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REVIEW ARTICLE

Harmful algal blooms and shellfish in the marine environment: an overview of the main molluscan responses, toxin dynamics, and risks for human health

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Abstract

Besides human health risks, phycotoxins may cause physiological injuries on molluscan shellfish and, consequently, damages to marine ecosystems and global fisheries production. In this way, this review aimed to present an overview of HABs impacts on marine shellfish by evaluating the effects of cultivated molluscs exposure to microalgae and cyanobacteria that form blooms and/or synthesize toxins. More specifically, it was assessed the main molluscan shellfish responses to harmful algae, trophic transfer and dynamics of phycotoxins, and the risks for human health. Of the 2420 results obtained from literature search, 150 scientific publications were selected after thorough inspections for subject adherence. In total, 70 molluscan species and 37 taxa of harmful algae were assessed from retrieved scientific publications. A significant positive correlation was found between the marine production of molluscs and the number of available studies by molluscan category. Molluscan responses to HABs and phycotoxins were categorized and discussed in three sub-sections: effects on grazing and behavior, metabolic and physiological reactions, and fitness consequences. The main histopathological injuries and toxin concentrations in molluscan tissues were also compiled and discussed. Bivalves often accumulate more toxins than gastropods and cephalopods, occasionally exceeding recommended levels for safe consumption, representing a risk for human health. Harmful algae impact on molluscan shellfish are complex to trace and predict; however, considering the perspective of increase in the occurrence and intensity of HABs, the intensification of efforts to expand the knowledge about HABs impacts on marine molluscs is crucial to mitigate the damages on economy and human health.

Keywords Aquatic environment · Bivalves · Malacoculture · Molluscs · Shellfish toxins · Phycotoxins · Public health risks · Seafood

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Introduction

Coastal areas, open oceans, and brackish systems have been affected worldwide by harmful algal blooms (HABs) over the last decades (Anderson et al. 2012; Hallegraeff 2010). Microalgal bloom events are characterized by the cellular proliferation and, occasionally, high biomass accumulation of toxic or noxious algal species that are harmful to aquatic fauna and food web dynamics (Neves and Rodrigues 2020). HABs occurrence has increased recently in various coastal regions around the globe which is likely due to natural dispersion of species by currents and winds, organisms transport via human activities (e.g., ballast water and aquaculture), increase in water column temperature, coastal eutrophication, and the better detection of HABs and their toxins in the environment (e.g., Glibert and Burkholder 2006; Gobler 2020; Granéli et al.

2011; Griffith and Gobler 2020; Wells et al. 2015; Xiao et al. 2019; Zohdi and Abbaspour 2019).

Many algal species synthesize toxins that are responsible for poisoning incidents worldwide. Most of these toxins are secondary metabolites produced by algal cells, but many other bioactive metabolites are simple molecules (e.g., polyunsaturated aldehydes in diatoms) derived from their primary metabolism (Ianora et al. 2011). Moreover, dissolved toxins released in the water by algal cells may surpass intracellular toxin levels in the late stages of algal growth (MacKenzie et al. 2004), which may be a risk factor for fauna survival (Castrec et al. 2018; Costa 2016). Generally, HABs are associated with fauna contamination by biotoxins that may eventually lead to mortality of marine species (Branch et al. 2013; Landsberg 2002; Shumway 1990). Among marine shellfish, bivalves are recognized as common vectors of toxins to their consumers regarding their intoxication susceptibility through filter-feeding on toxic algae (Basti et al. 2018; Deeds et al. 2008; Lopes et al. 2019; Neves et al. 2019), although, non-bivalve molluscs may also act as toxin vectors (Costa et al. 2005; Mafra Jr et al. 2019; Neves et al. 2015a; Shumway 1995). Deposit-feeders may accumulate toxins by the ingestion of biodeposits (e.g., pseudofeces, feces) containing toxins or directly by microalga consumption (e.g., Dowsett et al. 2011; Neves et al. 2015a; Persson et al. 2006, 2008; Persson and Smith 2009). In addition, carnivorous molluscs may accumulate toxins via trophic transfer by predation on contaminated prey (e.g., Bricelj et al. 2012; Carreto et al. 1996; Ito et al. 2004; Wekell et al. 1996).

The phylum Mollusca is the second largest in the animal kingdom, including living species and fossil records, and extremely diverse in terms of animal forms, feeding modes, and behaviors (Kershaw 1983). The four most abundant classes of living molluscs are the Polyplacophora (e.g., chitons), Bivalvia (e.g., bivalves), Gastropoda (e.g. snails), and Cephalopoda (e.g., squids and octopuses). Molluscs provide essential ecosystem services such as habitat structure, water purification through filtration, serve as food item for a wide range of predators—including humans, and are economically valuable (reviewed in Gutiérrez et al. 2003; Neves et al. 2020). The average annual growth rate of global food production in mariculture systems has increased 5.1% from 2010 to 2017 (FAO - Food and Agriculture Organization of the United Nations 2019), in which the world production of molluscs in marine waters comprised US$33.9 billion in 2018 (FAO - Food and Agriculture Organization of the United Nations 2016). Molluscan shellfish may be environmentally exposed to harmful algal blooms; thus, the edible mollusc may accumulate toxins and become unsafe for human consumption. The consumption of contaminated shellfish is a global public health concern since phycotoxins may lead to dangerous human poisonings (Neves and Rodrigues 2020). Besides human health risks, phycotoxin toxicity may cause physiological injuries in molluscan shellfish altering global fisheries production and the quality of marine ecosystems (Ajani et al. 2017; Khora and Jal 2018; Shumway 1990). In this way, this review aimed to present an overview of the main impacts of harmful algal blooms on molluscan shellfish by evaluating the exposure of cultivated molluscs in marine environments to microalgal and cyanobacteria species that form blooms and/or synthesizes toxins. Moreover, it was assessed the multiple responses of molluscs to HABs, the trophic transfer of phycotoxins, the dynamics of phycotoxins in molluscs, and the risks for human health. Finally, future perspectives were provided considering the economic importance of shellfish production and the impacts of contaminated molluscs on human health. The present review is within the context of the Sustainable Development Goal 14 (i.e., Life Below Water) of the United Nations by increasing the research efforts in marine sciences in order to improve the ocean health and environmental and human safety.

Material and methods

An extensive literature search limited to English was conducted using indexed databases (ISI Web of Science, Scopus, and Google Scholar) and reference lists of the retrieved papers searching for the effects of harmful alga and/or phycotoxins on marine molluscs, by applying a combination of the keywords "molluscs," "mollusks," "Mollusca," "phycotoxins;" and pairwise combinations of "harmful alga," "algal bloom," and "toxic algae." Publications included in the analysis were those that reported exposure of marine molluscs to harmful alga species and/or phycotoxins. All types of scientific publications were included except books that were not freely available online.

Of the 2420 results obtained from the literature search, 150 scientific publications were selected after thorough inspections for subject adherence and thus retrieved for further analyses (see Supplementary Material Table S1 to access all the reference list and publication details). Our analytical database consisted in data compiled from scientific studies published up to 2015. Considering that the first record on the effects of harmful alga and/or phycotoxins on marine molluscs dated back to 1972, our extensive literature search encompassed a time span of 44 years, ceasing intentionally in 2015 to coincide with the last scientific summary for policy makers (Kudela et al. 2015), provided by the SCOR-IOC Scientific Steering Committee of the Global Ecology and Oceanography of Harmful Algal Blooms (GEOHAB; UNESCO). The responses of molluscan species described in the literature were evaluated, compiled, and discussed here in three distinct subsections: (1) feeding and behavioral responses, (2) metabolic and physiological reactions, and (3) fitness consequences. A Spearman correlation was performed to test for statistical

significance between marine production of molluscs (in million tonne) and the relative number of available studies by molluscan category. Statistical analysis was performed using the software Statistica 8.0 (StatSoft).

Moreover, data from the available literature reporting values of phycotoxin concentrations in molluscs and their consumers were used to calculate the biomagnification factor (BMF), which is the ratio between the toxin concentration measured in aquatic consumers and their prey (sensu Gray 2002).

Results and discussion

Data overview

The number of published studies is highly asymmetric among molluscan groups, with 90% of studies focused on bivalves, 5.3% on cephalopods, and 4.7% on gastropods. The highest research effort on bivalves is likely related to the greater importance of this molluscan group as a food item, its higher commercial value, and the amount produced in mariculture systems. In addition, filter-feeder bivalves are traditionally monitored for human safety consumption; while carnivorous, herbivorous, and detritivorous molluscs were lately recognized as phycotoxin sources (e.g., Bricelj et al. 2012; Dowsett et al. 2011; Ito et al. 2004; Neves et al. 2015a; Persson et al. 2008; Persson and Smith 2009).

Production of farmed molluscs in 2013 (more than 21 million tonnes) represented 14% of the total seafood and fish produced worldwide (FAO - Food and Agriculture Organization of the United Nations 2014; Ritchie and Roser 2019). The amount of marine shellfish production varies according to each molluscan groups (FAO - Food and Agriculture Organization of the United Nations 2012): (1) clams, cockles, and arkshells ~5 million tonnes; (2) oysters ~4 to 5 million tonnes; (3) mussels ~2 million tonnes; (4) scallops and pectens ~2 million tonnes; (5) other marine molluscs, including cephalopods ~0.5 to 1 million tonne, and (6) gastropods ~0.5 million tonne (Fig. 1a). Aquaculture production of bivalves in marine waters accounts for more than 90% of the whole production of farmed molluscs. High production in mariculture systems demands monitoring of physical, chemical, and biological conditions and animal quality, which seems to reflect the higher number of studies focusing on harmful alga effects on bivalves (Fig. 1b). Among the molluscan categories, the impacts of harmful algae were similarly evaluated by scientific studies on clams, cockles, and arkshells (26.6% of retrieved papers), oysters (26.2%), and mussels (26.6%), followed by scallops and pectens (14.2%), and finally cephalopods (3.4%), and gastropods (3%) (Fig. 1b). A significant positive correlation was found between the marine production of molluscs (in million tonne) and the number of available studies by molluscan category (Spearman correlation, $\rho = 0.84$, $p < 0.05$).

The number of species addressed by retrieved scientific publications consisted of 56 bivalves, seven gastropods, and seven cephalopods. All species names are presented in Supplementary Material Table S1. Most of the information available, in the percentage of scientific studies, focused in only six bivalve species: the oysters *Crassostrea gigas* (19%) and *C. virginica* (12%), the mussels *Mytilus edulis* (14%) and *M. galloprovincialis* (9%), and the clams *Mercenaria mercenaria* and *Ruditapes philippinarum* (~7%). These six bivalve species have been listed by FAO as the major farmed molluscs in marine waters (FAO - Food and Agriculture Organization of the United Nations 2006-2020), which problably prompted more scientific efforts on these commercially valuable species.

Scientific studies compiled in this review addressed 36 different taxa of harmful microalgae (listed in Table 1), encompassing a great variety of toxins that may lead to shellfish poisoning syndromes in humans. Most of the studies evaluated the impacts of dinoflagellates exposure on molluscan shellfish, in which Dinophyceae class comprised 89% of all microalgal and cyanobacteria species. However, molluscan responses to marine cyanobacteria and diatoms have also been addressed in the retrieved studies. Dinoflagellates can produce a great variety of toxic compounds that are responsible for six of the seven human poisoning syndromes induced by

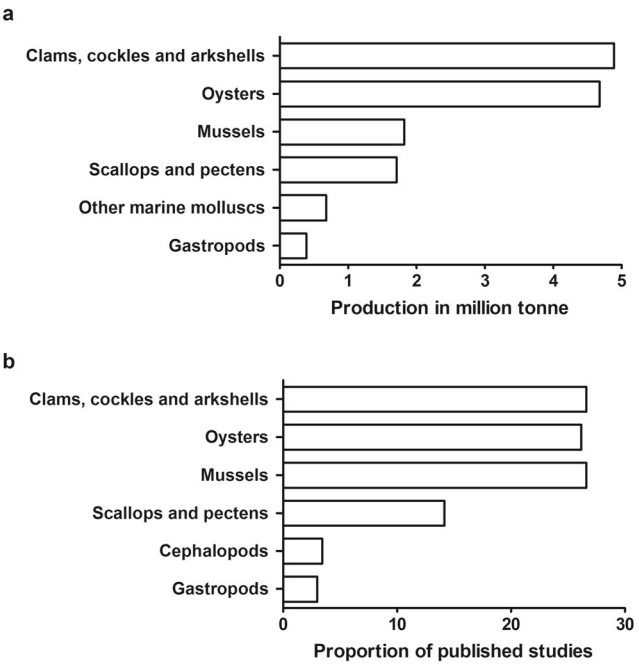

Fig. 1 **a** World aquaculture production of molluscs in marine waters (data compiled from FAO - Food and Agriculture Organization of the United Nations 2012). **b** Pencent proportion of retrieved scientific studies (n=150) among the six molluscan categories: clams, cockles, and arkshells; oysters; mussels; scallops and pectens; cephalopods; and gastropods

Table 1 Harmful algal or cyanobacteria species or higher taxonomic level addressed in the 150 compiled scientific studies, its geographic distribution (from Algae Base - Guiry and Guiry 2016), and the main toxins produced by each species

Phylum	Class	Genus	Species	Geographic Distribution	Toxins
Cyanobacteria					
	Cyanophyceae				
		Hydrocoleum			
			H. lyngbyaceum	Africa	Ciguatoxins-like
		Oscillatoria			
			O. cf *bonnemaisonii*	Africa Asia Europe Indian Ocean Islands New Zealand Pacific Islands	Ciguatoxins-like
		Phormidium			
			P. laysanense	Africa Caribbean Islands Indian Ocean Islands Pacific Islands	Ciguatoxins-like
		Microcystis			
			Microcystis sp.	World-wide distribution, with exception of subpolar regions	Microcystins
	Bacillariophyceae				
		Pseudo-nitzschia			
			P. australis	Africa Australia Europe New Zealand North America South America	Domoic acid
			P. multiseries	Asia Australia Europe New Zealand North America	Domoic acid
			P. pseudodelicatissima	Africa Asia Atlantic Islands Europe New Zealand North and South America	Domoic acid
	Pelagophyceae				
		Aureococcus			
			A. anophagefferens	North America	Not available
Miozoa					
	Dinophyceae				
		Alexandrium			
		A. *affine*		Asia Australia Europe New Zealand North America	Not available
		A. *catenella*		Africa Asia Australia Europe North and South America	Saxitoxins
		A. *fundyense*		Australia New Zealand North America	Saxitoxins
		A. *minutum*		Africa Asia Australia Europe New Zealand North and South America	Saxitoxins
		A. *monilatum*		Europe South America	Goniodomin
		A. *ostenfeldii*		Africa	Spirolides

Table 1 (continued)

