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Marine Toxins - A Potential Threat to Human Life

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Abstract

The development of harmful algal blooms is mainly due to the overgrowth of phytoplankton and it produces various toxins. The phytoplankton growth is also associated with transportation of encysted algae to the new environment or due to aquaculture practices. The toxins are classified into lipophilic and hydrophilic based on their solubility. The marine toxins have the ability to accumulate in fish, molluscs and crustaceans which are the basic diet for the human. The consumption of marine toxins causes severe neurological symptoms. The EU and USA has established the regulatory limits for the potential marine toxins. Hence, Continuous monitoring of algal blooms producing marine biotoxins helps in reducing potential impacts on human.

Introduction

Algal toxins are the organic molecules which are produced by a variety of algal species obtained from fresh, brackish and marine waters. Most of the human poisoning is occurred by the consumption of contaminated shellfish or fish, as well as mass killings of fish and shellfish, and the death of marine animals and birds. The human poisoning is mainly caused by the marine neurotoxins which have specific effects on the nervous system of animals, including humans, by interfering with nerve impulse transmission.

Different Types of Marine Toxins

The marine toxins are classified into various types based on both chemical structure and mechanism of action and they produce very distinct biological effects. The toxins can be grouped according to their polarity, lipophilic and hydrophilic nature. Hydrophilic toxins include Amnesic Shellfish poisoning and Paralytic shellfish poisoning whereas lipophilic toxins include Neurolytic Shellfish poisoning, Diarrhetic Shellfish poisoning, Yessotoxins, Azaspiracids and Cyclic Imines (Tamele *et al.*, 2019).

Hydrophilic Toxins

Paralytic Shellfish Poisoning (PSP)

Paralytic shellfish poisoning is produced by water-soluble tetrahydro purine toxins caused by dinoflagellates like *Alexandrium* sp., *Gymnodinium catenatum*, *Pyrodinium bahamense* and by cyanobacteria *Trichodesmium erythraeum*. These toxins are accumulated by shellfish through grazing on algae. The first PSP toxin chemically characterized is saxitoxin (STX) and it is highly carcinogenic. Tetrahydro purine compounds are divided into four groups such as carbamate (STX, neoSTX and gonyautoxins (GNTX1-4)), N-sulfo-carbamoyl (GNTX5-6, C1-4), decarbamoyl (dc-) (dcSTX, dcneoSTX,

dcGNTX1-4) and deoxydecarbamoyl (do-) (doSTX, doneoSTX and doGNTX1) components (Tamele *et al.*, 2019).

The saxitoxin has the ability to inhibit the transmission of nerve impulses by blocking voltage-gated sodium channels which is an important protein structure of cell membranes, nerves, skeletal, and cardiac muscle fibers, and cause death. Paralytic shellfish toxin intoxication causes many symptoms in human like slight tingling or numbness to complete respiratory paralysis, paresthesia, weakness, ataxia, floating or dissociative feeling, nausea, shortness of breath, dizziness, vomiting, headache, dysphagia and dysarthria (Gerssen *et al.*, 2010) whereas in fatal cases, respiratory paralysis or arrest occurs within 2-12 hours of consumption of the PSP toxins contaminated food. The EU has established a permitted level of 800 µg saxitoxin 2-HCl equivalents/kg shellfish.

Amnesic Shellfish Poisoning (ASP)

Amnesic shellfish toxins are polar cyclic amino acid toxins produced by diatoms like *Pseudo-nitzschia* sp., *Nitzschia* sp. and red algae *Chondria armata*. Domoic acid is responsible for amnesic shellfish poisoning. The most reported domoic acids analogs are of three groups. They are epi-domoic acid (epi-DA), domoic acid C5'-diastereomer and isodomoic acids. ASP toxin is a neurotoxin that binds with a high affinity to glutamate receptors and the binding leads to opening of the membrane channels which are permeable to sodium and leads to an increased sodium influx and membrane depolarization (Gerssen *et al.*, 2010). The ingestion of Amnesic shellfish toxins in humans cause nausea, vomiting, diarrhea or abdominal cramps within 24 hours and the neurological symptoms occurs after 48 hours. The EU has established a permitted level of 20 mg DA equivalents/Kg shellfish (Tamele *et al.*, 2019).

Lipophilic Toxins

Diarrheic Shellfish Poisoning

Okadaic acid is responsible for producing diarrheic shellfish poisoning (DSP). Okadaic acid (OA) and their analogs, dinophysistoxins -1, -2 and -3 (DTXs) are polyethers and produced by the dinoflagellates like *Procentrum* sp., *Dinophysis* sp. The polyethers are heat stable upto < 150 °C and the toxins are not affected by cooking procedures (Tamele *et al.*, 2019). Okadaic acid present in the toxins act as inhibitors of the serine/ threonine phosphoprotein phosphatases. The inhibition results in hyperphosphorylation of proteins which are involved in the cytoskeletal junctions as it regulates the permeability of the cell, resulting in a loss of cellular fluids. The symptoms caused by the toxins are diarrhea, nausea, vomiting, abdominal pain and tumour formation in the digestive system (Gerssen *et al.*, 2010). The EU has established a permitted level of 0.16 mg OA equivalents/Kg shellfish.

