Impact of cyanobacteria toxins

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Introduction

Cyanobacteria, or also known as blue-green algae is one of the bacteria phylum. It was classified as blue-green algae because it resembles eukaryotic green algae. Cyanobacteria are photosynthetic prokaryotes which have the ability to synthesize chlorophyll a. Chlorophyll a primarily absorbs most red and blue light, which allow cyanobacteria to obtain energy. This energy was then used to synthesize carbohydrate from carbon dioxide and water. Water is used as electron donor during the photosynthesis process and produces oxygen as a byproduct. Thus, the ability of cyanobacteria underwent the process of photosynthesis leading to the evolution of oxygen as they play an important role in increasing the amount of oxygen in Earth. Besides, cyanobacteria also called blue-green algae because of its ability to form the phycobilin pigment (phycocyanin). Phycocyanin is an accessory pigment where it works in conjunction with chlorophyll a. Phycocyanin pigment is the one that give bluish colour to cyanobacteria. According to Dittmann and Wiegand (2006), the lyses of a cyanobacterial bloom leads to release of high amounts of blue pigmented. However, the colour can degrade under condition of high exposure to light and heat (Jespersen et al., 2005).

Because cyanobacteria are prokaryote, it is usually small and unicellular. Usually individual cyanobacteria are round, oval, globular or string-like in shape. However, cyanobacteria often growth in colonies and, thus are large and easily to view. These colonies are built of many layers and can form filaments, sheets or even hallow ball depend on its species and environmental condition. Cyanobacteria have been classified into five groups based on their morphologies. There are chrooccales (I), pleurocapsales (II),

oscillatoriales (III), nostacales (IV) and stigonematales (V). Group l is unicellular cyanobacteria that divide by binary fusion or budding, while group II is unicellular form that divide by multiple fission. Then, group III is filamentous colonies that reproduce by trichome breakage (Henson, 2002). However, only groups IV and V are supported by phylogenetic studies and make up the heterocystous cyanobacteria. They have the ability to fix Nitrogen such as genera of Anabaena, Nostoc, and etc.

Cyanobacteria are extremely successful organism that can adapt in any condition depend on its species. The fossil record shows their existence since 3. 5 billion years ago and it are still around. According to Hitzfeld et al. (2000), the cyanobacteria inhabitants vary from hot springs to temporary frozen ponds in Antarctica. Cyanobacteria are gram negative that has cell wall made up of peptidoglycan and lipopolysaccharide layers that surrounded by gelatinous and mucilaginous sheath. The presence of the gelatinous sheath may help in survival of cyanobacteria during extreme conditions and desiccation (Duy et al., 2000). Cyanobacteria mostly found in brackish, freshwater, rivers, lakes, ponds and some reservoirs. They commonly live in such condition to get access of water and sunlight, as they do the photosynthesis process. The high accumulation of cyanobacteria is due to nutrient enrichment (eutrophication). The eutrophication is the process of water bodies gets the excess of nutrient and this promotes extremely growth of cyanobacteria. This nutrient may come from many sources, such as fertilizers applied to agriculture, erosion of soil containing nutrients and etc. The excess of nutrient lead to massive population of cyanobacteria, include the blooms, scums, and mats and biofilms (Codd et

al., 2005). The existence of cyanobacteria bloom can reduce dissolved oxygen in water and may cause other aquatic organisms died. Alperdoorn et al. (2007) suggest that complex interaction of high concentration of nutrients, sunlight, warm temperature, turbidity, pH, conductivity, salinity, carbon availability and slow-flowing stagnant water are involved in production of blooms. Besides, the bloom of cyanobacteria is related with toxins released.

Purpose of study

The purpose of study is to analyze the type of toxins produced by bloom of cyanobacterial. Growth of cyanobacteria bloom is favored by nutrient enrichment. The increase of mass population of cyanobacteria will lead to high amount of toxin produced. Then, relate how these toxins act in order to affect humans and animals health.