			Asia Atlantic Islands Australia Europe New Zealand North and South America	
A. *tamarense*			Africa Antarctic Islands Asia Australia Europe New Zealand North and South America	Saxitoxins
	Azadinium			
		A. spinosum	Europe	Azaspiracids
	Dinophysis			
	D. acuminata		Asia Atlantic Islands Australia Europe Central, North and South America New Zealand	Dinophysistoxins Okadaic acid Pectenotoxins
	D. acuta		Australia Europe New Zealand North America South-west Asia	Pectenotoxins
		D. caudata	Africa Asia Atlantic Islands Australia Caribbean Islands Central, North and South America Europe New Zealand	Pectenotoxins
		D. fortii	Africa Asia Atlantic Islands Australia Europe New Zealand South America	Dinophysistoxins Okadaic acid Pectenotoxins
		D. miles	Asia Australia New Zealand	Dinophysistoxins Okadaic acid
		D. norvegica	Asia Europe North America	Dinophysistoxins Okadaic acid
		D. sacculus	Australia Europe New Zealand South-west Asia	Dinophysistoxins Okadaic acid
	Gambierdiscus			
		G. polynesiensis	Pacific Islands New Zealand	Ciguatoxins
	Gymnodinium			
	G. catenatum		Asia Australia Central, North and South America Europe New Zealand	Saxitoxins
	Karenia			
		K. brevis	Asia Atlantic Islands Central and North America Europe New Zealand	Brevetoxins

Table 1 (continued)

	K. mikimotoi	Asia Australia Central and North America Europe New Zealand	Brevetoxins Gymnodimine
	K. selliformis	Australia New Zealand North America	Gymnodimine
	Karlodinium		
	K. veneficum	Asia Atlantic Islands Australia Europe New Zealand North America	Karlotoxins
	Ostreopsis		
	O. cf *ovata*	Africa Asia Atlantic Islands Europe Indian Ocean Islands New Zealand Pacific Islands South America	Palytoxin-like
	Pfiesteria		
	P. piscicida	Asia Australia New Zealand North America	*Pfiesteria* toxins
	P. shumwayae	North America	*Pfiesteria* toxins
	Prorocentrum		
	P. lima	Africa Asia Atlantic Islands Australia Central, North and South America Europe Indian Ocean islands New Zealand Pacific Islands	Okadaic acid
	P. minimum	Asia Australia Caribbean Islands Europe North America	Not available
	Pyrodinium		
	P. bahamense var. *compressum*	Asia	Saxitoxins
Ochrophyta			
	Raphidophyceae		
	Heterosigma		
	H. akashiwo	Asia Australia Europe New Zealand North and South America	Not available
	Natural plankton assemblage	Europe	Azaspiracids
	Azadinium spp. (Dinophyceae)	North and South America China	

phycotoxins (reviewed in James et al. 2010). A higher proportion of studies targeted the genus *Alexandrium* (37%), probably because of its wide geographic distribution and the high recurrence of its blooms (Van Dolah 2000).

The main responses of shellfish to marine harmful algae

Molluscs show a great variety of responses when exposed to marine harmful algae or directly to phycotoxins. In addition, bioactive extracellular compounds—noxious exudates released by harmful cells—can induce cytotoxic, allelopathic, and hemolytic effects upon marine bivalves (e.g., Basti et al. 2014a; Borcier et al. 2017; Ford et al. 2008; Smolowitz and Shumway 1997). A detailed compilation of the main routes of exposure to harmful algae or their toxic compounds and related responses of marine molluscan shellfish is graphically presented in Fig. 2.

Feeding and behavioral responses

The filtration and ingestion rates of most bivalve species, both juveniles and adults, decrease when they are exposed to harmful algal cells, either in suspension or deposited in the substrate (e.g., Haubois et al. 2007; May et al. 2010; Shumway et al. 2006; Springer et al. 2002). Exposure to bioactive extracellular compounds also inhibits clearance and ingestion rates of bivalves (Borcier et al. 2017; Matsuyama et al. 1997). However, an exception is the oyster *Ostrea edulis* that has increased its filtration rate when exposed to the toxic dinoflagellate *Alexandrium* (=*Protogonyaulax*) *tamarense* (Shumway and Cucci 1987). Moreover, molluscs that are periodically exposed to harmful algal blooms may have evolved mechanisms to exploit toxic algae as food with no harmful effects (Bricelj et al. 2005; Shumway and Cucci 1987; Twarog and Yamaguchi 1975).

Decreases in filtration and ingestion rates may be a consequence of active avoidance by the recognition of harmful cells. For example, selective feeding on non-toxic algal cells was described for the Manila clam *Ruditapes philippinarum* exposed to *Heterocapsa circularisquama* (Basti et al. 2011a, 2016). Reduction in filtration and ingestion rates can also be a consequence of behavioral and/or physiological changes in shell-valve activity and shell closures. Toxic alga exposure can induce short and incomplete shell-valve closure reactions (Basti et al. 2009), partial or complete closure of shells or valves (Estrada et al. 2007; Neves et al. 2015b; Romero-Geraldo et al. 2014), siphon retraction (Basti and Segawa 2010; Shumway and Cucci 1987), and increase in the reaction time and in the number of stimuli necessary for shell-valve closure response (Neves et al. 2019). In addition, molluscs exposed to *Alexandrium* species that synthesize paralytic

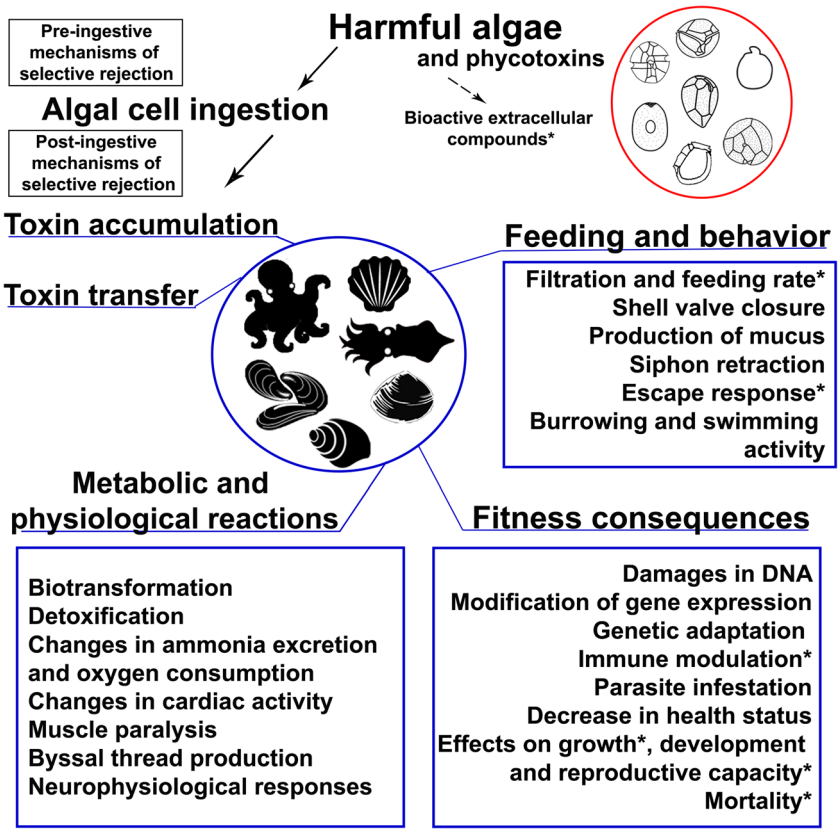

Fig. 2 Theoretical diagram of the main routes of exposure to harmful algae (e.g., exudates contact, algal cell ingestion, toxin accumulation) and related responses of marine molluscan shellfish based on the compiled literature. *Impacts attributed to bioactive extracellular compounds

shellfish toxins (PSTs) showed higher rates of shell-valve clapping (*Argopecten purpuratus*; Hégaret et al. 2012), an increase in the duration of shell-valve aperture and closure (*Crassostrea gigas*; Tran et al. 2010, 2015), and a negative correlation between shell-valve activity and toxic alga concentration (*C. gigas;* Haberkorn et al. 2011). Molluscs can also exhibit shorter duration of escape response, burrowing and swimming activity, byssal thread production, muscle paralysis, changes in cardiac activity, and neurophysiological responses when exposed to toxic algae (e.g., Basti et al. 2016; Escobedo-Lozano et al. 2012; reviewed in Gainey Jr and Shumway 1988; Hégaret et al. 2007a, 2012; Neves et al. 2015a; Shumway and Cucci 1987; reviewed in Shumway and Gainey Jr 1992). Behavioral responses in bivalve molluscs can indicate in vivo sensitivity to harmful algae and their toxins (Bricelj et al. 1996), making them more susceptible to predation and parasites infestation.

Algal cells can be avoided through pre-ingestive mechanisms (e.g., pseudo-feces) (e.g., Basti and Segawa 2010; Escobedo-Lozano et al. 2012; Estrada et al. 2007; Mafra Jr et al. 2009; Romero-Geraldo et al. 2014; Wikfors and Smolowitz 1995) or eliminated as viable cells or cysts in biodeposits of bivalves and gastropods (e.g., Hégaret et al. 2007a; May et al. 2010; Neves et al. 2015a, 2015b; Rolland et al. 2012; Shumway et al. 2006; Springer et al. 2002). The elimination of intact cells by molluscan species decreases the assimilation and digestion of toxic cells and the potential for toxins accumulation in their tissues during HABs.

Metabolic and physiological reactions

The elimination of accumulated toxins is an important protective strategy adopted by invertebrates. Toxin elimination occurs mainly through toxin release via excretion and detoxification mechanisms in some molluscan species (e.g., Bogan et al. 2007a; Choi et al. 2003; Contreras et al. 2012; Dowsett et al. 2011; Guéguen et al. 2008; Sephton et al. 2007; Suzuki et al. 2003). Detoxification in bivalves is composed by an initial fast depuration with elimination of unassimilated toxins and toxic cells, followed by a slow reduction in toxins that have been assimilated and incorporated in molluscan tissues (Cabado et al. 2020; Duan et al. 2021; Silvert et al. 1998). Metabolic and physiological reactions in molluscs as a consequence of digestive detoxification and/or use of toxins in metabolic processes may transform toxic compounds into products with different toxicities (Hégaret et al. 2009a). Some molluscan species biotransform toxic compounds into less toxic products; for example, the epimerization in shellfish tissues causes an 11-fold decrease in saxitoxin toxicity (e.g., Choi et al. 2003; FAO - Food and Agriculture Organization of the United Nations 2004; Fast et al. 2006; Gárate-Lizárraga et al. 2004). However, PSTs toxicity may also increase through an increase in the proportion of potent carbamate derivates (e.g., saxitoxin and decarbamoylsaxitoxin) compared to the less toxic N-sulfocarbamate forms (Doucette et al. 2006). Variations in toxin biotransformation within different tissues have also been described for bivalves. Digestive glands, followed by gills, have demonstrated higher toxin transformation activity while mantle, adductor muscle, and siphon tissues have shown a lower potential for toxin transformation (Fast et al. 2006).

Toxicity level varies widely among molluscan species depending on toxin retention, depuration rates, toxin nature, and density of microalga cells. Considering detoxification in bivalves, fast detoxifiers are those species that reduce toxins at rates between 6 and 17% per day (e.g., *Mercenaria mercenaria*, *Mytilus edulis*) (reviewed in Bricelj and Shumway 1998). Slow detoxifiers exhibit rates of toxin elimination smaller than 1% per day (e.g., *Placopecten magellanicus*, *Saxidomus nuttalli*), and these species could take several months or even years to reach safe toxin concentrations for consumption (reviewed in Bricelj and Shumway 1998). A similar time span for reduction in the content of paralytic toxins and brevetoxins has been experimentally demonstrated in molluscan shellfish during depuration phase: 23 days of depuration for the purple clam *Hiatula rostrata* (after 18 days of exposure to *Alexandrium minutum*; Chen and Chou 2001), 13 days of depuration for the noble scallop *Chlamys nobilis* and the green mussel *Perna viridis* (after 3 days of exposure to *A. tamarense,* Choi et al. 2003), 8 days of depuration for the Pacific oyster *Crassostrea gigas* (after 13 days of exposure to *A. minutum*, Guéguen et al. 2008), and 15 days of depuration for the eastern oyster *Crassostrea virginica* and the hard clam *Mercenaria mercenaria* (after 8 days of exposure to *Karenia brevis*, Griffith et al. 2013). Retention time of domoic acid varied from few hours to days in mussels and from several months to years in scallops, considering the time needed for species to reach toxin concentrations below regulatory levels (Fernández et al. 2004). Detoxification rates were not evaluated in cephalopods, and only one study evaluated toxin concentration in snails (*Littorina littorea*) during depuration phase after exposure to *A. minutum*, but no significant decrease in saxitoxin content was noticed during 6 days of depuration (Neves et al. 2015b).

Several methods have been tested to accelerate detoxification time of commercially important bivalves contaminated with phycotoxins as an effort to reduce the duration of harvest interdiction (e.g., Cabado et al. 2020; Guéguen et al. 2008; Lassus et al. 2005; Shumway et al. 1995). Osmotic stress, electric shocks, decrease in pH, and chlorination have not been effective (Shumway et al. 1995). Recently, thermal procedures were tested in naturally PSTs-contaminated mussels, clams, and scallops and showed promising results (Cabado et al. 2020).

Biotransformation of phycotoxins using enzymes is still under investigation, and assays with ozonization of seawater led to contradictory results (Lassus et al. 2005). The role of silt in depuration rates of molluscs has not been clearly established (Guéguen et al. 2008). The use of silt was suggested to accelerate detoxification process as it seems to have an effect on feeding physiology increasing the filtration rate (Kiørboe and Møhlenberg 1981). Active feeding during detoxification of molluscs seems to be important to accelerate the rates of gut evacuation and overall metabolism of toxins. Molluscs fed non-toxic algae during depuration phase were able to detoxify PSTs faster than molluscs held in filtered seawater (without food) (e.g., Bricelj and Shumway 1998; Guéguen et al. 2008; Lassus et al. 2005, 2007b). In addition, as the density of the non-toxic alga increases, the efficiency of mussel detoxification rate seems to enhance proportionately (Blanco et al. 1997). Alternative methods to reduce phycotoxin accumulation in shellfish molluscs have been also experimentally tested, in which mussels exposed to a phytochemical extract of cinnamaldehyde showed lower concentrations of DSTs in the digestive gland (Duan et al. 2021).

Mathematical models have been developed to predict the time duration of the phycotoxin detoxification process from economically important molluscan species (Blanco 2006; Blanco et al. 2005). The evaluation of the feasibility of detoxification models in terms of cost-effectiveness is necessary to meet the demand of shellfish industry and farmers for the implementation of an industrial-scale detoxification system that allows detoxification of contaminated shellfish in shorter time duration. The reduction in shellfish toxicity through toxin elimination and biotransformation into less toxic compounds has ecological and economic importance. When toxin content reaches levels below regulatory limits, shellfish may be harvested again, decreasing the risk of negative ecological effects and human health risks caused by the consumption of contaminated molluscs, as well as the economic losses for the producer. For example, a conservative estimate of the average annual economic impact resulting from HABs in the USA was close to US$ 75 million from 1987 to 2000 (Hoagland and Scatasta 2006).

Biological processes for toxin depuration and other cellular protection systems in marine molluscs are expensive in terms of energy requirements for organisms (Sokolova et al. 2011). Other physiological responses were also shown by molluscan shellfish after exposure to harmful algae and phycotoxins (e.g., changes in ammonia excretion and oxygen consumption and changes in cardiac activity, muscle paralysis, byssal thread production, and neurophysiological responses) (Fig. 2). Therefore, increased rates of molluscan metabolic activity to depurate phycotoxins, commonly related to stressful conditions, may be detrimental for individual fitness and the maintenance of populations exposed to HABs.

