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Global geographical and historical overview of cyanotoxin distribution and cyanobacterial poisonings

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Abstract

Cyanobacteria are photoautotrophic organisms which occur in aquatic and terrestrial environments. They have the potential to produce toxins which pose a threat to human and animal health. This review covers the global distribution of the common cyanotoxins and related poisoning cases. A total of 468 selected articles on toxic cyanobacteria, dating from the earliest records until 2018, were reviewed. Most of the articles were published after 2000 (72%; 337 out of 468), which is consistent with the recent growth in interest in the analysis, toxinology and ecotoxicology of cyanotoxins. Animal and/or human poisoning cases were described in more than a third of the overall publications (38%; 177 out of 468). The reviewed publications showed that there were 1118 recorded identifications of major cyanotoxins in 869 freshwater ecosystems from 66 countries throughout the world. Microcystins were the most often recorded cyanotoxins worldwide (63%; 699 out of 1118), followed by cylindrospermopsin (10%; 107 out of 1118), anatoxins (9%; 100 out of 1118), and saxitoxins (8%; 93 out of 1118). Nodularins were the most rarely recorded cyanotoxins (2%; 19 out of 1118); however, there were also reports where cyanotoxins were not analysed or specified (9%; 100 out of 1118). The most commonly found toxic cyanobacterial genera were *Microcystis* spp. (669 reports), *Anabaena* spp. (397 reports), *Aphanizomenon* spp. (100 reports), *Planktothrix* spp. (98 reports), and *Oscillatoria* spp. (75 reports). Furthermore, there were 183 recorded cyanotoxin poisonings of humans and/or animals. Out of all toxic cyanobacterial blooms reviewed in this paper, the highest percentage of associated poisonings was found in North and Central America (39%; 69 cases out of 179), then Europe (20%; 35 out of 179), Australia including New Zealand (15%; 27 out of 179), and Africa (11%; 20 out of 179), while the lowest percentage was related to Asia (8%; 14 cases out of 179) and South America (8%; 14 cases out of 179). Events where only animals were known to have been affected were 63% (114 out of 182), whereas 32% (58 out of 182) of the investigated events involved only humans. A historical overview of human and animal poisoning episodes associated with cyanobacterial blooms is presented. Further, geographical data on the occurrence of cyanotoxins and related poisonings based on the available literature are shown. Some countries (mainly European) have done very intensive research on the occurrence of toxic cyanobacteria and cyanotoxins, and reported related ecotoxicological observations, while in some countries the lack of data is apparent. The true global extent of cyanotoxins and associated poisonings is likely to be greater than found in the available literature, and it can be assumed that ecotoxicological and hygienic problems caused by toxic cyanobacteria may occur in more environments.

Keywords Cyanobacteria · Cyanotoxins · Poisoning · Health · Geographical distribution

Abbreviations

ATX-a Anatoxin-a
ATX-a(S) Anatoxin-a(S)

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BMAA	β-N-Methylamino-L-alanine
CYN	Cylindrospermopsin
HomoATXa	Homoanatoxin-a
MC	Microcystin
MC-LR	Microcystin-LR
NOD	Nodularin
NSTX	Neosaxitoxin
PLC	Primary liver cancer
STX	Saxitoxin

Extended author information available on the last page of the article

LC–MS/MS	Liquid chromatography with tandem mass spectrometric detection methods
LPS	Lipopolysaccharides
WHO	World Health Organization
N/A	Toxic cyanobacterial metabolites not analysed
ND	Not determined
N/S	Not stated
UR	Unknown reasons (group of cyanotoxins was not specified)

Introduction

Cyanobacteria are a group of ubiquitous prokaryotes which developed the Earth's aerobic biosphere via oxygenic photosynthesis (Yadav et al. 2011; Cardona et al. 2018). They are common inhabitants of freshwater lakes, rivers and reservoirs, and marine environments, as well as the illuminated surfaces of rocks and soils throughout the world. Cyanobacteria are able to tolerate extreme changes in salinity, temperature, desiccation and irradiance, which give them an extraordinary competitive advantage in these ecosystems (Chorus and Bartram 1999; Dantas et al. 2011; Whitton 2012). Furthermore, due to their ability to produce a diverse range of secondary metabolites (e.g. UV-protective pigments: scytonemin and mycosporine-like amino acids), this prokaryotic group successfully survives in extreme environmental conditions. Under favourable environmental conditions, cyanobacteria can attain high population densities in waterbodies (blooms), and may form visible scums on water surfaces (especially in eutrophic surface waters) and mats in shallow waters and along waterbody margins (Fogg et al. 1973; Codd 1995; Chorus and Bartram 1999; Whitton 2012; Huisman et al. 2018). In recent years, the increased anthropogenic eutrophication of water ecosystems has led to accelerated growth of cyanobacteria (Bláha et al. 2009). Moreover, consequences of global climate change are contributing to increases in the size, growth periods and spread of cyanobacterial populations (Codd et al. 2005a; Bláhová et al. 2008; Bláha et al. 2009; Huisman et al. 2018).