Objectives of study

- Production and mode of action of cyanobacteria
- Occurrence of cyanobacterial toxins in affects humans and animals - example case
- Routes of exposure
- Diseases in Humans and Animals
- Conclusion – further work

Production and mode of action of cyanobacteria toxins

Properties of cyanobacterial toxins

There are around 150 genera with about 2000 species of cyanobacteria has been recognized, as according to the current taxonomy. However, out of them, only 40 genera have been identified to produce toxins (Hitzfeld et al.,

2000). The toxins produced by bloom of cyanobacteria are sometimes called cyanotoxins. The genera that release toxins from cyanobacteria bloom are include Microcystis, Anabaena, Anabaenopsis, Plankthothrix, Aphanizomenon, Cylindrospermopsis, Raphidiopsis and Nodularia (Codd et al., 2005). Cyanotoxins are classified into two grouped, where one is based on their modes of toxin affect the animals cells or cell system, and the other one is based on their chemical composition and structure (Codd et al., 1999). The first grouped are divided into four types, which are hepatotoxins, neurotoxins, cytotoxin and irritant toxins (Codd et al., 2005). However, the second grouped is classify into three different chemical structure which are cyclic peptides, alkaloids and lipopolysaccharides (LPS) (Sivonen & Jones 1999). The production of cyanotoxin are highly variable depends on time and an individual bloom itself. Besides, the arrangement of the genes and their expression under certain environmental condition also contribute in released the toxins.

Hepatotoxins-cyclic peptides

Hepatotoxins class has the chemical structure of cyclic peptides. These kinds of toxins are released by bloom of cyanobacteria that ranging from freshwater to oceans. Among the common hepatotoxins produced are mycrocystins and nodularins. Microcystin is first found in the early 1980 and isolated from Microcystis aeruginosa. Thus, the toxins were named as microcystin (Sivonen & Jones 1999). Then, it was identified that microcystins also have been produced from the genera of Anabaena, Microcystis, Planktothrix, Nostoc and Anabaenopsis (Hitzfeld et al., 2000). Differ from microcystins, where nodularins only produced by the genera of Nodularia

and were names as nodularins after its producer, Nodularia spumigena (Falconer 1998). Both are widespread cyanotoxins because the presence of gas vesicle that provides buoyancy. Gas vesicles enable them to float up or sink in order to get sunlight and reach the site of nutrient-rich layers (Dittmann & Wiegand 2006). Enough of nutrient and sunlight enable the cyanobacteria to undergo the photosynthesis process and lead to excess growth. Therefore, the cyanotoxins of microcystins and nodularins could be produce enormously and can disturb the ecosystems

Microcystins are difference from nodularins based on their chemical structure of cyclic peptides. The chemical structures of microcystins have been identified as cyclic heptapeptides, while nodularins has chemical structure of cyclic pentapeptides (Codd et al., 1999). Cyclic heptapeptides refer to microcystins that contain seven peptide-linked amino acids. There are five common amino acids and another two L-amino acids are varied (Park et al., 1993). The five common amino acids are D-erythro-β-methylaspartic acid, D-alanine, N-methyldehydroalanine, D-glutamate and Adda-3-amino-9-methoxy-2, 6, 8-trimethyl- 10-phenyldeca-4, 6-dienoic acid. The variable L amino acids are located at position 2 and 4. The variable of L amino acids increased the variations in microcsytins structure and so far there are about 70 structural variables have been identified (Codd et al., 2005). Besides that, demethylation of D-erythro-β-methylaspartic acid and N-methyldehydroalanine amino acids also give variation in microcystin structure. In contrast, only about 6 variant of nodularins structure have been recognized (Codd et al. 1999).

Both microcystins and nodularins only release from cyanobacteria bloom once it was lyses. These toxins are potent inhibitors of eukaryotic protein phosphotases activity (Park et al., 1993). According to Codd et al, (2005), this inhibition can change the membrane integrity and causing tumor production and liver damage. Liver is the main targeting organ in this action of toxins.

Neurotoxin-alkaloids

Neurotoxins contain the chemical structure of alkaloids. Alkaloids are chemical compound that contains any basic nitrogen atoms and produced by cyanobacteria. It cause toxic that act on nerve cell (neuron).

