation of gene transcripts associated with stress response (Manfrin et al. 2010). In clams (*R. decussatus*), OA induced higher DNA damage to clams' gills than in hemocytes when exposed to lower OA concentrations, as opposed to when they were exposed to high OA concentrations for a shorter period of time (Flórez-Barrós et al. 2011). Mussels (*M. galloprovincialis*) presented similar results, with hemocytes having less DNA damage than gill tissue when exposed to OA, and gills presenting increased DNA damage at lower OA concentrations (Prego-Faraldo et al. 2015). Gills are the first tissue to come in contact with the toxin, and the lack of response when exposed to higher concentrations suggests: (i) very efficient defence mechanism in bivalves and (ii) detoxification pathways by metabolizing OA into less toxic compounds.

While the target protein phosphatases are as sensitive to OA *in vitro* exposure in blue mussels (*M. edulis*) as they are in other organisms (Svensson and Förlin 1998), there are no records of mussel mortalities due to OA exposure. Mussels can be exposed to OA throughout the year; thus, it is proposed that they possess detoxification mechanisms. Svensson et al. (2003), found that *M. edulis* can accumulate OA in the lysosomal system, therefore, preventing cellular damage in hematocytes.

Marine turtles have been found to accumulate OA in their tissues, produced by the epibenthic *Prorocentrum* spp., likely present on the surface of the algae that the turtles consume. Coincidentally, two DSP-producing *Prorocentrum* species (*P. lima* and *P. concavum*) occur where there is high risk of fibropapillomatosis, a neoplastic

Table 5. Documented cases of marine organisms exposed to and affected by brevetoxins (BTXs).

	Target species	Brevetoxin source	Route of exposure	Toxicity	Tissues analysed	Effects	Observations	References
Phytoplankton	*Asterionellopsis glacialis*	*K. brevis* extracellular exudates	Exposure to exudates	Up to 55 ng L^{-1} PbTx-2	-	Inhibition of growth	Indicates allelopathy	(Prince et al. 2008)
	Skeletonema costatum	*K. brevis* extracellular exudates	Exposure to exudates	Up to 55 ng L^{-1} PbTx-2	-	Inhibition of growth	Indicates allelopathy	(Prince et al. 2008)
	Prorocentrum minimum	*K. brevis* extracellular exudates	Exposure to exudates	Up to 55 ng L^{-1} PbTx-2	-	Inhibition of growth	Indicates allelopathy	(Prince et al. 2008)
Crustaceans	*A. tonsa*	*K. brevis*	Exposure to dinoflagellate cells	Up to 2400 cells ml^{-1}	-	Decreased survival and egg production	-	(Prince et al. 2006)
		Ptychodiscus brevis (now *K. brevis*)	Exposure to dinoflagellate cells	Up to 19567 cells ml^{-1}	-	Increased feeding rates	-	(Turner and Tester 1989)
		K. brevis	Exposure to dinoflagellate cells and brevetoxins	Up to 1×10^7 cells L^{-1} and 15 µg PbTx-2 L^{-1}	-	Increased mortality at higher concentrations	-	(Cohen et al. 2007)
	C. pacificus	*P. brevis* (now *K. brevis*)	Exposure to dinoflagellate cells	0.68 ng C $cell^{-1}$	-	Loss of motor control, increased heart rate and lethargy	-	(Huntley et al. 1987)
		P. brevis (now *K. brevis*)	Exposure to dinoflagellate cells	0.68 ng C $cell^{-1}$	-	Avoided feeding, increased heart rate and loss of motor control	-	(Huntley et al. 1986)
		P. brevis (now *K. brevis*)	Exposure to dinoflagellate cells	Up to 1000 ng C $cell^{-1}$	-	Increased heart rates and loss of motor control		(Sykes and Huntley 1987)