The colours, odours and associations with animal intoxications (mammals, birds, fish) of cyanobacterial scums, blooms and mats have undoubtedly brought these microbes to human notice throughout history. Anecdotal references, long before the advent of microscopy, clearly allude to cyanobacterial (and perhaps microalgal) mass populations in waterbodies. Traditional folk awareness of blooms is apparent in Canada and Australia from before European colonization (Codd et al. 2005b). In early Europe, the Roman naturalist, and military commander, Pliny the Elder, referred to apparent blooms in the River Dnieper in 77CE (Griffiths 1938). The aptly named “*Monasterium Viridis Stagnae*” in

the twelfth century, alongside Souleseat Loch in Scotland, appears to refer to blooms and scums (Codd 1996) and William Shakespeare may have assumed that his English audiences would be familiar in the 1590s with his allusion to pond scum in his play, *The Merchant of Venice* (Fogg et al. 1973). The occurrence of windblown summer scums in the Tuchomskie Lake, northern Poland, was reported by Kirkby (1672), which are likely to have been of buoyant cyanobacteria (Codd et al. 2015a). The continuing folk awareness of annual, episodic cyanobacterial bloom and scum phenomena is clearly apparent in the recognition of the “breaking of the meres” among communities around lakes (meres) in the northwest of England (Griffiths 1938). Thereafter, through time and space, there have been numerous described appearances of cyanobacterial scums and blooms. Eventually, people began to record and learn about the negative consequences of cyanobacteria and their metabolites.

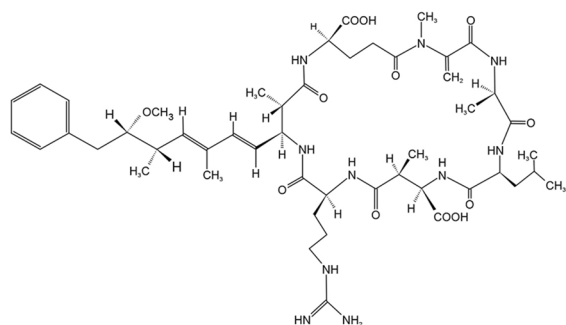
Cyanobacterial secondary metabolites exhibit various types of biological activities, and some of them have been identified as potent toxins: cyanotoxins (Fig. 1). Cyanotoxins can cause adverse effects on humans, terrestrial animals, aquatic organisms, as well as on the environment (Codd et al. 1999; Sivonen and Jones 1999; Metcalf and Codd 2012; Janssen 2019). They are recognized as one of the most lethal groups of biotoxins known, presenting high risks of illness and mortality (Chorus and Bartram 1999; Codd et al. 2005a).

A practice of classifying cyanobacterial mass populations as “toxic” or “non-toxic” has been developed without necessarily defining what is being meant by these terms. Since the toxicity of cyanobacterial components depends upon the presence and abundance of the substance(s) in question, the dose, exposure route and the target organism(s), it is necessary to specify these conditions when considering whether particular cyanobacterial compounds or blooms are “toxic” or “non-toxic” (Codd and Metcalf 2014). It should thus be borne in mind that most of the early surveys of cyanobacterial bloom and strain toxicity were determined by mouse intraperitoneal (i.p.) bioassay, and later by chemical analysis for the most commonly sought cyanotoxins, microcystins, with fewer analyses for, e.g. nodularins, anatoxins, saxitoxins and cylindrospermopsins (Carmichael 2001, 2008; Codd et al. 2005a). With the toxicity of cyanobacterial blooms and strains being defined as lethality by i.p. mouse bioassay, early surveys indicated an incidence of 25–75% (National Rivers Authority 1990; Codd 1995; Chorus 2001).

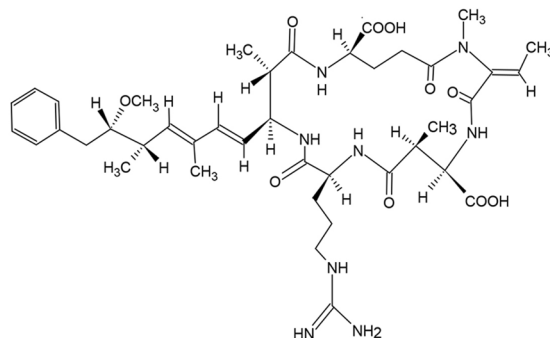
With reference to specific cyanotoxins, it is well established that differences exist between individual strains within species, between species in the same genus, and between genera: some biosynthesizing specific cyanotoxins, e.g. microcystins, and others not. With the exception of a structural role of the cyanobacterial lipopolysaccharide endotoxins as cell outer membrane components (Monteiro

HEPATOTOXINS

Microcystin-LR

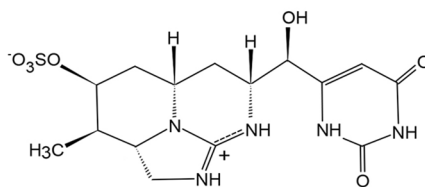


Nodularin



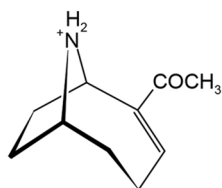
CYTOTOXIN AND GENOTOXIN

Cylindrospermopsin

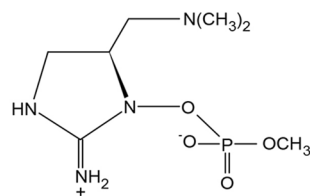


NEUROTOXINS

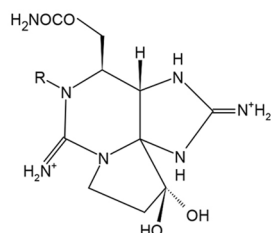
Anatoxin-a



Anatoxin-a(S)