Fitness consequences

Exposure to toxic algae may directly damage DNA structure or modify gene expression in shellfish. Physical damages have been described as morphological alteration in cytoplasmic and nuclear membrane, chromatin condensation, DNA fragmentation and release of fragments into the cytoplasm (Estrada et al. 2014), primary DNA lesions in digestive glands (Dizer et al. 2001), qualitative and quantitative impacts on DNA (Mat et al. 2013), and increase in DNA damage in gill tissues (Flórez-Barrós et al. 2011). Harmful algae may also change expression levels of genes involved in antioxidant defense, cell detoxification, immune system, stress response, and cell cycle regulation in bivalves (e.g., Fabioux et al. 2015; García-Lagunas et al. 2013; Mat et al. 2013; Medhioub et al. 2013; Rolland et al. 2014; Tran et al. 2015). For example, an increase in the transcription levels has been described for genes encoding for antioxidant enzymes (superoxide dismutase and catalase), mitochondrial enzymes (cytochome oxidase I and III, cytochrome b, ATP synthase-6, and ND1), ion channels (K^+ and Ca^{2+}), heat-shock proteins, bi-phase transcriptional response of *C-type lectin* and toll-*like receptor* genes, and expression of differential genes in molluscs immune cells (e.g., Astuya et al. 2015; Núñez-Acuña et al. 2013; Romero-Geraldo et al. 2014).

Populations from toxin-affected areas may undergo genetic adaptation to toxins with natural selection against individual's sensitive to toxins (Twarog 1974), as demonstrated for the softshell clam *Mya arenaria* (Bricelj et al. 2005, 2010; Connell et al. 2007). Populations that have been previously exposed to toxic algae seem to be less affected compared to naive populations. For example, individuals of *M. arenaria* from a naive population showed higher mortality rates (> 30%) compared to individuals from a population previously exposed to *Alexandrium tamarense* (2–8% of mortality; MacQuerrie and Bricelj 2008). Resistant populations are less sensitive to phycotoxicity and accumulate higher toxin amounts; thus, resistant individuals are potential toxin vectors representing an extra risk for human and ecosystem health.

Immune response in molluscs is modulated by stressful conditions and consists in a response to stress by specialized cells—the hemocytes (Barcia and Ramos-Martínez 2011). Hemocyte responses vary as a function of toxin type and concentration (Dizer et al. 2001; Flórez-Barrós et al. 2011), exposure time (Astuya et al. 2015; Jones et al. 1995), microalga species (Hégaret et al. 2011), and

the frequency of population exposure to harmful alga (Haberkorn et al. 2010; Hégaret and Wikfors 2005a). Even the exposure to bioactive extracellular compounds may induce deleterious effects on bivalve hemocytes, as demonstrated for *Alexandrium* species (Ford et al. 2008). The compilation of studies retrieved in the present review (see in the Supplementary Material Table S1) indicates that harmful algae usually induce an increase in total hemocyte counts (i.e., number) and production of reactive oxygen species (ROS), followed by a decrease in hemocyte viability, relative size, and intracellular complexity (e.g., Castrec et al. 2018; Galimany et al. 2008a; Hégaret and Wikfors 2005a, 2005b, Hégaret et al. 2010). Phagocytic activity has either decreased or increased after exposure to harmful algae depending on microalga and molluscan species (e.g., Galimany et al. 2008a; Hégaret et al. 2009b; Lassudrie et al. 2020), suggesting a species-specific response for this hemocyte parameter. Shifts in the ratio of hyalinocyte to granulocyte have also been reported and were associated with increases in granulocyte percentage (Hégaret and Wikfors 2005b). Granulocytes are the main cells in phagocytosis and encapsulation mechanisms; thus, shifts in hemocyte cellular types suggest changes in immune function. In summary, contradictory hemocyte responses were reported for molluscs exposed to harmful algae, and can be either immunostimulant or immunosuppressant. Some immunosuppressive effects evidenced by molluscs include decreases in hemocyte viability, phagocytosis, ROS production, and cell adhesion (e.g., Hégaret et al. 2009b, 2011). Immunosuppressive responses leave the organisms more susceptible to pathogens, and, therefore, harmful algae exposure may trigger bacteria proliferation (Galimany et al. 2008b), infection, and prevalence of protozoan and trematodes (e.g., *Perkinsus marinus* and *Bucephalus* sp.) in molluscan tissues (Hégaret et al. 2012; Lassudrie et al. 2015a).

Marine molluscs and other invertebrates are infected by several parasites, most often trematodes, that cause shifts in host resistance to environmental factors (reviewed in Berger and Kharazova 1997; Costello et al. 2021; Couch and Fournie 2021). More severe effects of phycotoxins are expected on parasitized molluscs. For example, toxic algae exposure of Manila clams (*Ruditapes philippinarum*) that were highly parasitized by protozoans (*Perkinsus olseni*) induced severe immune modulation (Hégaret et al. 2007b) and disrupted the pro/-anti-oxidant response of clams (Lassudrie et al. 2014). In addition, exposure to harmful algae may change the relationship of bivalves (i.e., hosts) with their parasite (e.g., *P. olseni*) and pathogen (e.g., herpesvirus, OSHv-1) reducing the prevalence and intensity of infection (da Silva et al. 2008; Lassudrie et al. 2015b). Negative effects of harmful algae and their exudates on parasitic protozoan viability, survival, and morphology were addressed by in vitro assays (da Silva et al. 2008; Hégaret et al. 2011). Harmful algae may act directly on the parasite providing paradoxally a short-duration relief for the host (Soudant et al. 2013). For example, the harmful alga *Prorocentrum minimum* and its exudates were found to induce mortality and morphological changes in the cells of the protozoan *Perkinsus olseni,* suggesting an antagonistic suppression of parasite transmission and proliferation in natural environment (Hégaret et al. 2011).

Beyond pathogens and environmental pollutants, harmful algae are agents of pathologies in molluscan tissues inducing (1) inflammatory responses, (2) tissue degeneration, (3) cell and tissue death, (4) alterations in cellular number, size and type, and (5) shifts in fluid accumulation within tissues (Table 2). In the view of studies retrieved in the present review (Table 2), the most frequent histopathologies induced by harmful microalgae are hemocyte infiltration and aggregation (inflammatory response), formation of ceroidosis and epithelial desquamation (tissue degeneration), and necrosis (cell and tissue death). Bioactive extracellular microalgal compounds may also induce tissue damages. For example, bioactive compounds released by *Alexandrium minutum* cells induced lesions on mantle and muscle tissues of the king scallop *Pecten maximus* (Borcier et al. 2017). Histopathological lesions primarily occur in tissues that interact with harmful cells, among them gills and mantle, are the most affected tissues in bivalves while digestive tissues are the most in gastropods (Supplementary Material Table S1). The intensity and prevalence of histopathologies depend on the density of toxic algae, duration of toxin exposure, and water temperature (Basti et al. 2015b). Damaged tissues of molluscs exposed to harmful algae may recover depending on the level in which those tissues were affected. Tissues of the blue mussel (*Mytilus edulis*) affected by the exposure to the toxic dinoflagellate *Alexandrium fundyense* have recovered fast (i.e., within 6 days) from inflammatory responses and tissue damage (i.e., lipofuchsin granules) (Galimany et al. 2008c). However, advanced histopathologies can cause non-reversible changes that compromise vital functions of molluscs and lead to the death of individuals (e.g., Akberali and Trueman 1985; Cuevas et al. 2015; Yee-Duarte et al. 2018).

Reproductive capacity may be negatively affected by toxic algae exposure with changes in production and morphology of spermatozoa, reduction in viability, motility and swimming velocity of spermatozoa, reduction in egg viability and fertilization, and increase in ROS production by oocytes (e.g., Basti et al. 2013; Le Goïc et al. 2014; Rolton et al. 2015). However, all the effects on reproductive cells were evaluated

Table 2 Types of histopathology in marine molluscan shellfish induced by harmful alga

	Histopathology	Reference
	Hemocyte aggregation in the tissues	Basti et al. 2015b; Carella et al. 2015; Estrada et al. 2007; Galimany et al. 2008b
Inflammatory response	Hemocyte degranulation, diapedesis, and hemocyte migration	Basti et al. 2015b; Galimany et al. 2008b, 2008c
	Hemocyte infiltration	Basti et al. 2015b; Borcier et al. 2017; Hégaret et al. 2009a; Neves et al. 2015b
Tissue degeneration	Formation of ceroidosis—lipofuchsin granules	Galimany et al. 2008c; Lassudrie et al. 2014; Neves et al. 2015b
	Increase in tissue melanization, myopathy, and muscle fibers degeneration	Basti et al. 2014a; Borcier et al. 2017; Hégaret et al. 2009b, 2012
	Lesions in the tissues of mantle and gills	Estrada et al. 2007; Smolowitz and Shumway 1997
	Lesions in the digestive system and kidney	Carella et al. 2015; Neves et al. 2015b
	Vacuolization in the digestive tubule and stomach epithelia	Neves et al. 2015b
	Matting and exfoliation of the ciliary structures of affected organs followed by epithelial desquamation	Basti et al. 2015b
	Degeneration of adductor muscle fibers	Lassudrie et al. 2015a
Death process of cells and tissues	Appearance of necrotic epithelial and/or connective tissues	Basti et al. 2014a, 2015b; Hégaret et al. 2009b
	Cell apoptosis	Estrada et al. 2014; Galimany et al. 2008b
Alterations in number, size, and differentiated-type of cells in tissues	Decrease in the height of absorptive cells	Smolowitz and Shumway 1997
	Increase in the lumen diameter	
	Thinning of digestive tubules	Galimany et al. 2014
	Reabsorption of the gonad	
	Decrease in gill ciliates	
	Hyperplasia, hypertrophy, and atrophy of epithelia	Basti et al. 2015b; Borcier et al. 2017
		Carella et al. 2015
	Increase in the area, perimeter, and circularity of lumen in the digestive tubules	
	Shifts in the percentage of tubule from adsorbing to atrophic profile	
Fluid accumulation within tissues	Formation of thrombi, edemas, and hemorrhage in the primary canals	Basti et al. 2015b
	Diverticular disease in hepatopancreas and in the lumen of intestine and stomach	

in only three oyster species (*Pinctada fucata martensii*, *Crassostrea virginica*, and *C. virginica*) exposed to dinoflagellates producers of saxitoxins and brevetoxins (Basti et al. 2013; Le Goïc et al. 2014; Rolton et al. 2015).

Larva and juvenile life stages are usually more affected by alga toxicity than adult individuals, and larval survival decreases with increased toxicity (Rolton et al. 2014; Talmage and Gobler 2012). Besides that, flagellated cells of the genus *Pfiesteria* have also reduced larval survival by attacking and consuming molluscan larvae (Shumway et al. 2006; Springer et al. 2002). Negative effects on larval growth, development, and lipid synthesis have been attributed to harmful algae exposure (e.g., Basti et al. 2011b; Mu and Li 2013; Rolton et al. 2014; Talmage and Gobler 2012; Wikfors and Smolowitz 1995). In addition, negative effects on embryo cleavage, inhibition of embryonic and newly hatched development, increased embryo abnormalities, damages to feeding and gut apparatus during embryonic development, reduction or interruption of embryo hatching, delay in metamorphosis of larval stages, and decrease in larval activity were shown in a few species of oysters and clams (e.g., Basti et al. 2013, 2014b, 2015a; Mu and Li 2013; Rolton et al. 2014, 2015).

Mass mortalities of marine invertebrates during HABs are attributed to the toxins produced by harmful species (Faimali et al. 2012). Lethal effects in adult bivalves have been related to toxic dinoflagellates exposure (e.g., Carella et al. 2015; MacQuerrie and Bricelj 2008; Shumway and Cucci 1987; Shumway et al. 2006; Smolowitz and Shumway 1997). However, mortality of marine bivalves may also be induced by other secondary

metabolites and/or unknown toxins produced by harmful algae, other than the characterized toxins. High mortalities of Japanese and noble scallops, respectively *Patinopecten yessoensis* and *Mimachlamys* (=*Chlamys*) *nobilis*, experimentally exposed to a strain of *Dinophysis caudata* that synthesizes pectenotoxin-2 (PTX-2), have been attributed to unknown toxins and/or secondary metabolites (Basti et al. 2014a). The implication of unknown toxins and/or secondary metabolites was suggested since mortality of scallops due to PTX-2 has never been observed, neither in the wild nor under laboratory conditions (Basti et al. 2014a).

Trophic transfer of phycotoxins

Contaminated molluscs act directly as toxin vectors to their consumers: carnivorous gastropods (Chen and Chou 1998; Wekell et al. 1996), cephalopods (Costa et al. 2009; Lopes et al. 2014), lobsters (Jiang et al. 2006), crabs (Oikawa et al. 2004), marine birds (Shumway et al. 2003), sea otters (Kvitek et al. 1991; Miller et al. 2010), and humans (García et al. 2004; Laurent et al. 2012). Moreover, molluscs may act indirectly as a source of phycotoxins following the elimination of toxic cells in their biodeposits, which makes the toxins available for deposit-feeders and coprophagous organisms (e.g., Hégaret et al. 2007c; Mafra Jr et al. 2009; Neves et al. 2015b, 2019). Toxins are transferred through the marine food web from the toxic algae to molluscs and then towards higher trophic levels, which is the typical pathway of phycotoxin bioaccumulation (reviewed in Basti et al. 2018; reviewed in Turner et al. 2021). Transfer of phycotoxins via food web interactions can have serious and deleterious effects on marine organisms (reviewed in Landsberg 2002), and lead to different human poisonings and even to death (García et al. 2004; reviewed in Neves and Rodrigues 2020).

Biomagnification is defined as an increase in the concentration of toxins in successively higher trophic levels (reviewed in Gray 2002). On the contrary, biodilution is defined as a decrease in toxin concentrations through the trophic web. For example, microcystins tend to biodilute rather than to biomagnify through trophic transfer in aquatic food webs (Ibelings et al. 2005; Kozlowsky-Suzuki et al. 2012; Sotton et al. 2014). The biomagnification factor indicates if trophic transfer is dominated by the process of biomagnification ($BMF_{\text{mean and 95\% CI}} > 1$) or biodilution ($BMF_{\text{mean and 95\% CI}} < 1$) (Kozlowsky-Suzuki et al. 2012). Only two studies, from the 150 scientific publications retrieved in this review, provided simultaneous measurements of toxin concentration in molluscs and their consumers: the scallop *Chlamys nobilis* and its predator the spiny lobster (Jiang et al. 2006), and the clam *Donax* sp. and its predator *Octopus vulgaris* (Lopes et al. 2014). Thus, data considered in the present review for BMF calculation was based only on concentrations of PSTs. We have found a tendency for toxin reduction, with BMF smaller than one (0.10 ±0.12), that suggests PST biodilution through trophic transfer. However, further studies including different species of molluscs and their potential predators, as well as diverse toxins are needed to properly evaluate BMFs of marine phycotoxins.