So far, three known families of neurotoxins are anatoxin-a, anatoxin-a(S) and saxitoxins. Anatoxin-a acts by mimic acetylcholine, while anatoxin-a(S) inhibit acetylcholinesterase. Next, saxitoxins which relatively associated with paralytic shellfish poisons (PSP) are works by block the sodium channels. These toxins have been reported found mostly in area of North America, Europe and Australia (Sivonen & Jones 1999). Devlin et al. (1977), identified anatoxins-a as a secondary amine 2-acetyl-9-azabicyclo (4-2-1)non-2-ene. Anatoxin-a is usually released by Anabaena flos-aquae, Anabaena spp, Anabaena planktonica, Oscillatoria, Aphanizomenon and Cylindrospermum (Sivonen and Jones, 1999). This toxins cause symptoms such as fasciculation, gasping and convulsion, when infection occurred in animals (Mazur et al., 2003). In contrast, Anatoxin-a(S) is guanidine methyl phosphate ester and produced by Anabaena flos-aquae and Anabaena lemmermannii (Codd et al., 2005). However, its structure still has not been recognized. Sanitoxins are group of carbonate alkaloids and about 20 of

structural variations has been recognized (Codd et al., 2005). Sanitoxins are produced by species of Anabaena, Aphanizomenon, Cylindrospermopsis, Lyngbya, Planktothrix and Trichodesmium (Carmichael et al., 2001)

Cytotoxin-alkaloids

Cylindrospermopsin is the example of cytotoxin released and has been found in tropical and subtropical water such as in lakes, rivers and water supply reservoir (Falconer 1998). According to Hitzfeld et al (2000) and Codd et al (1999), cylindrospermopsin could also be categorized as hepatotoxins because it affects liver damage. However, Codd et al (2005) and Falconer (1998) have categorized it under cytotoxin class because its action as an inhibitor of protein synthesis. This inhibition cause damage to tissue that rapidly synthesize protein such as pituitary gland, epithelia including gut lining, the pancreas, lymphoid tissue and the prostate gland, as well as the kidneys and liver (Falconer 1998). This toxin is also genotoxic, which can cause loss of chromosome and break of DNA strand (Humpage et al 2000). Cylindrospermopsin is a cyclic guanidine alkaloid and has been isolated mainly from cylindrospermopsis raciborskii and also from Aphanizomenon ovalisporum, Umezakia natans, Aphanizomenon flosaquae and Raphidiopsis curvata (Falconer and Humpage, 2006).

Irritant toxins

Irritant toxins are usually related with skin irritant (dermatoxin). Aplysiatoxin and lyngbyatoxin is alkaloid structure and both are the most toxins that cause skin irritation. Aplysiatoxin is produced by genera of Lyngbya, Oscillatoria and Schizothrix whereas Lyngbyatoxin is produced by Lyngbya (Codd et al 1999). Aplysiatoxin also is potent tumour promoters and

Lyngbyatoxin also caused severe oral and gastrointestinal inflammation (Sivonen and Jones, 1999). LPS endotoxin released by cyanobacteria is less potent than released by bacteria, such as Salmonella (Codd et al 1999). LPS is localized at outer membrane wall of cyanobacteria and contain lipid A that responsible for much of toxicity of cyanobacteria. LPS endotoxin in cyanobacteria is produced by Microcystis, Oscillatoria and Anabaena (Codd et al 1999). The signs and symptoms of this toxin are fever, rigors, headache, nausea, mild amnesia and diarrhea (Stewart et al., 2006). According to Codd et al (2005), it may contribute to inflammatory and gastrointestinal incidents.

Toxin	Chemical structure	Producer Genera	Primary targ
Hepatotoxins			
Microcystins	Cyclic heptapeptides	Microcystis, Anabaena, Planktothrix, Nostoc & Anabaenopsis	Liver
Nodularins	Cyclic pentaptides	Nodularia	Liver
Neurotoxins			
Anatoxin-a	Alkaloids	Anabaena, Oscillatoria and Aphanizomenon, Cylindrospermum & Microcystis	Nerve synaps
Anatoxin-a(s)	Alkaloids	Anabaena	Nerve synaps
Saxitoxins	Alkaloids	Aphanizomenon, Anabaena, Lyngbya &	Nerve axon

		Cylindrospermopsis	
Cytotoxins			
Cylindrospermosin	Cyclic guanidine alkaloids	Cylindrospermopsis, Aphanizomenon, Umezakia & Rhapidiopsis	Tissue damag include liver a kidney
Irritant toxins			
Lyngbyatoxin	Alkaloids	Lyngbya	Skin, GI tract
Aplysiatoxin	Alkaloids	Lyngbya, Oscillatoria & Schizothrix	Skin
Endotoxins	LPS	Microcystis, Oscillatoria & Anabaena	Potential irrit affect any ex tissues

Table 1: Updated from Codd et al. (1999) and Sivonen & Jones (1999). This shows the summaries of general features of cyanotoxins.