Saxitoxins



saxitoxin: R = H
neossaxitoxin: R = OH

Fig. 1 Examples of molecular structures of commonly recognized cyanotoxins

et al. 2017), the natural functions of cyanotoxins remain to be fully understood. It seems likely that no shared function can account for the biosynthesis of all of the remaining cyanotoxins and it is possible that multiple functions may account for the biosynthesis of a specific cyanotoxin (Codd et al. 2005b). One reason for the biosynthesis of cyanotoxins may be an adaptation that allows cyanobacteria in resource-limiting environments to ameliorate competition with other phototrophs and inhibit their growth (Arnold 1971; Smayda 1974; Gross et al. 1991), and also that of heterotrophic bacteria (Flores and Wolk 1986), and fungi (Patterson and Bolis 1997). Recent data suggest that in addition to conferring competitive advantage, some cyanotoxins may have roles as cyanobacterial physiological aides (e.g. in assisting nutrient uptake, iron scavenging, in protection against oxidative stress and/or in carbon–nitrogen metabolism, the maintenance of homeostasis and other roles as info-chemicals) (Holland and Kinner 2013; Makower et al. 2015).

Based on toxicological target(s) and chemical structures, cyanotoxins can be classified into several main groups (Table 1) (Sivonen and Jones 1999; Metcalf and Codd 2012; Corbel et al. 2014; Sanchez et al. 2014). The hepatotoxins include small cyclic peptides (microcystins and nodularins), and the cytotoxins include alkaloids (e.g. cylindrospermopsins). There are several groups of cyanobacterial neurotoxins, classified according to structure: alkaloids (anatoxin-a, homoanatoxin-a and saxitoxins), non-proteinogenic amino acids, e.g. BMAA, and the phosphate ester, anatoxin-a(S). One of the most studied mechanisms of cyanotoxin hepatotoxicity is the inhibition of serine/threonine protein phosphatases, which affects the regulation of cellular protein hyperphosphorylation (Yoshizawa et al. 1990; Mackintosh et al. 1990). Mechanisms of neurotoxicity include neuromuscular blockade (Codd et al. 1997; Funari and Testai 2008), anti-acetylcholinesterase activity, anti-phosphatase activity, postsynaptic cholinergic agonist activity (Metcalf and Codd 2004) and protein kinase C activators (Fujiki et al. 1990).

Illnesses associated with exposure to cyanotoxin-producing cyanobacterial blooms in recreational and drinking waters tend to have a range of symptoms including abdominal pain, vomiting, diarrhoea, weakness, severe oral and gastrointestinal inflammation, irritation of skin and mucous membrane of the eyes, nose and throat, asthma-like symptoms, muscle tremors, nausea, tingling in fingertips and toes, blurred vision, headache, dizziness, fever, hypoxia, cyanosis, paralysis and respiratory or cardiac arrest, potentially resulting in death (Moore 1984, 1996; Chorus and Bartram 1999; Metcalf and Codd 2012). Such effects can occur within minutes to days after exposure, depending on the types and concentration of cyanotoxins, exposure route(s), body weight and age of the affected persons.

Chronic exposure to cyanotoxins may present one of the factors responsible for carcinogenesis development. The

results of some epidemiological and experimental studies suggest that cyanobacterial blooms, associated with other risk factors, may cause a higher incidence of some cancers (primary liver cancer, brain cancer, heart, mediastinum and pleural cancer, kidney cancer, ovarian cancer, testicular cancer, gastric cancer, colorectal cancer, retroperitoneal and peritoneal cancer, leukaemia, and malignant skin melanoma) (Yu 1995; Ueno et al. 1996; Zhou et al. 2002; Fleming et al. 2002; Milutinović et al. 2006; Žegura et al. 2008; Li et al. 2009; Svirčev et al. 2014a). Long-term exposure to some amounts of cyanotoxins may be causally linked to neurodegenerative diseases in humans (Cox et al. 2003; Lobner et al. 2007; Holtcamp 2012; Delcourt et al. 2018) including amyotrophic lateral sclerosis–Parkinsonism–dementia complex (ALS/PDC) although further research is needed to verify this. In addition to the impact on animals and humans, cyanotoxins can also exert harmful effects on other biota including invertebrates (e.g. Blom et al. 2006; Metcalf et al. 2012) and plants, such as leaf necrosis, inhibition of photosynthesis and growth, and oxidative stress (Kós et al. 1995; Kurki-Helasma and Meriluoto 1998; McElhiney et al. 2001; M-Hamvas et al. 2003; Drobac et al. 2017).

The aim of this review is to collect and summarize the available, detailed data on the occurrence of cyanotoxins throughout the world and on the human and animal poisonings associated with particular cyanotoxins. This was achieved through (1) analyses and evaluation of available literature from refereed international journals, conference, technical- and situation-assessment reports; (2) a review of the distribution of well-known cyanotoxins: microcystins (MC), nodularins (NOD), cylindrospermopsins (CYN), anatoxins (ATX) and saxitoxins (STX), throughout the continents; (3) summary of the human and animal poisonings attributed to cyanotoxin exposure via drinking water supplies, water-based recreational activities and haemodialysis; (4) interpretation of the findings; and (5) making conclusions and recommendations concerning the need for future research.