Phycotoxin dynamics in molluscs and risks for human health

Most information on toxin accumulation in marine molluscs comes from routine monitoring programs for toxins in shellfish (Supplementary Material Table S1). Toxin content in molluscan shellfish may be related to its uptake, metabolism, depuration (Hégaret et al. 2009a), and differential sensitivity to toxins (Twarog 1974; Twarog et al. 1972). Toxin accumulation in molluscs varies widely among species (reviewed in Bricelj and Shumway 1998), even when considering species from the same taxonomic class (e.g., FAO/IOC/WHO- Food and Agriculture Organization of the United Nations/ Intergovernmental Oceanographic Commission of UNESCO/ World Health Organization 2004; Mello et al. 2010; Miller et al. 2010; Suzuki and Mitsuya 2001). Phycotoxin accumulation in molluscs may also be affected by environmental factors (e.g., temperature, exposure time, and salinity) and diverse toxin profiles in harmful alga species from distinct geographic regions (Lassus et al. 2007a; Molinet et al. 2010). Therefore, the equilibrium between the rates of uptake, metabolism, and elimination of toxins depends on several factors related to the toxic microalga, molluscan species, and the environmental conditions that influence both the HAB species and the molluscan shellfish (reviewed in Basti et al. 2018). In summary, the amount of accumulated toxins varies according to mollusc feeding mode and ingestion rates, size of individuals, species resistance and susceptibility to phycotoxins, density of toxic algae, and phycotoxin group (e.g., saxitoxin, domoic acid, okadaic acid).

Marine bivalves, cephalopods, and gastropods accumulate phycotoxins, occasionally exceeding maximum levels for safety consumption, and represent a risk for human health. Bivalves often accumulate higher toxin amounts than cephalopods and gastropods (Table 3). Mussels tend to accumulate high levels of toxins faster than other bivalves and usually eliminate them more quickly (e.g., Lassus et al. 1989; Mafra Jr et al. 2015; reviewed in Shumway et al. 1995; Wohlgeschaffen et al. 1992). The toxin dynamics in mussels make them interesting

Table 3 Concentration of phycotoxins in the tissues of marine molluscan shellfish. Minimum and maximum values are presented when data were available in the literature

Toxin	Mollusc	Toxin concentration (μg kg^{-1} tissue)	Species	Tissue	Reference
Azaspiracids	Clam	6100	*Tapes phillipinarium*	Whole tissue	Furey et al. 2003
	Cockle	2000	*Cardium edule*	Whole tissue	Furey et al. 2003
	Mussel	20 80–4200 240	*Mytilus chilensis* *Mytilus edulis* *Mytilus galloprovinci-alis*	Adductor muscle, digestive gland, non-visceral and whole tissue	Furey et al. 2003; Jauffrais et al. 2012a, 2012b; López-Rivera et al. 2010; Magdalena et al. 2003; Stobo et al. 2008
	Oyster	24,500	*Crassotrea gigas*	Whole tissue	Furey et al. 2003
	Scallop	200–4000	*Pecten maximus*	Whole tissue	Furey et al. 2003; Stobo et al. 2008
Brevetoxins (PbTX-3)	Clam	1200–1600 1000–2000	*Macoma baltica* *Mercenaria mercenaria*	Viscera and whole tissue	Echevarria et al. 2012; Griffith et al. 2013; Haubois et al. 2007
	Oyster	1900	*Crassostrea virginica*	Whole tissue	Griffith et al. 2013
Ciguatoxins (P-CTX-3C)	Clam	1.4–13.6	*Tridacna maxima*	Mantle, viscera, and whole tissue	Roué et al. 2016, 2018
Domoic acid	Clam	900–53,000 < 300 1500	*Donax trunculus* *Ensis siliqua* *Ruditapes decussatus*	Whole tissue	Amzil et al. 2001; James et al. 2005
	Cockle	39,000	*Cerastoderma edule*	Whole tissue	Vale and Sampayo 2001
	Mussel	15,000–243,000 200–90,000	*Mytilus edulis* *Mytilus galloprovinci-alis*	Whole tissue	Amzil et al. 2001; Mafra Jr et al. 2010; Vale and Sampayo 2001
	Oyster	< 5000 <10,000–22,000	*Crassostrea edulis* *Crassostrea virginica*	Whole tissue	James et al. 2005; Mafra Jr et al. 2010
	Cephalopod	< 500 1100–166,000	*Loligo opalescens* *Octopus vulgaris* *Sepia officinalis*	Branchial hearts, Digestive gland and tract, gills, gonad, kidney, mantle, stomach, and viscera	Bargu et al. 2008; Costa et al. 2004, 2005
	Scallops	7300–296,000	*Pecten maximus*	Adductor muscle, gonad, and hepatopancreas	Bogan et al. 2007b
Mycrocistins	Clam	295	*Tapes semidecussat-us*		
	Gastropod	175	*Tegula* spp.	Hepatopancreas	
	Mussel	979	*Mytilus edulis*		Miller et al. 2010
	Oyster	373	*Crassostrea gigas*		
Okadaic acid	Gastropod	4.7	*Haliotis discus hannai*	Digestive gland and foot muscle	Kim et al. 2012
	Mussel	1.7–87.9	*Perna perna*		Mello et al. 2010
	Oyster	6.8	*Crassostrea gigas*	Digestive gland	
Saxitoxins	Cephalopod	1200–14,900 2700–127,000 2400 2980–7000	*Eledone cirrhosa* *Eledona moschata* *Octopus (Abdopus)* sp.	Digestive gland, stomach, branchial hearts, salivary gland, kidney, digestive tract, gills, mantle	Costa et al. 2005, 2009; Monteiro and Costa 2011; Robertson et al. 2004

Table 3 (continued)

Toxin	Mollusc	Toxin concentration (μg kg^{-1} tissue)	Species	Tissue	Reference
			Octopus vulgaris		
	Clam	200–1000 17,500 82,000–770,000	*Atrina vexillum* *Hiatula rostrata* *Mya arenaria*	Digestive gland, visceral and non-visceral tissues, siphon, and whole tissue	Chen and Chou 2001; MacQuerrie and Bricelj 2008; Montojo et al. 2006
	Gastropod	20 50–300 720 480	*Haliotis laevigata* *Littorina littorea* *Nucella lamelosa* *Polinices lewissi*	Digestive gland, foot, and viscera	Dowsett et al. 2011; Neves et al. 2015a, 2015b; Wekell et al. 1996
	Mussel	360–880 1800–5000 350–220,000 5260–380,000	*Perna perna* *Perna viridis* *Mytilus chilensis* *Mytilus edulis*	Adductor muscle, digestive gland, gills, gonad, mantle, viscera, and whole tissue	Abouabdellah et al. 2008; Kwong et al. 2006; Molinet et al. 2010; Montojo et al. 2006; Schramm et al. 2006; Sephton et al. 2007
	Oyster	12–270 30–9700 60–180 3000–11,700	*Crassostrea virginica* *Crassostrea gigas* *Pinctada imbricata* *Spondylus squamosus*	Adductor muscle, digestive gland, non-visceral tissue, viscera, and whole tissue	Guéguen et al. 2008; Hégaret et al. 2007c; Lassus et al. 2007a; Montojo et al. 2006; Murray et al. 2009; Persson et al. 2006; Rolland et al. 2012
	Scallop	70–600 850 300–2900	*Argopecten ventricosus* *Chlamys nobilis* *Pecten novaezelandiae*	Digestive gland and whole tissue	Band-Schmidt et al. 2005; Contreras et al. 2012; Escobedo-Lozano et al. 2012; Jiang et al. 2006

candidates to be used as the most appropriate model, among molluscs, to allow early detection of HABs. In contrast, toxin concentration in gastropods is usually below regulatory levels for safe consumption (e.g., Dowsett et al. 2011; Kim et al. 2012; Neves et al. 2015a, 2015b), suggesting that gastropods accumulate less toxins than bivalves. Moreover, toxin accumulation in molluscs is not homogeneous; toxin content varies among tissues; and toxins migrate to different tissues during biotransformation. Data compilation from retrieved scientific studies indicates that in overall digestive glands concentrate more toxins (~81% total toxin) than other tissues-gonads (~12% total toxin), adductor muscles (~5% total toxin), and brachial hearts (~28% total toxin) (see Table 3). Higher toxin concentration in digestive glands seems to be directly related to their role in food digestion and absorption.

Routine monitoring programs for toxins in shellfish aim to reduce human risks by detecting phycotoxin concentration levels in molluscs which may lead to harvesting restrictions or closure to prevent human contamination. The European Commission (EC) regulates the production and marketing of live bivalves to ensure that contaminated shellfish are not placed on the market (European Commission, 2004 - EC 853/2004; European Commission, 2013 - EC 786/2013). Molluscs represent 11% of European Union (EU) seafood consumption, and EU production supplies 65% of its domestic mollusc demand (O'Mahony 2018). The National Shellfish Sanitation Program (NSSP), recognized by the U.S. Food and Drug Administration (FDA), is responsible for the sanitary control of shellfish production and sale for human consumption in the USA (FDA - U.S. Food and Drug Administration 2017). The current regulatory limits for marine phycotoxins are presented in Table 4.

Human health effects induced by shellfish poisonings include several general symptoms (e.g., nausea, diarrhea, vomiting, headache, fever) and symptoms specifically induced by the phycotoxin group, for example, tingling of fingers and toes and muscle paralysis (PSP), confusion and short-term memory loss (ASP), and cardiovascular symptoms (CFP) (reviewed in Nicolas et al. 2017).

Table 4 Regulatory limits applied to marine toxins established by U.S. Food and Drug Administration (FDA - U.S. Food and Drug Administration 2017) and European Union/ European Food Safety Authority (EC 853/2004 and 786/2013) and related human poisoning syndromes

Phycotoxins	Threshold values (μg phycotoxin-eq kg^{-1})		Human poisonings
	FDA	EFSA	
Azaspiracid	160	160	Azaspiracids poisoning (AZP)
Brevetoxins	800	-	Neurotoxic shellfish poisoning (NSP)
Ciguatoxins	0.01*	0.01*	Ciguatera poisoning (CP)
Domoic acid	20,000	20,000	Amnesic shellfish poisoning (ASP)
Okadaic acid[1], dinophysistoxins[1] and pectenotoxins[2]	160	160	Diarrhetic shellfish poisoning (DSP)[1] Pectenotoxin intoxication[2]
Saxitoxins	800	800	Paralytic shellfish poisoning (PSP)
Yessotoxins	-	3750	Yessotoxin intoxication

Phycotoxin group not regulated (-); * CTX concentration proposed by both FDA and EFSA (FAO and WHO - Food and Agriculture Organization of the United Nations/World Health Organization 2020); When available, superscript numbers refer to the human poisoning induced by a specific toxin

Conclusion and perspectives

Harmful algae impact on marine molluscan shellfish is complex to trace and predict, since they rely on molluscan species, harmful algae species, toxic compounds, and synergetic interactions of these and other barely known factors. Moreover, the few detected effects of HABs on gastropods and cephalopods indicate that more attention should be devoted to these molluscan groups for both ecological and human health considerations. Further studies including different species of molluscs and their potential prey and predators are also needed to evaluate the trophic transfer of marine biotoxins through food webs.

Considering the perspective of climate change which may favor an increase in the occurrence and intensity of HABs, the intensification of efforts to expand the knowledge about HABs impacts on marine molluscs is crucial to mitigate the damages on economy and human health. More information about the consequences of harmful algae exposure on reproductive features of marine molluscan shellfish is necessary in order to mitigate the impacts on cultivated shellfish and predict HABs impacts on farmed populations. Moreover, further investigations on the feasibility of detoxification in terms of cost-effectiveness are also needed to allow detoxification of contaminated shellfish in shorter periods and reduce the adverse effects for human health and excessive economic losses.

An increase in the research effort in the field of marine sciences is one of the targets of the Sustainable Development Goal 14 (United Nations Development Programme) in order to improve ocean health and, consequently, environmental and human safety. Moreover, the conservation and sustainable use of the oceans, seas, and marine resources can contribute to reduce the frequency and distribution of marine HABs and their impacts on public health, fishery, and marine ecosystems worldwide.

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Data availability All data generated or analyzed during this study are included in this published article and its supplementary material Table S1.

Declarations

Ethics approval and consent to participate Not applicable

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References

Abouabdellah R, Taleb H, Bennouna A, Erler K, Chafik A, Moukrim A (2008) Paralytic shellfish poisoning toxin profile of mussels *Perna perna* from southern Atlantic coasts of Morocco. Toxicon 51:780–786. https://doi.org/10.1016/j.toxicon.2007.12.004

Ajani P, Harwood D, Murray S (2017) Recent trends in marine phycotoxins from Australian coastal waters. Mar Drugs 15:33. https://doi.org/10.3390/md15020033

Akberali HB, Trueman ER (1985) Effects of environmental stress on marine bivalve molluscs. Adv Mar Biol 22:101–198. https://doi.org/10.1016/S0065-2881(08)60051-6

Amzil Z, Fresnel J, Le Gal D, Billard C (2001) Domoic acid accumulation in French shellfish in relation to toxic species of *Pseudo-nitzschia multiseries* and *P. pseudodelicatissima*. Toxicon 39:1245–1251. https://doi.org/10.1016/s0041-0101(01)00096-4

Anderson DM, Alpermann TJ, Cembella AD, Collos Y, Masseret E, Montresor M (2012) The globally distributed genus Alexandrium: multifaceted roles in marine ecosystems and impacts on human health. Harmful Algae 14:10–35. https://doi.org/10.1016/j.hal.2011.10.012

Astuya AP, Carrera C, Ulloa V, Aballay AE, Núñez-Acuña G, Hégaret H, Gallardo-Escárate C (2015) Saxitoxin modulates immunological parameters and gene transcription in *Mytilus chilensis* hemocytes. Int J Mol Sci 16:15235–15250. https://doi.org/10.3390/ijms160715235

Band-Schmidt CJ, Bustillos-Guzmán J, Gárate-Lizárraga I, Lechuga-Devéze CH, Reinhardt K, Luckas B (2005) Paralytic shellfish toxin profile in strains of the dinoflagellate *Gymnodinium catenatum* Graham and the scallop *Argopecten ventricosus* G.B. Sowerby II from Bahía Concepción, Gulf of California, Mexico. Harmful Algae 4:21–31. https://doi.org/10.1016/j.hal.2003.10.004

Barcia R, Ramos-Martínez JI (2011) Stress-based modulation of the immune response in molluscan hemocytes: a two-receptor model. ISJ-Invert Surviv J 8:56–58

Bargu S, Powell CL, Wang Z, Doucette GJ, Silver MW (2008) Note on the occurrence of *Pseudo-nitzschia australis* and domoic acid in squid from Monterey Bay, CA (USA). Harmful Algae 7:45–51. https://doi.org/10.1016/j.hal.2007.05.008

Basti L, Segawa S (2010) Mortality of the short-neck clam *Ruditapes philippinarum* induced by the toxic dinoflagellate *Heterocapsa circularisquama*. Fish Sci 76:625–631. https://doi.org/10.1007/s12562-010-0252-4

Basti L, Nagai K, Shimasaki Y, Oshima Y, Honjo T, Segawa S (2009) Effects of the toxic dinoflagellate *Heterocapsa circularisquama* on the valve movement behaviour of the Manila clam *Ruditapes philippinarum*. Aquaculture 291:41–47. https://doi.org/10.1016/j.aquaculture.2009.02.029