Occurrence of cyanobacterial toxins

The cases of cyanotoxins affect humans and animals have been reported occurred throughout the world. This include part of Europe (such as Belgium, France, Germany, UK, etc), America (at least 27 states), Middle East and Asia (such as Bangladesh, Saudi Arabia, Thailand), Australasia (such as Australia, New Zealand), Africa (Botswana, Morocco) and also Marine Atlantic Ocean (Baltic Sea, Caribbean sea) and Antarctica (McMurdo Ice Shelf) (Codd et al., 2005). From the case reported, cyanatoxins affect animals, include wild and domestic mammals, birds, amphibians and fish, while human cases ranging from acute to chronic (Hitzfeld et al., 2000).

The first case of cyanotoxins occurred in animals was the death of cattle, sheep, dogs, horses and pigs. This took placed in Lake Alexandrina, Australia in 1878. The death of these animals was due to drink the water that contains a scum of Nodularia spumigena (Francis, 1878) . After this case, numerous cases have been reported and most commonly involved death of farm animals after drinking the contaminated water with cyanobacterial bloom (Hitzfeld et al., 2000). For example, in 1991 the death of sheep has been recorded in Darling River, Australia. This death occurred after drinking from a farm dam contaminated with saxitoxins, released by Anabaena circinalis (Goodman et al., 1999). Besides, the cases of dog deaths after swimming in, or eating, cyanobacteria also occurred. In 1992, death of dogs at Loch Insh, Scotland happened after swimming was due to release of Anatoxin-a by Oscillatoria sp. into the water (Edwards et al., 1992).

Among the earliest reported cases involving acute effect in humans was a series of town along the Ohio River, US in 1931. It start when the water of a side branch of the river develop a cyanobacteria bloom because of low rainfall. This water was then washed into the main river and caused a series of gastroenteritis once it moves downstream (Tisdale 1931). However, the toxins caused this outbreak is unknown and the organism that released this toxins was unspecified. Then, another case involving the same diseased, (gastroenteritis) was reported in Harare, Zimbabwe in 1966. This time Microcystis aeruginosa was the one that has been identified responsible in this case, but the toxins released was still not known (Hitzfeld et al., 2000). Children living in this area developed gastroenteritis each year as they use

the water reservoir which contains a natural bloom of Microcystis (Zilberg 1966).

The case of chronic effects in humans may be present due to short exposure to toxins (Goodman et al., 1999). The incidence in China, 1995 due to microcystins have lead to chronic of liver injury, hepatocellular carcinoma. This is primary cancer of the liver and most are secondary to hepatitis B infection. From the case analyzed, cyanobacteria are abundant in surface waters of south east China, where the incidence of hepatocellular carcinoma is highest. Thus, it has been concluded that microcystins in the drinking water are responsible for the increased of liver cancer (Falconer 1998).

Compare to all cyanotoxins, cyclic peptides (mostly microcystins) has high risk because of their potential to develop diseases in long term time, even when exposed to low concentration of cyanotoxins. This was confirmed after examined all the cases reported, where the major injury is hepatotoxicosis, cause liver damage. In contrast, neurotoxin mostly shows acute effect in mammals (Goddman et al., 1999).

Routes of exposure

There are many ways where humans and animals can be exposed to cyanotoxins. From the cases reported, animals usually infected by cyanotoxins orally via drinking contaminated water. For instance, the case reported of cattle deaths in Alpine Lakes, Switzerland (1974-1994). The cattle died because of liver damage after drinking the water which contains bloom of cyanobacteria (Hitzfeld et al., 2000). Besides, human can get infection of cyanotoxins during the recreational activity involving direct

contact with water such as swimming, canoeing and paddling (Apeldoorn et al., 2007). In 1989, UK, some of army recruits showed symptoms of infected by cyanotoxins after swimming and canoes training in water with dense bloom of Mocrocystis. The signs of symptoms were vomiting, diarrhea, blistering of the lips, sore throat and central abdominal pain (Turner et al., 1990). The person that worked in the area of water such as boatmen and environmental scientists are also easily to get infection. According to Dittmann and Wiegand (2006), the consumption of blue green algae containing food and dietary supplements, such as pills or capsules, also can lead to gain the toxicity of cyanobacteria.