Description of workflow and classification of publications

An extensive literature review was performed to investigate the presence of the most commonly found cyanotoxins in various freshwater ecosystems worldwide, as well as numerous cases of associated human and animal poisonings. To achieve this goal, the first step was to examine a wide range of environmental and other scientific literature via the Scopus database which includes PubMed, Web of Science and Science Direct. Searches were performed using the following key words: “cyanotoxin”, “microcystin”, “nodularin”, “cylindrospermopsin”, “anatoxin”, “saxitoxin”, and

Table 1 Principle classes of cyanotoxins with summaries of modes of action, health effects, cyanobacterial producers and toxicities to mice

Toxins/structure (number of known analogs)	Mechanism of action and target organ	Health effects	Examples of toxicogenic genera/species	LD ₅₀ (i.p. mouse, µg/kg b.w.)	LD ₅₀ (oral, µg/kg b.w.)	References
Hepatotoxins						
Microcystins/cyclic heptapeptides (~250)	Irreversible inhibition of protein phosphatases (PP1, PP2A, PPP4, PPP5), membrane integ- rity and conductance disruption; primary site of action: liver (also affect other tissues— kidney, reproductive tissue, colon, brain)	Nausea; vomiting; diar- rhoea; renal damage; hepatotoxic; tumour promoters; death (in some cases)/immediate up to 24 h	<i>Microcystis</i> , <i>Anabaena</i> , <i>Nostoc</i> , <i>Planktothrix</i> , <i>Anabaenopsis</i> , <i>Aphano- capsa</i> , <i>Hapalosiphon</i> , <i>Aphanizomenon</i> , <i>Meris- mopedia</i> , <i>Oscillatoria</i> , <i>Phormidium</i> , <i>Syn- echococcus</i> , <i>Snowella</i> , <i>Arthrospira</i> , <i>Pleurocap- salean</i> , <i>Gloeotrichia</i> , <i>Fischerella</i> , <i>Radiocys- tis</i> , <i>Woronichinia</i>	MC-LR-50; MC-LA-50; MC-YR-70; MC-RR- 300-600; ([6Z]-Adda] MC-RR)-1000	MC-LR-5000 (Cr1:CD-1(ICR) BR mice); 10,900 (Balb/c mice); > 5000 (rats)	Rinehart et al. (1988), Sivonen et al. (1992), Fawell et al. (1994), Yoshida et al. (1997), Mahakhan- t et al. (1998), dos Vieira et al. (2003), Ballot (2004), Botha et al. (2004), Ballot et al. (2005), Carey et al. (2007), Fiore et al. (2009), Chen et al. (2015), Spoof and Catherine (2017)
Nodularins/cyclic pentapeptides (10)	Inhibition of protein phosphatases (PP1 and PP2A); primary site of action: liver	Hepatotoxic; tumour pro- moters; carcinogenic	<i>Nodularia</i> , <i>Nostoc</i>	30–60	ND	Sivonen et al. (1989), Resson et al. (1994), Carmichael and Boyer (2016), Spoof and Catherine (2017)
Cytotoxins						
Cylindrosper- mopsins/guanidine alkaloids (3)	Irreversible inhibitor of protein biosynthesis, genotoxicity; primary site of action: liver (also to kidneys, spleen, lungs, heart, intestine, thymus, skin)	Nausea; vomiting; bloody diarrhoea; kidney damage; headache; dehydration; genotoxic/ up to a week	<i>Cylindrospermopsis</i> , <i>Anabaena</i> , <i>Aphani- zomenon</i> (<i>ovalisporum</i>), <i>Raphidiopsis</i> (<i>curvata</i>), <i>Umezakia</i> (<i>natans</i>), <i>Oscillatoria</i> , <i>Sphaero- spermopsis</i> , <i>Lyngbya</i> (<i>wallei</i>), <i>Chrysochlorum</i> (<i>bergii</i>), <i>Anabaena</i> (<i>lappinica</i>)	200 (6 days)–2100 (24 h)	4400–6900 (2–6 days)	Ohtani et al. (1992), Li et al. (2001), Schembri et al. (2001), Svreck and Smith (2004), Spoof et al. (2006), Seifert et al. (2007)
Neurotoxins						
Anatoxin-a/alkaloids (8)	Postsynaptic, depolar- izing neuromuscu- lar blockers, bind irreversibly to nicotinic acetylcholine receptors; primary site of action: nerve synapse	Tingling in fingers and toes; dizziness; convul- sions; paralysis; muscle fasciculation; gasping; death (in some cases)/ immediate up to 1–2 h	<i>Aphanizomenon</i> , <i>Ana- baena</i> , <i>Raphidiopsis</i> , <i>Microcystis</i> , <i>Oscil- latoria</i> , <i>Planktothrix</i> , <i>Cylindrospermum</i> , <i>Arthrospira</i> , <i>Tychonema</i> (<i>bourrellyi</i>)	200–375	>5000	Devlin et al. (1977), Carmichael and Gorham (1978), Sivonen et al. (1989), Fawell and James (1994), Fitzgeorge et al. (1994), Resson et al. (1994), Sivonen and Jones (1999), Ballot (2004), Ballot et al. (2005), Van Apeldoorn et al. (2007), Shams et al. (2015), Car- michael and Boyer (2016)