Basti L, Endo M, Segawa S (2011a) Physiological, pathological, and defense alterations in Manila clams (short-neck clams), *Ruditapes philippinarum*, induced by *Heterocapsa circularisquama*. J Shellfish Res 30:829–844. https://doi.org/10.2983/035.030.0324

Basti L, Go J, Higuchi K, Nagai K, Segawa S (2011b) Effects of the toxic dinoflagellate *Heterocapsa circularisquama* on larvae of the Pearl Oyster *Pinctada fucata martensii* (Dunker, 1873). J Shellfish Res 30:177–186. https://doi.org/10.2983/035.030.0125

Basti L, Nagai K, Tanaka Y, Segawa S (2013) Sensitivity of gametes, fertilization, and embryo development of the Japanese pearl oyster, *Pinctada fucata martensii*, to the harmful dinoflagellate, *Heterocapsa circularisquama*. Mar Biol 160:211–219. https://doi.org/10.1007/s00227-012-2079-2

Basti L, Uchida H, Kanamori M, Matsushima R, Suzuki T, Nagai S (2014a) Mortality and pathology of Japanese scallop, *Patinopecten* (*Mizuhopecten*) *yessoensis*, and noble scallop, *Mimachlamys nobilis*, fed monoclonal culture of PTX-producer, *Dinophysis caudata*. In: AL MK (ed) Proceedings of the 16th International Conference on Harmful Algae. Cawthron Institute and the International Society for the Study of Harmful Algae (ISSHA), New Zealand, pp 105–108

Basti L, Nagai S, Nagai K, Go J, Okano S, Watanabe R, Suzuki T, Tanaka Y (2014b) Harmful algal blooms affect early life-stages of Japanese pearl oyster, *Pinctada fucata martensii*. In: AL MK (ed) Proceedings of the 16th International Conference on Harmful Algae. Cawthron Institute and the International Society for the Study of Harmful Algae (ISSHA), New Zealand, pp 94–97

Basti L, Nagai S, Go J, Okano S, Nagai K, Watanabe R, Suzuki T, Tanaka Y (2015a) Differential inimical effects of *Alexandrium* spp. and *Karenia* spp. on cleavage, hatching, and two larval stages of Japanese pearl oyster *Pinctada fucata martensii*. Harmful Algae 43:1–12. https://doi.org/10.1016/j.hal.2014.12.004

Basti L, Endo M, Segawa S, Shumway SE, Tanaka Y, Nagai S (2015b) Prevalence and intensity of pathologies induced by the toxic dinoflagellate, *Heterocapsa circularisquama*, in the Mediterranean mussel, *Mytilus galloprovincialis*. Aquat Toxicol 163:37–50. https://doi.org/10.1016/j.aquatox.2015.03.012

Basti L, Nagai S, Watanabe S, Oda T, Tanaka Y (2016) Neuroenzymatic activity and physiological energetics in Manila clam, *Ruditapes philippinarum*, during short-term sublethal exposure to harmful alga, *Heterocapsa circularisquama*. Aquat Toxicol 176:76–87. https://doi.org/10.1016/j.aquatox.2016.04.011

Basti L, Hégaret H, Shumway SE (2018) Harmful algal blooms and shellfish. In: Shumway SE, Burkholder JM, Morton SL (eds) Harmful algal blooms: a compendium desk reference. Wiley, Chichester, pp 135–190. https://doi.org/10.1002/9781118994672.ch4

Berger VJ, Kharazova AD (1997) Mechanisms of salinity adaptations in marine molluscs. Hydrobiologia 355:115–126. https://doi.org/10.1023/A:1003023322263

Blanco J (2006) Modelling phycotoxins accumulation in bivalves: a review. In: Henshilwood K (ed) Proceedings of the fifth International Conference on Molluscan Shellfish Safety. Marine Institute, California, pp 258–269

Blanco J, Moroño A, Franco J, Reyero MI (1997) PSP detoxification kinetics in the mussel *Mytilus galloprovincialis*. One and two-compartment models and the effect of some environmental variables. Mar Ecol Prog Ser 158:165–175

Blanco J, Moroño A, Fernandez ML (2005) Toxic episodes in shellfish produced by lipohilic phycotoxins: an overview. Revista Galega de Recursos Mariños 1:1–70

Bogan YM, Harkin AL, Gillespie J, Kennedy DJ, Hess P, Slater JW (2007a) The influence of size on domoic acid concentration in king scallop, *Pecten maximus* (L.). Harmful Algae 6:15–28. https://doi.org/10.1016/j.hal.2006.05.005

Bogan YM, Kennedy DJ, Harkin AL, Gillespie J, Vause BJ, Beukers-Stewart BD, Hess P, Slater JW (2007b) Variation in domoic acid concentration in king scallop (*Pecten maximus*) from fishing grounds around the Isle of Man. Harmful Algae 6:81–92. https://doi.org/10.1016/j.hal.2006.07.002

Borcier E, Morvezen R, Boudry P, Miner P, Charrier GG, Laroche J, Hégaret H (2017) Effects of bioactive extracellular compounds and paralytic shellfish toxins produced by *Alexandrium minutum* on growth and behaviour of juvenile great scallops *Pecten maximus*. Aquat Toxicol 184:142–154. https://doi.org/10.1016/j.aquatox.2017.01.009

Branch GM, Bustamante RH, Robinson TB (2013) Impacts of a "black tide" harmful algal bloom on rocky-shore intertidal communities on the West Coast of South Africa. Harmful Algae 24:54–64. https://doi.org/10.1016/j.hal.2013.01.005

Bricelj VM, Shumway SE (1998) Paralytic shellfish toxins in bivalve molluscs: occurrence, transfer kinetics, and biotransformation. Rev Fish Sci 6:315–383. https://doi.org/10.1080/10641269891314294

Bricelj V, Cembella A, Laby D, Shumway S, Cucci T (1996) Comparative physiological and behavioral responses to PSP toxins in two bivalve molluscs, the softshell clam, *Mya arenaria*, and surfclam *Spisula solidissima*. In: Yasumoto T, Oshima Y, Fukuyo Y (eds) Harmful and Toxic Algal Blooms. UNESCO, Japan, pp 405–408

Bricelj VM, Connell L, Konoki K, MacQuarrie SP, Scheuer T, Catterall WA, Trainer VL (2005) Sodium channel mutation leading to saxitoxin resistance in clams increases risk of PSP. Nature 434:763–767. https://doi.org/10.1038/nature03415

Bricelj VM, MacQuarrie SP, Doane JAE, Connell LB (2010) Evidence of selection for resistance to paralytic shellfish toxins during the early life history of soft-shell clam (*Mya arenaria*) populations. Limnol Oceanogr 55:2463–2475. https://doi.org/10.4319/lo.2010.55.6.2463

Bricelj VM, Haubois AG, Sengco MR, Pierce RH, Culter JK, Anderson DM (2012) Trophic transfer of brevetoxins to the benthic macrofaunal community during a bloom of the harmful dinoflagellate *Karenia brevis* in Sarasota Bay, Florida. Harmful Algae 16:27–34. https://doi.org/10.1016/j.hal.2012.01.001

Cabado AG, Lago J, González V, Blanco L, Paz B, Diogène J, Ferreres L, Rambla-Alegre M (2020) Detoxification of paralytic shellfish poisoning toxins in naturally contaminated mussels, clams and scallops by an industrial procedure. Food Chem Toxicol 141:111386. https://doi.org/10.1016/j.fct.2020.111386

Carella F, Sardo A, Mangoni O, Di Cioccio D, Urciuolo G, De Vico G, Zingone A (2015) Quantitative histopathology of the Mediterranean mussel (*Mytilus galloprovincialis L.*) exposed to the harmful dinoflagellate *Ostreopsis cf. ovata*. J Invertebr Pathol 127:130–140. https://doi.org/10.1016/j.jip.2015.03.001

Carreto JI, Elbusto C, Sancho H, Carignan M, Yasumoto T, Oshima Y (1996) Comparative studies on paralytic shellfish toxin profiles of marine snails, mussels and an *Alexandium tamarense* isolate from The Mar del Plata Coast (Argentina). Rev Invest Desarr Pesq 10:101–107

Castrec J, Soudant P, Payton L, Tran D, Miner P, Lambert C, Le Goïc N, Huvet A, Quillien V, Boullot F, Amzil Z, Hégaret H, Fabioux C (2018) Bioactive extracellular compounds produced by the dinoflagellate *Alexandrium minutum* are highly detrimental for oysters. Aquat Toxicol 199:188–198. https://doi.org/10.1016/j.aquatox.2018.03.034

Chen CY, Chou HN (1998) Transmission of the paralytic shellfish poisoning toxins, from dinoflagellate to gastropod. Toxicon 36:515–522. https://doi.org/10.1016/s0041-0101(97)00093-7

Chen CY, Chou HN (2001) Accumulation and depuration of paralytic shellfish poisoning toxins by purple clam *Hiatula rostrata Lighttoot*. Toxicon 39:1029–1034. https://doi.org/10.1016/s0041-0101(00)00242-7

Choi MC, Hsieh DPH, Lam PKS, Wang WX (2003) Field depuration and biotransformation of paralytic shellfish toxins in scallop *Chlamys nobilis* and green-lipped mussel *Perna viridis*. Mar Biol 143:927–934. https://doi.org/10.1007/s00227-003-1148-y

Connell LB, MacQuarrie SP, Twarog BM, Iszard M, Bricelj VM (2007) Population differences in nerve resistance to paralytic shellfish toxins in softshell clam, *Mya arenaria*, associated with sodium channel mutations. Mar Biol 150:1227–1236. https://doi.org/10.1007/s00227-006-0432-z

Contreras AM, Marsden ID, Munro MHG (2012) Physiological effects and biotransformation of PSP toxins in the New Zealand scallop, *Pecten novaezelandiae*. J Shellfish Res 31:1151–1159. https://doi.org/10.2983/035.031.0426

Costa PR (2016) Impact and effects of paralytic shellfish poisoning toxins derived from harmful algal blooms to marine fish. Fish Fish 17:226–248. https://doi.org/10.1111/faf.12105

Costa PR, Rosa R, Sampayo MAM (2004) Tissue distribution of the amnesic shellfish toxin, domoic acid, in *Octopus vulgaris* from the Portuguese coast. Mar Biol 144:971–976. https://doi.org/10.1007/s00227-003-1258-6

Costa PR, Rosa R, Duarte-Silva A, Brotas V, Sampayo MAM (2005) Accumulation, transformation and tissue distribution of domoic acid, the amnesic shellfish poisoning toxin, in the common cuttlefish, *Sepia officinalis*. Aquat Toxicol 74:82–91. https://doi.org/10.1016/j.aquatox.2005.01.011

Costa PR, Botelho MJ, Rodrigues SM (2009) Accumulation of paralytic shellfish toxins in digestive gland of *Octopus vulgaris* during bloom events including the dinoflagellate *Gymnodinium catenatum*. Mar Pollut Bull 58:1747–1750. https://doi.org/10.1016/j.marpolbul.2009.08.005

Costello KE, Lynch SA, O'Riordan RM, McAllen R, Culloty SC (2021) The importance of marine bivalves in invasive host–parasite introductions. Front Mar Sci 8:1–14. https://doi.org/10.3389/fmars.2021.609248

Couch JA, Fournie JW (2021) Pathobiology of marine and estuarine organisms. Advances in Fisheries Science Book 2, CRC Press, 555 p.

Cuevas N, Zorita I, Costa PM, Franco J, Larreta J (2015) Development of histopathological indices in the digestive gland and gonad of mussels: integration with contamination levels and effects of confounding factors. Aquat Toxicol 162:152–164. https://doi.org/10.1016/j.aquatox.2015.03.011

da Silva PM, Hégaret H, Lambert C, Wikfors GH, Le Goïc N, Shumway SE, Soudant P (2008) Immunological responses of the Manila clam (*Ruditapes philippinarum*) with varying parasite (*Perkinsus olseni*) burden, during a long-term exposure to the harmful alga, *Karenia selliformis*, and possible interactions. Toxicon 51:563–573. https://doi.org/10.1016/j.toxicon.2007.11.006

Deeds J, Landsberg J, Etheridge S, Pitcher G, Longan S (2008) Non-traditional vectors for paralytic shellfish poisoning. Mar Drugs 6:308–348. https://doi.org/10.3390/md6020308

Dizer H, Fischer B, Harabawy ASA, Hennion MC, Hansen PD (2001) Toxicity of domoic acid in the marine mussel *Mytilus edulis*. Aquat Toxicol 55:149–156. https://doi.org/10.1016/s0166-445x(01)00178-3

Doucette G, Maneiro I, Riveiro I, Svensen C (2006) Phycotoxin pathways in aquatic food webs: transfer, accumulation and degradation. In: Granéli E, Turner J (eds) Ecology of harmful algae. Ecological Studies, vol 189. Springer, Berlin, Heidelberg, pp 283–295

Dowsett N, Hallegraeff G, Van Ruth P, Van Ginkel R, McNabb P, Hay B, O'Connor W, Kiermeier A, Deveney M, McLeod C (2011) Uptake, distribution and depuration of paralytic shellfish toxins from *Alexandrium minutum* in Australian greenlip abalone, *Haliotis laevigata*. Toxicon 58:101–111. https://doi.org/10.1016/j.toxicon.2011.05.010

Duan GF, Liu Y, Zhang LN, Li HY, Liu JS, Yang WD (2021) Cinnamaldehyde could reduce the accumulation of diarrhetic shellfish toxins in the digestive gland of the mussel *Perna viridis* under laboratory conditions. Mar Drugs 19:63. https://doi.org/10.3390/md19020063

Echevarria M, Naar JP, Tomas C, Pawlik JR (2012) Effects of *Karenia brevis* on clearance rates and bioaccumulation of brevetoxins in benthic suspension feeding invertebrates. Aquat Toxicol 106–107:85–94. https://doi.org/10.1016/j.aquatox.2011.10.011

Escobedo-Lozano AY, Estrada N, Ascencio F, Contreras G, Alonso-Rodriguez R (2012) Accumulation, biotransformation, histopathology and paralysis in the pacific calico scallop *Argopecten ventricosus* by the paralyzing toxins of the dinoflagellate *Gymnodinium catenatum*. Mar Drugs 10:1044–1065. https://doi.org/10.3390/md10051044

Estrada N, De Jesús RM, Campa-Córdova A, Luna A, Ascencio F (2007) Effects of the toxic dinoflagellate, *Gymnodinium catenatum* on hydrolytic and antioxidant enzymes, in tissues of the giant lions-paw scallop *Nodipecten subnodosus*. Comp Biochem Physiol C Toxicol

Pharmacol 146:502–510. https://doi.org/10.1016/j.cbpc.2007.06.003

Estrada N, Ascencio F, Shoshani L, Contreras RG (2014) Apoptosis of hemocytes from lions-paw scallop *Nodipecten subnodosus* induced with paralyzing shellfish poison from *Gymnodinium catenatum*. Immunobiology 219:964–974. https://doi.org/10.1016/j.imbio.2014.07.006

European Commission (2004) Commission regulation (EU) No 853/2004 of the European Parliament and of the Council of 29 April 20004 laying down specific hygiene rules for on the hygiene of foodstuffs. Official Journal of the European Union, L 139/55.