	Centropages typicus	*P. brevis* (now *K. brevis*)	Exposure to dinoflagellate cells	Up to 19567 cells ml^{-1}	-	Decreased feeding rates	-	(Turner and Tester 1989)
		K. brevis	Exposure to dinoflagellate cells and brevetoxins	Up to 1×10^7 cells L^{-1} and 15 µg PbTx-2 L^{-1}	-	Increased mortality at higher concentrations	-	(Cohen et al. 2007)
	Labidocera aestiva	*P. brevis* (now *K. brevis*)	Exposure to dinoflagellate cells	Up to 19567 cells ml^{-1}	-	Increased feeding rates	-	(Turner and Tester 1989)
	Oncaea venusta	*P. brevis* (now *K. brevis*)	Exposure to dinoflagellate cells	Up to 19567 cells ml^{-1}	-	Increased feeding rates	-	(Turner and Tester 1989)
	Paracalanus quasimodo	*P. brevis* (now *K. brevis*)	Exposure to dinoflagellate cells	Up to 845 cells ml^{-1}	-	Decreased feeding rates	-	(Turner and Tester 1989)
	Temora turbinata	*K. brevis*	Exposure to dinoflagellate cells and brevetoxins	Up to 5×10^6 cells L^{-1} and 15 µg PbTx-2 L^{-1}	-	Suppressed swimming behaviour	-	(Cohen et al. 2007)
Molluscs	*A. irradians*	*P. brevis* (now *K. brevis*)	Exposure to dinoflagellate cells	-	-	Decreased recruitment	-	(Summerson and Peterson 1990)
		K. brevis	Exposure to dinoflagellate cells and extracts	Up to 22000 cells ml^{-1}		Reduction in clearance rates		(Leverone et al. 2007)
	C. virginica	*K. brevis*	Exposure to dinoflagellate cells and extracts	Up to 24600 cells ml^{-1}	-	Reduction in clearance rates		(Leverone et al. 2007)
	M. mercenaria	*K. brevis*	Exposure to dinoflagellate cells and extracts	Up to 23100 cells ml^{-1}	-	Reduction in clearance rates		(Leverone et al. 2007)

Table 5 contd. ...

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	Target species	Brevetoxin source	Route of exposure	Toxicity	Tissues analysed	Effects	Observations	References
	P. viridis	*K. brevis*	Exposure to dinoflagellate cells and extracts	Up to 23800 cells ml^{-1}	-	Reduction in clearance rates		(Leverone et al. 2007)
Fish	Larval *Sciaenops ocellatus*	*P. brevis* (now *K. brevis*)	Exposure to dinoflagellate cells	Up to 2040 cells ml^{-1}	-	Deformities, abnormal swimming, paralysis and death	-	(Riley et al. 1989)
Sea turtles	*Caretta caretta*	*K. brevis*	Likely through prey	-	-	Death	-	(Landsberg et al. 2009)
	Chelonia mydas	*K. brevis*	Likely through prey	-	-	Death	-	(Landsberg et al. 2009)
	Lepidochelys kempii	*K. brevis*	Likely through prey	-	-	Death	-	(Landsberg et al. 2009)
Seabirds	*Aythya affinis*	*G. breve* (now *Karenia brevis*)	Prey (contaminated clams)	-	-	Lethargy, ataxia, death	Over 6000 specimens found dead or moribund	(Forrester et al. 1977)
		G. breve (now *K. brevis*)	Prey (contaminated clams)	-	-	Weakness, inability to dive, unresponsiveness, loss of reflexes, death	-	(Quick and Henderson 1974)
		G. breve (now *K. brevis*)	Prey (contaminated clams)	-	-	Dead or weakened		(Schreiber et al. 1975)
	Phalacrocorax auritus	*K. brevis*	Prey (contaminated fish)	-	-	Cerebellar ataxia, death	-	(Kreuder et al. 2002)