Table 1 (continued)

Toxins/structure (number of known analogs)	Mechanism of action and target organ	Health effects	Examples of toxicogenic genera/species	LD ₅₀ (i.p. mouse, µg/kg b.w.)	LD ₅₀ (oral, µg/kg b.w.)	References
Homoanatoxin-a/alkaloids (1)	Similar to anatoxin-a, causes potent neuromuscular blockade; primary site of action: nerve synapse	Staggering; gasping; muscle fasciculation; convulsions; coma; cyanosis; hyper salivation; death	<i>Phormidium (Oscillatoria) formosa</i> , <i>Raphidiopsis mediterranea</i>	250–330	ND	Skulberg et al. (1992), Ressom et al. (1994), Codd et al. (1997), Namikoshi et al. (2003)
Anatoxin-a(S)/guanidine methyl phosphate ester (1)	Irreversibly inhibits acetylcholinesterase, nerve hyper-excitability; primary site of action: peripheral nervous system	Hyper salivation; diarrhoea; paralysis; asphyxiation; decreased movement; exaggerated abdominal breathing; cyanosis; convulsions; and ultimately death. Survival time of 10–30 min	<i>Anabaena lemmermannii</i> , <i>A. flos-aquae</i> , <i>A. spiroides</i>	20–40	ND	Mahmood and Carmichael (1987), Matsunaga et al. (1989), Carmichael et al. (1990), Stewart (2004), Van Apeldoorn et al. (2007), Aráoz et al. (2010)
Saxitoxins/carbamate alkaloids (56)	Bind and block sodium channels inhibiting nerve axon conduction; primary site of action: nerve axons	Numbness around mouth; spreading to arms and hands; respiratory muscle paralysis; difficulty breathing; death/immediate up to 24 h	<i>Aphanizomenon (gracile)</i> , <i>Lyngbya (wollet)</i> , <i>D. (circinale)</i> , <i>Planktoniopsis</i> , <i>Phormidium uncinatum</i> , <i>Scytonema</i> , <i>Geitlerinema</i> spp., <i>Raphidiopsis (brookii)</i> , <i>Cuspidolthrix (issatschenkoi)</i> , <i>Cylindropspermopsis (raciborskii)</i>	5–30	263	Carmichael (1992), Humpage et al. (1994), Mons et al. (1998), Beltran and Neilan (2000), WHO (2003), Pearson et al. (2010), Wiese et al. (2010), Borges et al. (2015), Cirés and Ballot (2016)
Dermatotoxins (irritants)						
Lyngbyatoxin/modified cyclic dipeptide (3)	Protein kinase C activators; primary site of action: skin, gastrointestinal tract	Inflammatory agents; dermatitis; necrosis; blisters; dermatotoxins; tumor promoters	<i>Lyngbya</i> , <i>Schizotrix</i> , <i>Oscillatoria</i>	250 µg/kg (LD ₁₀₀)	ND	Fujiki et al. (1983), Moore (1984, 1996), Ito et al. (2002), Jiang et al. (2014), Carmichael and Boyer (2016)
Aplysiatoxin/phe-nolic bislactones (> 2)	Protein kinase C activators; primary site of action: skin	Inflammatory agents; dermatitis; necrosis; blisters; dermatotoxins; tumor promoters	<i>Lyngbya</i> , <i>Schizotrix</i> , <i>Oscillatoria</i>	300	ND	Fujiki et al. (1983), Moore (1984), Ito et al. (2002)
Debromoaplysiatoxin/phenolic bislactones	Inflammatory toxins operate through mechanisms similar to those of phorbol esters; primary site of action: skin	Inflammatory agents; dermatitis; blisters and necrosis in mammals	<i>Lyngbya</i> , <i>Schizotrix</i> , <i>Oscillatoria</i>	107–117 µg/kg	ND	Moore et al. (1984), Carmichael and Boyer (2016)

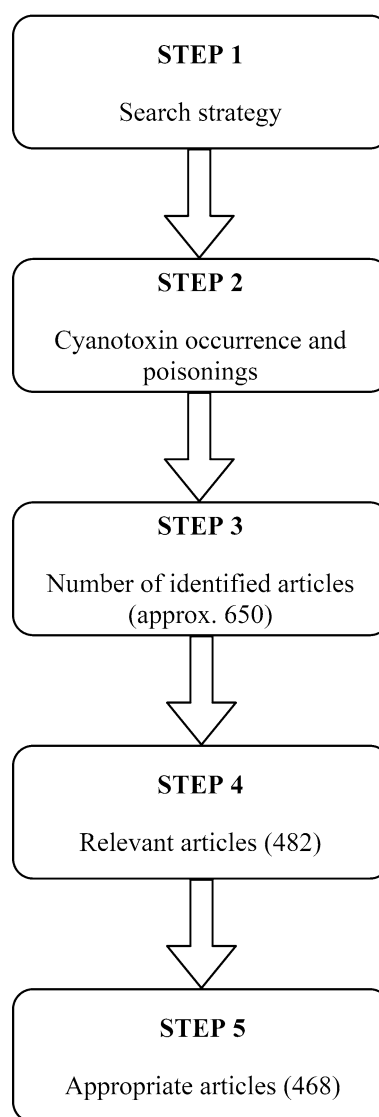
Table 1 (continued)