European Commission (2013) Commission regulation (EU) No 786/2013 of the European Parliament and of the Council of 16 August 2013 amending Annex III to Regulation (EC) No 853/2004 as regards the permitted limits of yessotoxins in live bivalve molluscs. Official Journal of the European Union, L 220/14.

Fabioux C, Sulistiyani Y, Haberkorn H, Hégaret H, Amzil Z, Soudant P (2015) Exposure to toxic *Alexandrium minutum* activates the detoxifying and antioxidant systems in gills of the oyster *Crassostrea gigas*. Harmful Algae 48:55–62. https://doi.org/10.1016/j.hal.2015.07.003

Faimali M, Giussani V, Piazza V, Garaventa F, Corrà C, Asnaghi V, Privitera D, Gallus L, Cattaneo-Vietti R, Mangialajo L, Chiantore M (2012) Toxic effects of harmful benthic dinoflagellate *Ostreopsis ovata* on invertebrate and vertebrate marine organisms. Mar Environ Res 76:97–107. https://doi.org/10.1016/j.marenvres.2011.09.010

FAO - Food and Agriculture Organization of the United Nations (2004) Marine biotoxins. FAO Food and Nutrition Paper 80, Rome. http://www.fao.org/3/a-y5486e.pdf

FAO - Food and Agriculture Organization of the United Nations (2006-2020) Fisheries and aquaculture software. FishStat Plus - Universal software for fishery statistical time series. In: FAO Fisheries and Aquaculture Department. Rome. http://www.fao.org/fishery/

FAO - Food and Agriculture Organization of the United Nations (2012) The state of world fisheries and aquaculture. FAO Fisheries and Aquaculture Department, Rome http://www.fao.org/docrep/016/i2727e/i2727e.pdf

FAO - Food and Agriculture Organization of the United Nations (2014) The state of world fisheries and aquaculture. FAO Fisheries and Aquaculture Department, Rome http://www.fao.org/3/a-i3720e.pdf

FAO - Food and Agriculture Organization of the United Nations (2016) AQUASTAT Main Database, FAO. Website accessed on 18/07/2020.

FAO - Food and Agriculture Organization of the United Nations (2019) FAO yearbook. Fishery and Aquaculture Statistics 2017, Rome. ISBN 978-92-5-131669-6. http://www.fao.org/fishery/static/Yearbook/YB2017_USBcard/index.htm

FAO and WHO - Food and Agriculture Organization of the United Nations/World Health Organization (2020) Report of the expert meeting on ciguatera poisoning, Rome, 19-23 November 2018. Food Safety and Quality n° 9, Rome. https://doi.org/10.4060/ca8817en

FAO/IOC/WHO- Food and Agriculture Organization of the United Nations/ Intergovernmental Oceanographic Commission of UNESCO/ World Health Organization (2004) Report of the joint FAO/IOC/WHO ad hoc expert consultation on biotoxins in bivalve molluscs. FAO/IOC/WHO, Oslo http://ftp.fao.org/es/esn/food/biotoxin_report_en.pdf

Fast MD, Cembella AD, Ross NW (2006) *In vitro* transformation of paralytic shellfish toxins in the clams *Mya arenaria* and *Protothaca staminea*. Harmful Algae 5:79–90. https://doi.org/10.1016/j.hal.2005.05.005

FDA - U.S. Food and Drug Administration (2017) National Shellfish Sanitation Program (NSSP) – Guide for the control of molluscan shellfish. http://www.fda.gov/Food/GuidanceRegulation/FederalStateFoodPrograms/ucm2006754.htm

Fernández ML, Shumway SE, Blanco J (2004) Management of shellfish resources. In: Hallegraef GM, Anderson DM, Cembella AD (eds) Manual of Harmful Marine Microalgae. UNESCO, Paris, pp 657–692

Flórez-Barrós F, Prado-Alvarez M, Méndez J, Fernández-Tajes J (2011) Evaluation of genotoxicity in gills and hemolymph of clam *Ruditapes decussatus* fed with the toxic dinoflagellate *Prorocentrum lima*. J Toxicol Environ Health A 74:971–979. https://doi.org/10.1080/15287394.2011.582025

Ford SE, Bricelj VM, Lambert C, Paillard C (2008) Deleterious effects of a nonPST bioactive compound(s) from *Alexandrium tamarense* on bivalve hemocytes. Mar Biol 154:241–253. https://doi.org/10.1007/s00227-008-0917-z

Furey A, Moroney C, Magdalena ABA, Fidalgo Saez MJ, Lehane M, James KJ (2003) Geographical, temporal, and species variation of the polyether toxins, azaspiracids, in shellfish. Environ Sci Technol 37:3078–3084. https://doi.org/10.1021/es020246z

Gainey LF Jr, Shumway SE (1988) A compendium of the responses of bivalve molluscs to toxic dinoflagellates. J Shellfish Res 7:623–628

Galimany E, Place AR, Ramón M, Jutson M, Pipe RK (2008a) The effects of feeding *Karlodinium veneficum* (PLY # 103; *Gymnodinium veneficum* Ballantine) to the blue mussel *Mytilus edulis*. Harmful Algae 7:91–98. https://doi.org/10.1016/j.hal.2007.05.004

Galimany E, Sunila I, Hégaret H, Ramón M, Wikfors GH (2008b) Pathology and immune response of the blue mussel (*Mytilus edulis* L.) after an exposure to the harmful dinoflagellate *Prorocentrum minimum*. Harmful Algae 7:630–638. https://doi.org/10.1016/j.hal.2008.01.001

Galimany E, Sunila I, Hégaret H, Ramón M, Wikfors GH (2008c) Experimental exposure of the blue mussel (*Mytilus edulis*, L.) to the toxic dinoflagellate *Alexandrium fundyense*: histopathology, immune responses, and recovery. Harmful Algae 7:702–711. https://doi.org/10.1016/j.hal.2008.02.006

Galimany E, Rose JM, Alix J, Dixon MS, Wikfors GH (2014) Responses of the ribbed mussel, *Geukensia demissa*, to the harmful algae *Aureococcus anophagefferens* and *Heterosigma akashiwo*. J Molluscan Stud 80:123–130. https://doi.org/10.1093/mollus/eyt055

Gárate-Lizárraga I, Bustillos-Guzmán JJ, Alonso-Rodríguez R, Luckas B (2004) Comparative paralytic shellfish toxin profiles in two marine bivalves during outbreaks of *Gymnodinium catenatum* (Dinophyceae) in the Gulf of California. Mar Pollut Bull 48:397–402. https://doi.org/10.1016/j.marpolbul.2003.10.032

García C, Del Carmen Bravo MA, Lagos M, Lagos N (2004) Paralytic shellfish poisoning: post-mortem analysis of tissue and body fluid samples from human victims in the Patagonia fjords. Toxicon 43:149–158. https://doi.org/10.1016/j.toxicon.2003.11.018

García-Lagunas N, Romero-Geraldo R, Hernández-Saavedra NY (2013) Genomics study of the exposure effect of *Gymnodinium catenatum*, a paralyzing toxin producer, on *Crassostrea gigas* defense system and detoxification genes. PLoS One 8:e72323. https://doi.org/10.1371/journal.pone.0072323

Glibert PM, Burkholder JM (2006) The complex relationships between increasing fertilization of the earth, coastal eutrophication and proliferation of harmful algal blooms. In: Granéli E, Turner J (eds) Ecology of harmful algae. Springer, Berlin, pp 341–354

Gobler CJ (2020) Climate change and harmful algal blooms: insights and perspective. Harmful Algae 91:101731. https://doi.org/10.1016/j.hal.2019.101731

Granéli E, Vidyarathna NK, Funari E, Cumaranatunga PRT, Scenati R (2011) Can increases in temperature stimulate blooms of the toxic benthic dinoflagellate *Ostreopsis ovata*? Harmful Algae 10:165–172. https://doi.org/10.1016/j.hal.2010.09.002

Gray JS (2002) Biomagnification in marine systems: the perspective of an ecologist. Mar Pollut Bull 45:46–52. https://doi.org/10.1016/S0025-326X(01)00323-X

Griffith AW, Gobler CJ (2020) Harmful algal blooms: a climate change co-stressor in marine and freshwater ecosystems. Harmful Algae 91: 101590. https://doi.org/10.1016/j.hal.2019.03.008

Griffith AW, Shumway SE, Volety AK (2013) Bioaccumulation and depuration of brevetoxins in the eastern oyster (*Crassostrea virginica*) and the northern quahog (= hard clam, *Mercenaria mercenaria*). Toxicon 66:75–81. https://doi.org/10.1016/j.toxicon.2013.01.016

Guéguen M, Bardouil M, Baron R, Lassus P, Truquet P, Massardier J, Amzil Z (2008) Detoxification of pacific oyster *Crassostrea gigas* fed on diets of *Skeletonema costatum* with and without silt, following PSP contamination by *Alexandrium minutum*. Aquat Living Resour 21:13–20. https://doi.org/10.1051/alr:2008010

Guiry MD, Guiry GM (2016) AlgaeBase. World-wide electronic publication, National University of Ireland, Galway http://www.algaebase.org

Gutiérrez JL, Jones CG, Strayer DL, Iribarne OO (2003) Mollusks as ecosystem engineers: the role of shell production in aquatic habitats. Oikos 101:79–90. https://doi.org/10.1034/j.1600-0706.2003.12322.x

Haberkorn H, Lambert C, Le Goïc N, Guéguen M, Moal J, Palacios E, Lassus P, Soudant P (2010) Effects of *Alexandrium minutum* exposure upon physiological and hematological variables of diploid and triploid oysters, *Crassostrea gigas*. Aquat Toxicol 97:96–108. https://doi.org/10.1016/j.aquatox.2009.12.006

Haberkorn H, Tran D, Massabuau JC, Ciret P, Savar V, Soudant P (2011) Relationship between valve activity, microalgae concentration in the water and toxin accumulation in the digestive gland of the Pacific oyster *Crassostrea gigas* exposed to *Alexandrium minutum*. Mar Pollut Bull 62:1191–1197. https://doi.org/10.1016/j.marpolbul.2011.03.034

Hallegraeff GM (2010) Ocean climate change, phytoplankton community responses, and harmful algal blooms: a formidable predictive challenge. J Phycol 46:220–235. https://doi.org/10.1111/j.1529-8817.2010.00815.x

Haubois AG, Bricelj VM, Naar J (2007) Transfer of brevetoxins to a Tellinid bivalve by suspension- and deposit-feeding and its implications for clay mitigation of *Karenia brevis* blooms. Mar Biol 151: 2003–2012. https://doi.org/10.1007/s00227-007-0637-9

Hégaret H, Wikfors GH (2005a) Effects of natural and field-simulated blooms of the dinoflagellate *Prorocentrum minimum* upon hemocytes of eastern oysters, *Crassostrea virginica*, from two different populations. Harmful Algae 4:201–209. https://doi.org/10.1016/j.hal.2003.12.005

Hégaret H, Wikfors GH (2005b) Time-dependent changes in hemocytes of eastern oysters, *Crassostrea virginica*, and northern bay scallops, *Argopecten irradians irradians*, exposed to a cultured strain of *Prorocentrum minimum*. Harmful Algae 4:187–199. https://doi.org/10.1016/j.hal.2003.12.004

Hégaret H, Wikfors GH, Shumway SE (2007a) Diverse feeding responses of five species of bivalve mollusc when exposed to three species of harmful algae. J Shellfish Res 26:549–559. https://doi.org/10.2983/0730-8000(2007)26[549:DFROFS]2.0.CO;2

Hégaret H, da Silva PM, Wikfors GH, Lambert C, De Bettignies T, Shumway SE, Soudant P (2007b) Hemocyte responses of Manila clams, *Ruditapes philippinarum*, with varying parasite, *Perkinsus olseni*, severity to toxic-algal exposures. Aquat Toxicol 84:469–479. https://doi.org/10.1016/j.aquatox.2007.07.007

Hégaret H, Wikfors G, Soudant P, Lambert C, Shumway S, Bérard J, Lassus P (2007c) Toxic dinoflagellates (*Alexandrium fundyense* and *A. catenella*) have minimal apparent effects on oyster hemocytes. Mar Biol 152:441–447. https://doi.org/10.1007/s00227-007-0703-3

Hégaret H, Wikfors GH. Shumway SE (2009a) Biotoxin contamination and shellfish safety. In: Shumway SE, Rodrick GE (eds) Shellfish safety and quality. Woodhead Publishing Limited and CRC Press, pp 43-80.

Hégaret H, da Silva PM, Sunila I, Shumway SE, Dixon MS, Alix J, Wikfors GH, Soudant P (2009b) *Perkinsosis* in the Manila clam *Ruditapes philippinarum* affects responses to the harmful-alga, *Prorocentrum minimum*. J Exp Mar Biol Ecol 371:112–120. https://doi.org/10.1016/j.jembe.2009.01.016

Hégaret H, Smolowitz RM, Sunila I, Shumway SE, Alix J, Dixon M, Wikfors GH (2010) Combined effects of a parasite, QPX, and the harmful-alga, *Prorocentrum minimum* on northern quahogs, *Mercenaria mercenaria*. Mar Environ Res 69:337–344. https://doi.org/10.1016/j.marenvres.2009.12.008

Hégaret H, da Silva PM, Wikfors GH, Haberkorn H (2011) *In vitro* interactions between several species of harmful algae and haemocytes of bivalve molluscs. Cell Biol Toxicol 27:249–266. https://doi.org/10.1007/s10565-011-9186-6

Hégaret H, Brokordt KB, Gaymer CF, Lohrmann KB, García C, Varela D (2012) Effects of the toxic dinoflagellate *Alexandrium catenella* on histopathogical and escape responses of the Northern scallop *Argopecten purpuratus*. Harmful Algae 18:74–83. https://doi.org/10.1016/j.hal.2012.04.006

Hoagland P, Scatasta S (2006) The economic effects of harmful algal blooms. In: Granéli E, Turner J (eds) Ecology of harmful algae - ecological studies. Springer, Berlin, pp 391–419

Ianora A, Bentley MG, Caldwell GS, Casotti R, Cembella AD, Engström-öst J, Halsband C, Sonnenschein E (2011) The relevance of marine chemical ecology to plankton and ecosystem function: an emerging field. Mar Drugs 9:1625–1648. https://doi.org/10.3390/md9091625

Ibelings BW, Bruning K, De Jonge J, Wolfstein K, Pires LMD, Postma J, Burger T (2005) Distribution of microcystins in a lake foodweb: no evidence for biomagnification. Microb Ecol 49:487e500. https://doi.org/10.1007/s00248-004-0014-x

Ito K, Asakawa M, Beppu R, Takayama H, Miyazawa K (2004) PSP-toxicification of the carnivorous gastropod *Rapana venosa* inhabiting the estuary of Nikoh River, Hiroshima Bay, Hiroshima Prefecture, Japan. Mar Pollut Bull 48:1116–1121. https://doi.org/10.1016/j.marpolbul.2003.12.020

James KJ, Gillman M, Amandi MF, López-Rivera A, Puente PF, Lehane M, Mitrovic S, Furey A (2005) Amnesic shellfish poisoning toxins in bivalve molluscs in Ireland. Toxicon 46:852–858. https://doi.org/10.1016/j.toxicon.2005.02.009

James KJ, Carey B, O'Halloran J, Van Pelt FN, Skrabakova Z (2010) Shellfish toxicity: human health implications of marine algal toxins. Epidemiol Infect 138:927–940. https://doi.org/10.1017/S0950268810000853

Jauffrais T, Contreras A, Herrenknecht C, Truquet P, Séchet V, Tillmann U, Hess P (2012a) Effect of *Azadinium spinosum* on the feeding behaviour and azaspiracid accumulation of *Mytilus edulis*. Aquat Toxicol 124:179–187. https://doi.org/10.1016/j.aquatox.2012.08.016

Jauffrais T, Marcaillou C, Herrenknecht C, Truquet P, Séchet V, Nicolau E, Tillmann U, Hess P (2012b) Azaspiracid accumulation, detoxification and biotransformation in blue mussels (*Mytilus edulis*) experimentally fed *Azadinium spinosum*. Toxicon 60:582–595. https://doi.org/10.1016/j.toxicon.2012.04.351

Jiang TJ, Niu T, Xu YX (2006) Transfer and metabolism of paralytic shellfish poisoning from scallop (*Chlamys nobilis*) to spiny lobster (*Panulirus stimpsoni*). Toxicon 48:988–994. https://doi.org/10.1016/j.toxicon.2006.08.002

Jones TO, Whyte JNC, Ginther NG, Townsend LD, Iwama GK (1995) Haemocyte changes in the pacific oyster, *Crassostrea gigas*, caused by exposure to domoic acid in the diatom *Pseudonitzschia pungens* f. *multiseries*. Toxicon 33:347–353. https://doi.org/10.1016/0041-0101(94)00170-D

Kershaw DR (1983) Phylum Mollusca. In: Kershaw DR (ed) Animal diversity. Springer, Dordrecht, pp 169–191. https://doi.org/10.1007/978-94-011-6035-3_10

Khora SS, Jal S (2018) Occurrence of natural toxins in seafood. In: Holban AM, Grumezescu AM (eds), Microbial contamination and food degradation, Handbock of food bioengineering. Volume 10, Academic Press and Elsevier, pp 177-233. https://doi.org/10.1016/B978-0-12-811515-2/00007-X.