	Sterna maxima	*K. brevis*	-	Up to 33.1 PbTx ng g^{-1}	Kidney, liver, testes, heart muscle, stomach, intestines, lung	Death	Analysis performed on beached specimens	(Vargo et al. 2006)
	Larus atricilla	*K. brevis*	-	16.2 PbTx ng g^{-1}	Kidney	Death	Analysis performed on beached specimens	(Vargo et al. 2006)
Marine Mammals	*Trichechus manatus latirostris*	*K. brevis*	Aerosols or ingested seawater	-	-	Death following pulmonary oedema and hemmorhage, congestion of liver and kidneys	Over 100 manatees died	(Bossart et al. 1998)
		K. brevis	Contaminated seagrass	Up to 300 ng g^{-1}	Liver	Death	~ 30 manatees died	(Flewelling et al. 2005)
		G. breve (now *K. brevis*)	Possibly ingestion of contaminated ascidians	-	-	Congestion and hemorrhage in brain tissue, death	~ 40 manatees died	(O'Shea et al. 1991)
	Tursiops truncatus	*K. brevis*	Prey	Up to 613 ng g^{-1}	Feces	Death	Over 100 dolphins died	(Flewelling et al. 2005)
		P. brevis (now *K. brevis*)	Likely through prey	Up to 15820 ng g^{-1}	Liver	Death	Over 700 dolphins died	(Geraci 1989)
		G. breve (now *K. brevis*)	Prey	-	-	Death	Over 100 dolphins died	(Mase et al. 2000)
		K. brevis	Prey	Up to 2896 ng g^{-1}	Stomach contents	Death	-	(Fire et al. 2007)

disease specific to sea turtles. Therefore, OA may play an important role in this disease's etiology (Landsberg 2002, Landsberg et al. 1999).

Although not positively linked to DSTs, many seabird deaths occurred after DSP and other toxin's outbreaks (Shumway et al. 2003). The presence of DSTs is likely to decrease the organism's fitness and well-being, making them more vulnerable to other toxicants.

Despite being regarded as a less dangerous toxin, OA has been shown to cause a wide array of responses and effects in marine organisms, highlighting the potential of this toxin to affect many other organisms, including human populations chronically ingesting low doses of a tumour promoting toxin.

Future Directions and Concluding Remarks

It is predicted that many changes in the world's oceans will occur. Increasing temperature and CO_2 concentrations are but two of the many factors affecting HAB distribution, frequency and intensity. HAB ecology is complex, and it is dependent on the interaction of many factors, including ocean stratification, oceanic currents, nutrient availability and precipitation (Wells et al. 2015). Currently, there are a number of studies on the effect of climate change in HABs. However, the interactions simulated are scarce and do not allow for species adaptation and plasticity. Temperature fluctuations directly affect phytoplankton communities. Typically, with increasing temperatures, phytoplanktonic species tend to have higher growth rates until a species-specific temperature threshold is met (Wells et al. 2015). There is growing evidence that HABs are increasing in frequency and intensity throughout the globe (Dolah 2000), and further studies are needed to better understand the shifts in HAB ecology and physiology in these new conditions.

It is evident from the present work that there is a great lack of knowledge on the effects that HAB toxins have on early stages of development, a very sensitive and critical stage in an organism's life. Moreover, most toxins may be chronically accumulated and, in many cases, not elicit outward signs of toxicity. Here, we reviewed the effects that HAB toxins have on marine organisms, more specifically, the four main groups of toxins (PSP, ASP, NSP and DSP). Still, there has been growing evidence that in addition to the increasing intensity and toxicity of these blooms, new and emerging toxins, such as palytoxins, cyclic imines, tetrodotoxins and ciguatoxins, are occurring in regions previously undetected (Soliño et al. 2014). Also, the co-occurrence of emerging toxins with endemic HAB-toxins may lead to additive, synergistic or antagonistic effects on marine organisms; however, the available data is not sufficient to confirm and characterize such effects. Multidisciplinary studies are necessary to comprehensively understand the effects of exposure to multiple toxins. Thus, there is great need to reach out to policy makers and work alongside with the monitoring programs already implemented in many countries worldwide, to better understand the risk faced by organisms exposed to marine toxins in the natural environment, the consequences on an ecosystem's stability and to develop models of biotoxins kinetics useful to predict the toxic effects highlighted in this study.

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