Neurotoxic Shellfish Poisoning (NSP)

Neurotoxic shellfish poisoning is called as brevetoxins. The shellfish poisoning is caused by algae species like *Karenia brevis* or *Gymnodium brevis* (Visciano *et al.*, 2010). The mechanism of the toxins leads to the opening of voltage gated sodium channels and block the excitation of neurons (Tamele *et al.*, 2019). The contamination of shellfish by brevetoxins caused by inhalation of aerosols and cause symptoms include nausea, vomiting, diarrhea, paresthesia, cramps, bronchoconstriction, paralysis occurs in 30 minutes to 3 hours. In USA, the Food and Drug Administration (FDA) established the regulatory limit is 800 µg brevetoxin equivalents/kg shellfish (Gerssen *et al.*, 2010).

Yessotoxins

Yessotoxins are sulphated polycyclic polyethers and the toxins are produced by the dinoflagellates like *Protoceratium reticulatum*, *Lingulodinium polyedrum* and *Gonyaulax spinifera* and accumulated in Shellfish (Gerssen *et al.*, 2010). YTX was first isolated from the digestive glands of Japanese scallops (*P. yessoensis*). The Structures of toxins are similar to brevetoxins and ciguatoxins. Initially the toxins are classified under Diarrheic Shellfish poisoning but the Yessotoxins does not cause diarrhea and has no association with human intoxication. Yessotoxins are less toxic compared to that of DSP toxins because the toxins have decreased mitochondrial membrane potential, cell detachment, total nucleic acid content and DNA fragmentation, plasma membrane integrity *etc.* The mechanism of Yessotoxins involved in phosphodiesterase activation, modulation of calcium migration at several levels, alteration of protein disposal and induces apoptosis within 12 hours (Tamele *et al.*, 2019). The EU has established a permitted level of 3.75 mg YTX equivalents/Kg of shellfish meat.

Ciguatoxins

Ciguatoxins are lipid-soluble cyclic polyethers structurally similar to brevetoxins. The toxins are caused by dinoflagellate *Gambierdiscus toxicus* (Visciano *et al.*, 2016) which get adheres to dead coral surfaces and bottom associated algae. Humans are exposed to toxins after consuming the carnivore fishes like grouper, red snapper, and barracuda which feed on the dinoflagellate. Ciguatoxins has the ability to elevate calcium ion concentration and activate non-selective cation channels in the cells and leads to cause neurological symptoms in human (Tamele *et al.*, 2019). The symptom occurs in human after ingestion of toxins are vomiting, diarrhea, nausea, tingling, itching, hypotension, bradycardia whereas in extreme cases, death occurs through respiratory failure in 30 minutes to 48 hours after consumption of toxin contaminated fish. The USA has established a permitted level of 0.01 µg P-CTX-1 equivalents/kg of fish.

Azaspiracid Shellfish Poisoning (AZP)

Azaspir acid is a fat-soluble nitrogen-containing polyether amino acid toxin. The poisoning is caused by consumption of mussels *Mytilus edulis* (Furey *et al.*, 2010) contaminated by the dinoflagellates like *Proto-peridinium crassipes* and *Azadinium spinosum*. Azaspir acid toxins are the potential inhibitors of Ca²⁺ channels, store-operated channels (SOC), and non-SOC channels. The consumption of AZA-contaminated shellfish results in severe acute symptoms similar to DSP toxins are nausea, vomiting, diarrhea, and stomach cramps. The EU has established a permitted level of 160 µg AZA/kg whole shellfish meat (Tamele *et al.*, 2019).

Cyclic Amines

Cyclic amines are a heterogeneous group composed of Spirolides (SPXs), *Gymnodimines* (GYMs), *Pinnatoxins* (PnTXs) and *Pteriatoxins* (PtTXs) and the toxins are produced by the dinoflagellates like *Alexandrium* sp., *Gymnodium* sp., and *Vulcanodinium rugosum*. The structure consists of imine functional group and spiro-linked ether moieties (Tamele *et al.*, 2019). These neurotoxins have the ability to inhibit the nicotinic and muscarinic acetylcholine receptors respectively in the nervous system and at the neuromuscular junction. The symptoms are not specific but it may cause gastric distress and tachycardia in humans.

Conclusion

Harmful algal blooms are responsible for the productions of marine toxins. The marine toxins get accumulated in the shellfish and affect the humans. There are several methods like biological (in-vivo and in-vitro), biochemical

and chemical methods for the detection of marine toxins and it helps to close the shellfish harvesting areas where the occurrences of harmful algal blooms are more. Further, monitoring programs are also able to mitigate the harmful effects by toxins to the human.

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