Kim JH, Lee KJ, Suzuki T, Mok JS, Park K, Kwon JY, Son KT, Song KC (2012) First report of contamination of the abalone *Haliotis discus hannai* by okadaic acid and yessotoxin. J Shellfish Res 3:1199–1203. https://doi.org/10.2983/035.031.0431

Kiørboe T, Møhlenberg F (1981) Particle selection in suspension-feeding bivalves. Mar Ecol Prog Ser 5:291–296

Kozlowsky-Suzuki B, Wilson AE, Ferrão-Filho ADS (2012) Biomagnification or biodilution of microcystins in aquatic foodwebs? Meta-analyses of laboratory and field studies. Harmful Algae 18:47–55. https://doi.org/10.1016/j.hal.2012.04.002

Kudela RM, Berdalet E, Bernard S, Burford M, Fernand L, Lu S, Roy S, Tester P, Usup G, Magnien R, Anderson DM, Cembella A, Chinain M, Hallegraef G, Reguera B, Zingone A, Enevoldsen H, Urban E (2015) Harmful algal blooms. In: A scientific summary for policy makers. IOC/UNESCO, Paris

Kvitek RG, DeGange AR, Beitler MK (1991) Paralytic shellfish poisoning toxins mediate feeding behavior of sea otters. Limnol Oceanogr 36:393–404. https://doi.org/10.4319/lo.1991.36.2.0393

Kwong RWM, Wang WX, Lam PKS, Yu PKN (2006) The uptake, distribution and elimination of paralytic shellfish toxins in mussels and fish exposed to toxic dinoflagellates. Aquat Toxicol 80:82–91. https://doi.org/10.1016/j.aquatox.2006.07.016

Landsberg JH (2002) The effects of harmful algal blooms on aquatic organisms. Rev Fish Sci 10:113–390. https://doi.org/10.1080/20026491051695

Lassudrie M, Soudant P, Richard G, Henry N, Medhioub W, da Silva PM, Donval A, Bunel M, Le Goïc N, Lambert C, de Montaudouin X, Fabioux C, Hégaret H (2014) Physiological responses of Manila clams *Venerupis* (=*Ruditapes*) *philippinarum* with varying parasite *Perkinsus olseni* burden to toxic algal *Alexandrium ostenfeldii* exposure. Aquat Toxicol 154:27–38. https://doi.org/10.1016/j.aquatox.2014.05.002

Lassudrie M, Wikfors GH, Sunila I, Alix JH, Dixon MS, Combot D, Soudant P, Fabioux C, Hégaret H (2015a) Physiological and pathological changes in the eastern oyster *Crassostrea virginica* infested with the trematode *Bucephalus* sp. and exposed to the toxic dinoflagellate *Alexandrium fundyense*. J Invertebr Pathol 126:51–63. https://doi.org/10.1016/j.jip.2015.01.011

Lassudrie M, Soudant P, Nicolas JL, Fabioux C, Lambert C, Miner P, Le Grand J, Petton B, Hégaret H (2015b) Interaction between toxic dinoflagellate *Alexandrium catenella* exposure and disease associated with herpesvirus OsHV-1μVar in Pacific oyster spat *Crassostrea gigas*. Harmful Algae 45:53–61. https://doi.org/10.1016/j.hal.2015.04.007

Lassudrie M, Hégaret H, Wikfors GH, da Silva PM (2020) Effects of marine harmful algal blooms on bivalve cellular immunity and infectious diseases: a review. Dev Comp Immunol 108:103660. https://doi.org/10.1016/j.dci.2020.103660

Lassus P, Fremy JM, Ledoux M, Bardouil M, Bohec M (1989) Patterns of experimental contamination by *Protogonyaulax tamarensis* in some French commercial shellfish. Toxicon 27:1313–1321. https://doi.org/10.1016/0041-0101(89)90063-9

Lassus P, Bardouil M, Baron R, Bérard J, Masselin P, Truquet P, Pitrat JP (2005) Improving detoxification efficiency of PSP-contaminated oysters (Crassostrea gigas Thunberg). Aquaculture Europe. http://archimer.ifremer.fr/doc/00000/2271/

Lassus P, Amzil Z, Baron R, Séchet V, Barillé L, Abadie E, Bardouil M, Sibat M, Truquet P, Bérard JB, Gueguen M (2007a) Modelling the accumulation of PSP toxins in Thau Lagoon oysters (*Crassostrea gigas*) from trials using mixed cultures of *Alexandrium catenella* and *Thalassiosira weissflogii*. Aquat Living Resour 20:59–67. https://doi.org/10.1051/alr:2007016

Lassus P, Gowland D, McKenzie D, Kelly M, Braaten B, Marcaillou-Martin C, Blanco J (2007b) Industrial scale detoxification of phycotoxin-contaminated shellfish: myth or reality? In: Busby P (ed) Proceedings of the sixth International Conference on Molluscan Shellfish Safety. The Royal Society of New Zealand, Blenheim, pp 289–297

Laurent D, Kerbrat AS, Darius HT, Rossi F, Yeeting B, Haddad M, Golubic S, Pauillac M, Chinain M (2012) Ciguatera shellfish poisoning (CSP): a new ecotoxicological phenomenon from cyanobacteria to humans via giant clams. In: Jensen MA, Muller DW (eds) Food chains. New Research, Nova Science, pp 1-43.

Le Goïc N, Hégaret H, Boulais M, Béguel JP, Lambert C, Fabioux C, Soudant P (2014) Flow cytometric assessment of morphology, viability, and production of reactive oxygen species of *Crassostrea gigas* oocytes. Application to Toxic dinoflagellate (*Alexandrium minutum*) exposure. Cytometry A 85:1049–1056. https://doi.org/10.1002/cyto.a.22577

Lopes VM, Baptista M, Repolho T, Rosa R, Costa PR (2014) Uptake, transfer and elimination kinetics of paralytic shellfish toxins in common octopus (*Octopus vulgaris*). Aquat Toxicol 146:205–211. https://doi.org/10.1016/j.aquatox.2013.11.011

Lopes VM, Costa PR, Rosa R (2019) Effects of harmful algal bloom toxins on marine organisms. In: Duarte B, Caçador I (eds) Ecotoxicology of marine organisms. CRC Press, Boca Raton, p 47. https://doi.org/10.1201/b22000

López-Rivera A, O'Callaghan K, Moriarty M, O'Driscoll D, Hamilton B, Lehane M, James KJ, Furey A (2010) First evidence of azaspiracids (AZAs): a family of lipophilic polyether marine toxins in scallops (*Argopecten purpuratus*) and mussels (*Mytilus chilensis*) collected in two regions of Chile. Toxicon 55:692–701. https://doi.org/10.1016/j.toxicon.2009.10.020

MacKenzie L, Beuzenberg V, Holland P, McNabb P, Selwood A (2004) Solid phase adsorption toxin tracking (SPATT): a new monitoring tool that simulates the biotoxin contamination of filter feeding bivalves. Toxicon 44:901–918. https://doi.org/10.1016/j.toxicon.2004.08.020

MacQuerrie SP, Bricelj VM (2008) Behavioral and physiological responses to PSP toxins in *Mya arenaria* populations in relation to previous exposure to red tides. Mar Ecol Prog Ser 366:59–74. https://doi.org/10.3354/meps07538

Mafra LL Jr, Bricelj VM, Ouellette C, Léger C, Bates SS (2009) Mechanisms contributing to low domoic acid uptake by oysters feeding on *Pseudo-nitzschia* cells. I. Filtration and pseudofeces production. Aquat Biol 6:201–212. https://doi.org/10.3354/ab00121

Mafra LL Jr, Bricelj VM, Ouellette C, Bates SS (2010) Feeding mechanics as the basis for differential uptake of the neurotoxin domoic acid by oysters, *Crassostrea virginica*, and mussels, *Mytilus edulis*. Aquat Toxicol 97:160–171. https://doi.org/10.1016/j.aquatox.2010.01.009

Mafra LL Jr, Ribas T, Alves TP, Proença LAO, Schramm MA, Uchida H, Suzuki T (2015) Differential okadaic acid accumulation and detoxification by oysters and mussels during natural and simulated *Dinophysis* blooms. Fish Sci 81:749–762. https://doi.org/10.1007/s12562-015-0882-7

Mafra LL Jr, Nolli PKW, Mota LE, Domit C, Soeth M, Luz LFG, Sobrinho BF, Leal JG, Di Domenico M (2019) Multi-species okadaic acid contamination and human poisoning during a massive bloom of *Dinophysis acuminata* complex in southern Brazil. Harmful Algae 89:101662. https://doi.org/10.1016/j.hal.2019.101662

Magdalena AB, Lehane M, Krys S, Fernández ML, Furey A, James KJ (2003) The first identification of azaspiracids in shellfish from France and Spain. Toxicon 42:105–108. https://doi.org/10.1016/s0041-0101(03)00105-3

Mat AM, Haberkorn H, Bourdineaud JP, Massabuau JC, Tran D (2013) Genetic and genotoxic impacts in the oyster *Crassostrea gigas* exposed to the harmful alga *Alexandrium minutum*. Aquat Toxicol 140-141:458–465. https://doi.org/10.1016/j.aquatox.2013.07.008

Matsuyama Y, Uchida T, Honjo T (1997) Toxic effects of the dinoflagellate *Heterocapsa circularisquama* on clearance rate of the blue mussel *Mytilus galloprovincialis*. Mar Ecol Prog Ser 146:73–80

May SP, Burkholder JM, Shumway SE, Hégaret H, Wikfors GH, Frank D (2010) Effects of the toxic dinoflagellate *Alexandrium monilatum* on survival, grazing and behavioral response of three ecologically important bivalve molluscs. Harmful Algae 9:281–293. https://doi.org/10.1016/j.hal.2009.11.005

Medhioub W, Ramondenc S, Vanhove AS, Vergnes A, Masseret E, Savar V, Amzil Z, Laabir M, Rolland JL (2013) Exposure to the neurotoxic dinoflagellate, *Alexandrium catenella*, induces apoptosis of the hemocytes of the oyster *Crassostrea gigas*. Mar Drugs 11: 4799–4814. https://doi.org/10.3390/md11124799

Mello DF, Proença LAO, Barracco MA (2010) Comparative study of various immune parameters in three bivalve species during a natural bloom of *Dinophysis acuminata* in Santa Catarina Island, Brazil. Toxins 2:1166–1178. https://doi.org/10.3390/toxins2051166

Miller MA, Kudela RM, Mekebri A, Crane D, Oates SC, Tinker MT, Staedler M, Miller WA, Toy-Choutka S, Dominik C, Hardin D, Langlois G, Murray M, War K, Jessup DA (2010) Evidence for a novel marine harmful algal bloom: cyanotoxin (microcystin) transfer from land to sea otters. PLoS One 5:e12576. https://doi.org/10.1371/journal.pone.0012576

Molinet C, Niklitschek E, Seguel M, Díaz P (2010) Trends of natural accumulation and detoxification of paralytic shellfish poisoning in two bivalves from the Northwest Patagonian inland sea. Rev Biol Mar Oceanogr 45:195–204. https://doi.org/10.4067/S0718-19572010000200001

Monteiro A, Costa PR (2011) Distribution and selective elimination of paralytic shellfish toxins in different tissues of *Octopus vulgaris*. Harmful Algae 10:732–737. https://doi.org/10.1016/j.hal.2011.06.004

Montojo UM, Sakamoto S, Cayme MF, Gatdula NC, Furio EF, Relox JR Jr, Shigeru S, Fukuyo Y, Kodama M (2006) Remarkable difference in accumulation of paralytic shellfish poisoning toxins among bivalve species exposed to *Pyrodinium bahamense* var. *compressum* bloom in Masinloc bay, Philippines. Toxicon 48:85–92. https://doi.org/10.1016/j.toxicon.2006.04.014

Mu C, Li Q (2013) Effects of the dinoflagellate *Alexandrium catenella* on the early development of the Pacific oyster *Crassostrea gigas*. J Shellfish Res 32:689–694. https://doi.org/10.2983/035.032.0310

Murray SA, O'Connor WA, Alvin A, Mihali TK, Kalaitzis J, Neilan BA (2009) Differential accumulation of paralytic shellfish toxins from *Alexandrium minutum* in the pearl oyster, *Pinctada imbricata*. Toxicon 54:217–223. https://doi.org/10.1016/j.toxicon.2009.04.005

Neves RAF, Rodrigues ET (2020) Harmful algal blooms: effect on coastal marine ecosystems. In: Azul AM, Brandli L, Leal Filho W, Özuyar PG., Wall T (eds) Encyclopedia of the UN Sustainable Development Goals. Life Below Water. Springer Internacional Publishing

Neves RAF, Valentin JL, Figueiredo GM, Hégaret H (2015a) Responses of the common periwinkle *Littorina littorea* to exposure to the toxic dinoflagellate *Alexandrium minutum*. J Molluscan Stud 81:308–311. https://doi.org/10.1093/mollus/eyu092

Neves RAF, Figueiredo GM, Valentin JL, Da Silva PM, Hégaret H (2015b) Immunological and physiological responses of the periwinkle *Littorina littorea* during and after exposure to the toxic dinoflagellate *Alexandrium minutum*. Aquat Toxicol 160:96–105. https://doi.org/10.1016/j.aquatox.2015.01.010