Toxins/structure (number of known analogs)	Mechanism of action and target organ	Health effects	Examples of toxicogenic genera/species	LD ₅₀ (i.p. mouse, µg/kg b.w.)	LD ₅₀ (oral, µg/kg b.w.)	References
Endotoxins (irritants)						
Lipopolysaccharides (LPS)/lipopolysaccharides (3)	LPS form complexes with proteins and phospholipids; primary site of action: affects any exposed tissue (skin and mucosa)	Inflammatory agents; headache; fever; skin irritations; gastrointestinal, allergic and respiratory reactions	All cyanobacteria	40,000–190,000	ND	Weise et al. (1970), Chorus and Bartram (1999), Stewart et al. (2006a), Monteiro et al. (2017)
Other toxins						
Non-proteinogenic amino acids, e.g. β-N-methylamino-L-alanine (BMAA)	Potentiation and enhancement of motor neuron death; agonist for N-methyl-D-aspartate and glutamate R5 receptors; oxidative stress	Potential neurodegenerative agents; neurotoxic	<i>Aphanizomenon</i> , <i>Cylindrospermopsis</i> , <i>Dolichospermum</i> , <i>Planktothrix</i> (<i>Oscillatoria</i>), <i>Microcystis</i> , <i>Nodularia</i> , <i>Synechococcus</i> , <i>Synechocystis</i>	ND	ND	Cox et al. (2005), Lobner et al. (2007), Carmichael and Boyer (2016)

ND not determined

“poisoning”, “intoxication”, “incident”, “death”, “mortality”, “health”, “health effects”, “adverse effects”, “exposure”, “drinking water”, and “recreation”. Cyanotoxins are comprised of a wide number of compounds including their structural variants. To simplify representation of some well-known cyanotoxins and their distribution, variants were included in an appropriate cyanotoxin group.

In step two, a review of the individual results was carried out to assess and determine their relevance to the topic of this manuscript. The number of identified articles (step three), through data processing and quality assessment until February 2018, is presented in Fig. 2. Publications that were not included in the scope of the study consisted of (a) investigations performed under experimental conditions in the absence of field investigations or intoxication events; (b)

**Fig. 2** Search strategy for the systematic review of cyanotoxin occurrence and poisoning incidents

publications of some lesser known cyanotoxins (e.g. BMAA and dermatotoxins) and other cyanobacterial toxic metabolites; (c) uncharacterized toxic metabolites whose molecular structure has not been determined; (d) papers about cyanotoxins from ecosystems other than freshwater, including cyanotoxin occurrences in some extreme environments; and (e) news, reports and other unverified online data.

Previous refereed review papers were considered relevant, as well as papers dealing with similar scope but which did not contain key information (e.g. ecosystems were not defined, reports of other, less known cyanotoxins, etc.); therefore, they were not analysed further (step four). Such systematic and large-scale investigations on cyanotoxin occurrences from 12 different countries have been presented and summarized in Table 2. These papers present valuable information on 2250 different freshwater ecosystems where identification of MCs was most often found; however, individual blooming ecosystems could not be associated with cyanotoxin identifications in some cases (e.g. in Germany 15 MCs were isolated from 11 unspecified lakes and reservoirs). Therefore, these data are important for the scope of this overview but could not be presented on the global and particular maps.

Publications that contained most of the necessary information (e.g. investigated freshwater ecosystem and geographical location, cyanotoxins and cyanobacteria identified, symptoms/effects manifested with possible causal connections to cyanobacteria/cyanotoxins) were found to be acceptable and were retained for final analysis (step five). The chosen literature consisted mostly of published, peer-reviewed scientific papers, rather than conference proceedings, books, newspaper articles, Ph.D. dissertations, Master and Bachelor theses. The acceptable publications regarding cyanotoxin occurrence and poisoning incidents (468) were analysed within an internal database used for the production of this paper (in the text referred to as database). Although the database contains a large amount of information, the focus of this study was solely on the cyanotoxin occurrences and poisoning incidents. Therefore, the database could represent the basis for different studies as well, such as analysis of potentially toxic cyanobacterial species, more detailed statistics, and freshwater ecosystem distribution. All of the acceptable articles were classified according to publication date and continent, and are presented in Table 3.

Based on the selected references from the database, the number of publications on cyanotoxins appears to have increased exponentially over recent decades. Most papers have dealt with the ecosystems and cyanobacterial problems found in European countries, mostly in recent decades. 38% (177 out of 468) of the papers reported poisoning cases involving animals and/or humans. Until 1949, authors appear to have reported poisoning incidents only. In the period from 1950 to 1999, the vast majority of the publications dealt

with poisoning cases, except in Asia, Europe, and South America. On the other hand, recently only 22% (74 out of 337) of the papers documented and presented cyanobacterial poisoning cases with more emphasis on the reports of cyanotoxin occurrence. In Australia and New Zealand, 63% (32 out of 51) of all reported references to the occurrence of the cyanobacteria dealt with associated poisonings. Conversely, in Asia, only 21% (16 out of 78) of the publications dealt with poisoning cases; in South America 27% (17 out of 63), and in Europe 30% (39 out of 128).