According to Codd et al (1999), there are four routes of exposure where human can get infection of cyanotoxins (Table 2). The first one is via oral routes, taken by ingestion during recreational activity, drinking water, food and dietary supplements that contain dried cyanotoxins. The oral route has caused the outbreak of many diseased, such as gastroenteritis and hepatoenteritis after drinking water (Codd et al 1999). Infection by pulmonary route occurs either by inhalation of cyanobacteria bloom during recreational activity or work practices in industrial spray water (Codd et al., 1999). Next, dermal route is associated with skin or mucosal contact the contaminated water. This can lead to skin irritation and allergic reaction. Lastly, haemodialysis route can occurred via water used in haemodialysis treatment. Among the cases of this route, is the case of major fatal incident at haemodialysis clinic in Caruaru, Brazil. This case happened in 1996, where the patients with dialysis treatment were treated with water from local reservoir. All patients experienced symptoms of nausea, vomiting, muscle

weakness and painful hepatomegaly. Then, these patients developed acute liver failure and acute neurotoxicity signs. From all the treated patients, 60 have been recorded as dead. Microcystins released by Aphanizomenon and Oscillatoria have been recognized as the toxins that responsible for this death (Codd et al., 1999).

Exposure route Exposure medium

Oral (ingestion) drinking water, recreational water, food (shellfish, finfish if toxin if toxin accumulation

has occurred during production), dietary supplements (pills, capsules) if contains dried

cyanobacterial cells with toxins.

Pulmonary

(inhalation, aspiration) water: aerosols, spray during recreation, work, showering

Dermal water during recreation, work, showering

(skin, mucosal contact)

Haemodialysis water used for haemodialysis

Table 2: Taken from Codd et al., 2005. This figure summaries the human exposure route and exposure medium for cyanotoxins.

Diseases in Animals and Humans

Hepatoenteritis – Liver damage

Hepatoenteritis is described as hepatitis-like illness, where associated with liver problem. This diseased can infect both human and animals. The outbreak of hepatoenteritis disease was reported in 1979 and occurred in Palm Island of the Queensland, Australia. Thus, this case also name as " Palm Island Mystery Disease" because the water drinking is supply from Palm Island reservoir (Ohtani et al., 1992). Investigation have shown that the reservoir contain the bloom of Cylindrospermopsis raciborskii. This species released cylindrospermopsin and responsible for developed of severe hepatoenteritis among the 140 children and 10 adults. The common symptoms of this disease are malaise, anorexia, vomiting, painful liver enlargement, dehydration and bloody diarrhea. This toxin is very water soluble and infect into body by oral route via drinking water. According to Falconer and Humpage (2006), the mechanism of action for cylindrospermopsin is relatively slow. It work by inhibit protein synthesis at ribosome during the peptide chain elongation step. Besides, the toxins also released CYP450 oxidation that work to inhibit the glutathione synthesis. Both inhibitions caused major changes in liver, particularly hepatocytes. First, accumulation of ribosomes in the cytoplasm of hepatocytes and followed by membrane proliferation. Next, the accumulation of lipid in the central portion of hepatic lobules and all this lead to severe liver necrosis (Duy et al., 2000). Kidney, lung, heart, spleen and thymus also might be affects.

The toxins of microcystins are majorly involved in liver damage. Most of microcystins types are hydrophilic and thus, not able to penetrate vertebrate

cell membrane. It only can uptake into cell membrane via transporter. Once the microcystins are uptake by mammals, it is transport into the blood from the ileum via bile acid type transporter, that present in hepatocytes (Apeldoorn et al 2007). As a result, the present of microcystins is higher in liver due to active uptake by hepatocytes. Once inside the hepatocytes, microcystins act as potent inhibitor of eukaryotic protein phosphatases 1 and 2A. These inhibitions cause changes in cytoskeletal proteins, and thus results in deformation of hepatocytes. The liver may undergo changes in term of a disruption of hepatocytes structure due to damage of cytoskeleton, loss of sinusoidal structure, increased in liver weight because of intrahepatic haemorrhage, heart failure and death.