Neves RAF, Santiago TC, Carvalho WF, Silva ES, da Silva PM, Nascimento SM (2019) Impacts of the toxic benthic dinoflagellate *Prorocentrum lima* on the brown mussel *Perna perna*: Shell-valve closure response, immunology, and histopathology. Mar Environ Res 146:35–45. https://doi.org/10.1016/j.marenvres.2019.03.006

Neves RAF, Naveira C, Miyahira IC, Portugal SGM, Krepsky N, Santos LN (2020) Are invasive species always negative to aquatic ecosystem services? The role of dark false mussel for water quality improvement in a multi-impacted urban coastal lagoon. Water Res 184:116108. https://doi.org/10.1016/j.watres.2020.116108

Nicolas J, Hoogenboom RLAP, Hendriksen PJM, Bodero M, Bovee TFH, Rietjens IMCM, Gerssen A (2017) Marine biotoxins and associated outbreaks following seafood consumption: prevention and surveillance in the 21st century. Glob Food Sec 15:11–21. https://doi.org/10.1016/j.gfs.2017.03.002

Núñez-Acuña G, Aballay AE, Hégaret H, Astuya AP, Gallardo-Escárate C (2013) Transcriptional responses of *Mytilus chilensis* exposed *in vivo* to saxitoxin (STX). J Molluscan Stud 79:323–331. https://doi.org/10.1093/mollus/eyt030

O'Mahony M (2018) Eu regulatory risk management of marine biotoxins in the marine bivalve mollusc food-chain. Toxins 10:118. https://doi.org/10.3390/toxins10030118

Oikawa H, Fujita T, Saito K, Watabe S, Satomi M, Yano Y (2004) Comparison of paralytic shellfish poisoning toxin between carnivorous crabs (*Telmessus acutidens* and *Charybdis japonica*) and their prey mussel (*Mytilus galloprovincialis*) in an inshore food chain. Toxicon 43:713–719. https://doi.org/10.1016/j.toxicon.2004.03.003

Persson A, Smith BC (2009) Consumption of *Scrippsiella lachrymosa* resting cysts by the eastern oyster (*Crassostrea virginica*). J Shellfish Res 28:221–225. https://doi.org/10.2983/035.028.0227

Persson A, Smith BC, Wikfors GH, Quilliam M (2006) Grazing on toxic *Alexandrium fundyense* resting cysts and vegetative cells by the eastern oyster (*Crassostrea virginica*). Harmful Algae 5:678–684. https://doi.org/10.1016/j.hal.2006.02.004

Persson A, Smith BC, Dixon MS, Wikfors GH (2008) The eastern mudsnail, *Ilyanassa obsoleta*, actively forages for, consumes, and digests cysts of the dinoflagellate, *Scrippsiella lachrymosa*. Malacologia 50:341–345. https://doi.org/10.4002/0076-2997-50.1-2.341

Ritchie H, Roser M (2019) Seafood Production. http://ourworldindata.org/seafood-production

Robertson A, Stirling D, Robillot C, Llewellyn L, Negri A (2004) First report of saxitoxin in octopi. Toxicon 44:765–771. https://doi.org/10.1016/j.toxicon.2004.08.015

Rolland JL, Pelletier K, Masseret E, Rieuvilleneuve F, Savar V, Santini A, Amzil Z, Laabir M (2012) Paralytic toxins accumulation and tissue expression of α-amylase and lipase genes in the pacific oyster *Crassostrea gigas* fed with the neurotoxic dinoflagellate *Alexandrium catenella*. Mar Drugs 10:2519–2534. https://doi.org/10.3390/md10112519

Rolland JL, Medhioub W, Vergnes A, Abi-Khalil C, Savar V, Abadie E, Masseret E, Amzil Z, Laabir M (2014) A feedback mechanism to control apoptosis occurs in the digestive gland of the oyster *Crassostrea gigas* exposed to the paralytic shellfish toxins producer *Alexandrium catenella*. Mar Drugs 12:5035–5054. https://doi.org/10.3390/md12095035

Rolton A, Vignier J, Soudant P, Shumway SE, Bricelj VM, Volety AK (2014) Effects of the red tide dinoflagellate, *Karenia brevis*, on early development of the eastern oyster *Crassostrea virginica* and northern quahog *Mercenaria mercenaria*. Aquat Toxicol 155:199–206. https://doi.org/10.1016/j.aquatox.2014.06.023

Rolton A, Soudant P, Vignier J, Pierce R, Henry M, Shumway SE, Bricelj VM, Volety AK (2015) Susceptibility of gametes and embryos of the eastern oyster, *Crassostrea virginica*, to *Karenia brevis* and its toxins. Toxicon 99:6–15. https://doi.org/10.1016/j.toxicon.2015.03.002

Romero-Geraldo RDJ, García-Lagunas N, Hernández-Saavedra NY (2014) Effects of *in vitro* exposure to diarrheic toxin producer *Prorocentrum lima* on gene expressions related to cell cycle

regulation and immune response in *Crassostrea gigas*. PLoS One 9: e97181. https://doi.org/10.1371/journal.pone.0097181

Roué M, Darius HT, Picot S, Ung A, Viallon J, Gaertner-Mazouni N, Sibat M, Amzil Z, Chinain M (2016) Evidence of the bioaccumulation of ciguatoxins in giant clams (*Tridacna maxima*) exposed to *Gambierdiscus* spp. cells. Harmful Algae 57:78–87. https://doi.org/10.1016/j.hal.2016.05.007

Roué M, Darius H, Ung A, Viallon J, Sibat M, Hess P, Amzil Z, Chinain M (2018) Tissue distribution and elimination of ciguatoxins in *Tridacna maxima* (Tridacnidae, Bivalvia) fed *Gambierdiscus polynesiensis*. Toxins 10:189. https://doi.org/10.3390/toxins10050189

Schramm MA, Tamanaha MS, Beirão LH, Proença LA (2006) Toxinas paralisantes em mexilhão *Perna perna* em áreas de cultivo da costa sul do Brasil: estudo de caso. Braz J Food Nutr 17:443–450

Sephton DH, Haya K, Martin JL, Legresley MM, Page FH (2007) Paralytic shellfish toxins in zooplankton, mussels, lobsters and caged Atlantic salmon, *Salmo salar*, during a bloom of *Alexandrium fundyense* off Grand Manan Island, in the Bay of Fundy. Harmful Algae 6:745–758. https://doi.org/10.1016/j.hal.2007.03.002

Shumway SE (1990) A review of the effects of algal blooms on shellfish and aquaculture. J World Aquacult Soc 21:65–104. https://doi.org/10.1111/j.1749-7345.1990.tb00529.x

Shumway SE (1995) Phycotoxin-related shellfish poisoning: bivalve molluscs are not the only vectors. Rev Fish Sci 3:1–31. https://doi.org/10.1080/10641269509388565

Shumway SE, Cucci TL (1987) The effects of the toxic dinoflagellate *Protogonyaulax tamarensis* on the feeding and behaviour of bivalve molluscs. Aquat Toxicol 10:9–27. https://doi.org/10.1016/0166-445X(87)90024-5

Shumway SE, Gainey LF Jr (1992) A review of physiological effects of toxic dinoflagellates on bivalve molluscs. In: Gittenberger E, Goud J (eds) Proceedings of Ninth International Malacological Congress. Unitas Malacologica, Leiden, pp 357–362

Shumway SE, van Egmond HP, Hurst JW, Bean LL (1995) Management of shellfish resources. In: Hallegraeff GM, Anderson DM, Cembella AD (eds) Manual of Harmful Marine Microalgae. IOC Manuals and Guides vol. 33, UNESCO, pp 436-463.

Shumway SE, Allen SM, Dee Boersma P (2003) Marine birds and harmful algal blooms: sporadic victims or under-reported events? Harmful Algae 2:1–17. https://doi.org/10.1016/S1568-9883(03)00002-7

Shumway SE, Burkholder JM, Springer J (2006) Effects of the estuarine dinoflagellate *Pfiesteria shumwayae* (Dinophyceae) on survival and grazing activity of several shellfish species. Harmful Algae 5:442–458. https://doi.org/10.1016/j.hal.2006.04.013

Silvert W, Bricelj M, Cembella A (1998) Dynamic modelling of PSP toxicity in the surfclam (*Spisula solidissima*): multicompartimental kinetics and biotransformation. In: Reguera B, Blanco J, Fernández ML, Wyatt T (eds) Harmful Algae. Xunta de Galicia and IOC of UNESCO, Santiago de Compostela, pp 437–440

Smolowitz R, Shumway SE (1997) Possible cytotoxic effects of the dinoflagellate, *Gyrodinium aureolum*, on juvenile bivalve molluscs. Aquac Int 5:291–300. https://doi.org/10.1023/A:1018355905598

Sokolova IM, Sukhotin AA, Lannig G (2011) Stress effects on metabolism and energy budgets in mollusks. In: Abele D, Vázquez-Medina JP, Zenteno-Savín T (eds) Oxidative Stress in Aquatic Ecosystems. John Wiley & Sons, Chichester, pp 261–280

Sotton BT, Guillard J, Anneville O, Maréchal M, Savichtcheva O, Domaizon I (2014) Trophic transfer of microcystins through the lake pelagic food web: evidence for the role of zooplankton as a vector in fish contamination. Sci Total Environ 466-467:152–163. https://doi.org/10.1016/j.scitotenv.2013.07.020

Soudant P, Chu FLE, Volety A (2013) Host-parasite interactions: marine bivalve molluscs and protozoan parasites, *Perkinsus* species. J Invertebr Pathol 114:196–216. https://doi.org/10.1016/j.jip.2013.06.001

Springer JJ, Shumway SE, Burkholder JM, Glasgow HB (2002) Interactions between the toxic estuarine dinoflagellate *Pfiesteria piscicida* and two species of bivalve molluscs. Mar Ecol Prog Ser 245:1–10. https://doi.org/10.3354/meps245001

Stobo LA, Lacaze JPCL, Scott AC, Petrie J, Turrell EA (2008) Surveillance of algal toxins in shellfish from Scottish waters. Toxicon 51:635–648. https://doi.org/10.1016/j.toxicon.2007.11.020

Suzuki T, Mitsuya T (2001) Comparison of dinophysistoxin-1 and esterified dinophysistoxin-1 (dinophysistoxin-3) contents in the scallop *Patinopecten yessoensis* and the mussel *Mytilus galloprovincialis*. Toxicon 39:905–908. https://doi.org/10.1016/s0041-0101(00)00205-1

Suzuki T, Ichimi K, Oshima Y, Kamiyama T (2003) Paralytic shellfish poisoning (PSP) toxin profiles and short-term detoxification kinetics in mussels *Mytilus galloprovincialis* fed with the toxic dinoflagellate *Alexandrium tamarense*. Harmful Algae 2:201–206. https://doi.org/10.1016/S1568-9883(03)00042-8

Talmage SC, Gobler CJ (2012) Effects of CO_2 and the harmful alga *Aureococcus anophagefferens* on growth and survival of oyster and scallop larvae. Mar Ecol Prog Ser 464:121–134. https://doi.org/10.3354/meps09867

Tran D, Haberkorn H, Soudant P, Ciret P, Massabuau JC (2010) Behavioral responses of *Crassostrea gigas* exposed to the harmful algae *Alexandrium minutum*. Aquaculture 298:338–345. https://doi.org/10.1016/j.aquaculture.2009.10.030

Tran D, Ciutat A, Mat A, Massabuau JC, Hégaret H, Lambert C, Le Goïc N, Soudant P (2015) The toxic dinoflagellate *Alexandrium minutum* disrupts daily rhythmic activities at gene transcription, physiological and behavioral levels in the oyster *Crassostrea gigas*. Aquat Toxicol 158:41–49. https://doi.org/10.1016/j.aquatox.2014.10.023

Turner AD, Lewis AM, Bradley K, Maskrey BH (2021) Marine invertebrate interactions with harmful algal blooms –iImplications for one health. J Invertebr Pathol:107555. https://doi.org/10.1016/j.jip.2021.107555.

Twarog BM (1974) "Immunity" to paralytic shellfish toxin in bivalve molluscs. In: Cameron AM (ed) Proceedings of the Second International Coral Reef Symposium. Great Barrier Reef Committee, Brisbane, pp 505–512

Twarog BM, Yamaguchi H (1975) Resistance to paralytic shellfish toxins in bivalve molluscs. In: Lo Cicero VR (ed) Proceedings of the First International Conference on Toxic Dinoflagellate Blooms. Mass Science and Technology Foundation, Wakefield, pp 381–393

Twarog BM, Hidaka T, Yamaguchi H (1972) Resistance to tetrodotoxin and saxitoxin in nerves of bivalve molluscs. Toxicon 10:273–278. https://doi.org/10.1016/0041-0101(72)90012-8

Vale P, Sampayo MAM (2001) Domoic acid in Portuguese shellfish and fish. Toxicon 39:893–904. https://doi.org/10.1016/S0041-0101(00)00229-4

Van Dolah FM (2000) Marine algal toxins: origins, health effects, and their increased occurrence. Environ Health Perspect 108:133–141. https://doi.org/10.1289/ehp.00108s1133

Wekell JC, Lorenzana RM, Hogan M, Barnett H (1996) Survey of paralytic shellfish poison and domoic acid in Puget Sound predatory gastropods. J Shellfish Res 15:231–236

Wells ML, Trainer VL, Smayda TJ, Karlson BSO, Trick CG, Kudela RM, Ishikawa A, Bernard S, Wulff A, Anderson DM, Cochlan WP (2015) Harmful algal blooms and climate change: learning from the past and present to forecast the future. Harmful Algae 49:68–93. https://doi.org/10.1016/j.hal.2015.07.009

Wikfors GH, Smolowitz RM (1995) Experimental and histological studies of four life-history stages of the eastern oyster, *Crassostrea virginica*, exposed to a cultured strain of the dinoflagellate *Prorocentrum minimum*. Biol Bull 188:313–328. https://doi.org/10.2307/1542308

Wohlgeschaffen GD, Mann KH, Subba Rao DV, Pocklington R (1992) Dynamics of the phycotoxin domoic acid: accumulation and excretion in two commercially important bivalves. J Appl Phycol 4:297–310. https://doi.org/10.1007/BF02185786

Xiao X, Agustí S, Pan Y, Yu Y, Li K, Wu J, Duarte CM (2019) Warming amplifies the frequency of harmful algal blooms with eutrophication in Chinese coastal waters. Environ Sci Technol 53:13031–13041. https://doi.org/10.1021/acs.est.9b03726

Yee-Duarte JA, Ceballos-Vázquez BP, Arellano-Martínez M, Camacho-Mondragón MA, Uría-Galicia E (2018) Histopathological alterations in the gonad of *Megapitaria squalida* (Mollusca: Bivalvia) inhabiting a heavy metals polluted environment. J Aquat Anim Health 30:144–154. https://doi.org/10.1002/aah.10015

Zohdi E, Abbaspour M (2019) Harmful algal blooms (red tide): a review of causes, impacts and approaches to monitoring and prediction. Int J Environ Sci Technol 16:1789–1806. https://doi.org/10.1007/s13762-018-2108-x