Several important findings were made during production this manuscript based on the formed database that should be clarified. There were

- 468 acceptable articles;
- 1118 recorded cyanotoxin identifications (MCs, CYNs, ATXs, STXs, NODs) or reports where cyanotoxins were not analysed or specified (UR, N/A) (sometimes more than one cyanotoxin was identified in one ecosystem at different times);
- 183 recorded cyanotoxin poisonings of humans and/or animals;
- 869 investigated freshwater ecosystems (some were investigated more than once by different authors or at different point in time);
- 1017 inputs in the database are presented in supplementary tables (S1–S6) that refer to the different freshwater ecosystems that were investigated with complete data at one point in time.

The publications and findings related to the presence of cyanotoxins and poisonings are presented on the maps of continents and subcontinents and in several supplementary tables (S1–S6) and are further discussed in the following sections.

Distribution of cyanotoxins on a global scale

An investigation on global cyanotoxin distribution presents a daunting task since it includes review of a very large number of publications. Constant progress in science together with the increased concerns associated with cyanobacterial blooms have undoubtedly contributed to the increase in the number of publications on cyanotoxins over recent decades (from about hundred to three hundred articles per year since the 1990s) (e.g. Merel et al. 2013b). In December 2012, the Thomson Reuters Web of Science database retrieved 18,642 publications related to cyanobacteria, of which 20% were related to cyanobacterial blooms. In the same period, 5293 publications were related to cyanotoxins, but these publications were mostly unevenly distributed between the different

Table 2 Cyanobacterial and cyanotoxin occurrence in some countries based on the publications with incomplete information required for database

Investigated period	Country, ecosystem (lakes, reservoirs, rivers)	Species reported	Toxin(s) detected	References
1989–1992	Portugal 12 samples: 2 natural lakes, 2 Iberian rivers and 5 reservoirs	<i>Microcystis aeruginosa</i> , <i>Microcystis wesenbergii</i> , <i>Anabaena flos-aquae</i> , <i>Nostoc</i> sp.	7 different toxins isolated: MC-LR, -RR, -YR, [D-Asp ³]MCYST-LR, MCYST-HiLR, [L-MeSer]MCYST-LR and [DhaT] MCYST-LR	Vasconcelos et al. (1996)
1995–1996	Germany 11 lakes and reservoirs	<i>Microcystis</i> spp., <i>Planktothrix agardhii</i> , <i>Planktothrix rubescens</i>	15 MCs isolated: MC-RR, MC-YR, MC-LR, [D-Asp ³] MC-LR, [D-Asp ³] MC-YR, [Dha ⁷] MC-LR, [Dha ⁷] MC-RR, [Dha ⁷] MC-YR, MC-WR, [D-Asp ³] MC-HtyR, [H ₄] MC-YR	Fastner et al. (1999)
August 1996–October 1997	South Korea 10 large reservoirs	<i>Microcystis</i> spp.	MC	Kim et al. (1999)
October 1997–June 1999	Australia 47 reservoirs and weir pools	<i>Cylindrospermopsis raciborskii</i> (recorded in 22 of 24 reservoirs and in 13 of 23 weir pools sampled), <i>Limnospira</i> aff. <i>redekei</i> , <i>Pseudanabaena limnetica</i> , <i>Planktolyngbya subtilis</i>	CYN	McGregor and Fabbro (2000)
1999	Germany 400 samples from eight ecoregions, 325 analysed for cyanobacteria, 155 lakes	55% contained cyanobacteria populations and 26% contained toxigenic cyanobacteria (<i>M. aeruginosa</i> , <i>Planktothrix</i> sp., <i>Limnospira</i> sp.)	MC (MC-LR, MC-RR, MC-YR)	Frank (2002)
N/S	Czech Republic 8 water treatment plants (40 samples in total)	<i>Oscillatoria</i> spp., <i>Phormidium autumnale</i>	MC-LR 61% of raw and 38% of treated waters contained detectable	Bláha and Maršálek (2003)
2002	Bangladesh 79 ponds	<i>Microcystis</i> , <i>Planktothrix</i> , <i>Anabaena</i> , <i>Oscillatoria</i> sp., <i>Merismopedia</i> sp., <i>Pseudanabaena</i> sp., <i>Anabaenopsis</i> sp., <i>Aphanizomenon</i> sp.	MCs (MC-RR, MC-YR, MC-LR) in 39 ponds	Welker et al. (2004)
May–September 2000–2001	USA 241 lakes in Missouri, Iowa, northeastern Kansas, and southern Minnesota (800 lake visits)	<i>Anabaena</i> , <i>Coelosphaerium</i> , <i>Microcystis</i> , <i>Oscillatoria</i>	MC	Graham et al. (2004)
Mid-July and August 2003 and 2004	Czech Republic 18 eutrophic, recreational, and/or drinking water reservoirs	<i>Microcystis</i> spp. (<i>M. aeruginosa</i> , <i>M. viridis</i> , <i>M. ichthyoblabe</i> , <i>M. flos-aquae</i> , <i>M. wesenbergii</i>), <i>Woronichinia naegeliiana</i> , <i>Anabaena</i> (<i>A. lemmermannii</i> , <i>A. flos-aquae</i> , <i>A. crassa</i> , <i>A. circinalis</i> , <i>A. spirroides</i> , <i>A. mendotae</i> , <i>A. planctonica</i>), <i>Aphanizomenon</i> (<i>Aph. klebahnii</i> , <i>Aph. yezoense</i> , <i>Aph. flos-aquae</i> , <i>Aph. issatschenkoi</i>), <i>Planktothrix agardhii</i>	MC (MC-LR, MC-RR, MC-YR) MCs detected in 90% of the samples	Znachor et al. (2006)