Gastroenteritis

Gastroenteritis is inflammation of the gastrointestinal tract, where involved stomach and intestine. This diseased can be cause by infection from cyanobacteria bloom of Microcystis sp and Anabaena sp. Acording to Hitzfeld et al (2000), the cases of gastroenteritis that have been recorded due to cyanobacteria bloom were occured in Ohio River, US (1931), Harare, Zimbabwe (1966) and Itaparica Dam, Brazil (1993). However, the toxins that responsible for this diseased still remain unknown because lack of available toxin analysis method and knowledge of candidate toxins at the time (Codd et al., 1999).

Recently, there is case where LPS endotoxin is responsible for gastroenteritis incidents (Codd et al., 2005). Gastroenteritis is categorized under acute effect and mostly results in diarrhea. Besides, the symptoms shows are nausea and vomiting, loss of appetite, fever, headaches and abnormal pain.

Respiratory problem

Neurotoxins effects can lead to progressive paralysis and death because of respiratory failure. The case of livestock death in Europe and the US have been reported due to anatoxin-a, released from the genera of Oscillatoria, Aphanizomenon and Anabaena (Falconer, 1998). Anatoxin-a acts as a potent postsynaptic depolarizing neuromuscular blocking agent, where it binds to neuronal nicotinic acetylcholine receptors of neuromuscular junction (Goodman et al., 1999) . This cause postsynaptic sodium channel of neuron is remain open and lead to continuous stimulation of sodium ion influx and continuously generates action potential. Consequently, the muscle contraction is over react and might be followed by fatigue and respiratory failure (Dittmann and Wiegand, 2006). This toxin can cause rapidly death depending on the species and amount of toxin ingested. The clinical sign of this infection are muscle fasciculation, decreased movement, abdominal breathing, cyanosis, and death by respiratory failure. Saxitoxins are another type of neurotoxins that can infect both human and animals. As mention before, the case of Darling River in Australia (1990-1991) involved the deaths of sheep and cattle due to saxitoxins. Then, in human, saxitoxins have been the cause of paralytic shellfish poisoning (PSP). Saxitoxins acts as a blocking agent of sodium channel in nerve axons. In mammals, this induces muscle paralyzed (respiratory muscle) and can follow by death due to respiratory failure (Apeldoorn et al., 2007).

Skin irritation and allergic

Lyngbya majuscula is one of the cyanobacteria that released aplysiatoxin and lyngbyatoxin. These toxins act as potent skin tumour promoters. Both toxins, especially aplysiatoxin, cause skin irritation after contact with bloom

of Lyngbya majuscula. Swimmers of Hawaii and Okinawa got acute dermatitis (causing itch), erythematous wheals and desquamation after contact with Lyngbya majuscule (Codd et al., 1999). Besides, symptoms have included rashes, blisters, allergic reaction, asthma, conjunctivitis, and eye irritation.

Conclusion

The development of cyanobacterial bloom tends to be favored by nutrient enrichment (eutrophication). Therefore, enough nutrients will provide extremely growth of cyanobacteria bloom and thus, lead to high production of cyanotoxins once it is lyses. The most clearly study of toxins is microcystins due to widespread of its production among the cyanobacteria blooms. Besides, their existences that usually can be found in lakes, rivers and water supply reservoirs also lead to increased the chance to affect humans and animals health compare to the other toxins. As mention above, there are four routes where infection of cyanotoxins could occurs, which are by oral route, dermal route, pulmonary route and lastly via haemodialysis route. Once the toxins get inside humans and animals, they will start reacts and disturb the system inside the body according to its modes of actions. Therefore, it leads to outbreak of many diseased such as hepatoenteritis, gastroenteritis, respiratory problem and skin irritation and allergic.

However, till now there are some mechanism of toxins that still not understood, such as lyngbyatoxins (Goodman et al., 1999). Then, further work also need to be done in order to solve the cases of unknown toxic affect humans and animals that have been recorded. For example, the case of the outbreak of gastroenteritis diseased occurred in Ohio River, US (1931),

Harare, Zimbabwe (1966) and Itaparica, Dam, Brazil (1993), where no actual toxins have been identified (Hitzfeld et al., 2000). All the features of cyanobacterial cell include their type of the toxins released and their mode of action is needed to understand clearly, in order to monitor and control their growth from continuously affect humans and animals. Thus, guidelines and regulatory standard could be developed to increased awareness of actual and potential of cyanotoxins.

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