Table 2 (continued)

Investigated period	Country, ecosystem (lakes, reservoirs, rivers)	Species reported	Toxin(s) detected	References
Summer 2003	USA 33 lake and reservoir raw water sources (206 samples + 77 effluents) reservoirs, dams, creeks, lakes	N/S	MC-LR equiv. in 7% of the samples (14 samples)	Haddix et al. (2007)
July–September 2004	Czech Republic 94 water reservoirs (206 water samples collected)—27 for drinking water supply	<i>Microcystis</i> spp., <i>M. aeruginosa</i> , <i>M. wesenbergii</i> , <i>Woronichinia</i> spp., <i>Planktothrix</i> spp., <i>Aphanizomenon</i> spp., <i>Cylindrospermopsis</i> spp.	MC detected in 70% of all samples (145 waters)	Bláhová et al. (2007)
June–September 2005	Germany 21 lakes (115 samples)	<i>C. raciborskii</i> , <i>Anabaena bergii</i> , <i>Anabaena</i> spp., <i>Anabaenopsis</i> spp., <i>Aphanizomenon</i> spp., <i>Aph. gracile</i> , <i>Aph. flos-aquae</i> , <i>Aph. aphanizomenoides</i> , <i>Aph. issatschenkoi</i> , <i>Raphidiopsis mediterranea</i> , <i>Planktothrix agardhii</i>	CYN detected in 19 lakes (102 samples)	Rücker et al. (2007)
May and October 2007	USA 1161 lakes	<i>Anabaena</i> , <i>Anabaenopsis</i> , <i>Aphanizomenon</i> , <i>Aphanocapsa</i> , <i>Coleosphaerium</i> , <i>Cylindrospermum</i> , <i>Cylindrospermopsis</i> , <i>Leptolyngbya</i> , <i>Limnolthrix</i> , <i>Lyngbya</i> , <i>Microcystis</i> , <i>Nodularia</i> , <i>Oscillatoria</i> , <i>Phormidium</i> , <i>Planktolingbya</i> , <i>Planktothrix</i> , <i>Pseudanabaena</i> , <i>Raphidiopsis</i> , <i>Snowella</i> , <i>Synechococcus</i> , <i>Synechocystis</i>	CYN, MC, STX, ATX, NOD	Lofin et al. (2016b)
July 2011–March 2012	China 25 urban reservoirs for drinking water supply in Dongguan City of South China (86 samples)	<i>C. raciborskii</i> , <i>Raphidiopsis</i> sp., <i>Limnolthrix</i> sp. (<i>Limnolthrix redekei</i>), <i>Microcystis</i> sp.	CYN detected in more than one half of the reservoirs MCs detected in 12 reservoirs	Lei et al. (2014)
1930–2012	Serbia 65 freshwaters (4 canals, 4 multi-use reservoirs, 6 lakes, 7 ponds, 8 fish-ponds, 11 reservoirs for irrigation, 12 reservoirs for drinking water supply, 13 rivers)	<i>M. aeruginosa</i> , <i>Aphanizomenon flos-aquae</i> , <i>Oscillatoria agardhii</i> , <i>Microcystis flos-aquae</i> , <i>Oscillatoria rubescens</i> , <i>Anabaena flos-aquae</i> , <i>Anabaena solitaria</i> , <i>Pseudanabaena limnetica</i> , <i>Anabaena spiroides</i> , <i>Gomphosphaeria lacustris</i> , <i>Microcystis wesenbergii</i> , <i>Phormidium foveolarum</i> , <i>Anabaena circinalis</i> , <i>Gomphosphaeria saponina</i> , <i>Jaaginema subtilissimum</i> , <i>Microcystis viridis</i> , <i>C. raciborskii</i>	MC	Svirčev et al. (2014b, 2017a)
2013	USA Puget Sound area lakes	<i>Anabaena</i> spp., <i>Microcystis</i> spp.	MC	Preece et al. (2015)

Table 2 (continued)

Investigated period	Country, ecosystem (lakes, reservoirs, rivers)	Species reported	Toxin(s) detected	References
2009–2014	USA Washington lakes	<i>Anabaena</i> , <i>Aphanizomenon</i> , <i>Microcystis</i> , <i>Gloeotrichia</i>	MC, ATX, CYN, STX	Trainer and Hardy (2015)
June 2014	USA 75 Wadeable streams, Piedmont region	24 March 1993 and 14 September 2011: <i>Leptolyngbya</i> sp. (33%), <i>Phormidium</i> sp. (27%), <i>Pseudanabaena</i> sp. (15%), <i>Anabaena</i> sp. (9.9%) <i>Microcystis</i> spp.	MC	Loftin et al. (2016a)
1980–2014	Uruguay 64 ecosystems		MC, STX, CYN	Bonilla et al. (2015)
2000–2015	Bulgaria 120 waterbodies	210 taxa (207 species, 1 variety and 2 forms) from 69 genera of Cyanoprokaryota: <i>Dolichospermum spirroides</i> , <i>Dolichospermum scheremetieviae</i> , <i>M. wesenbergii</i> , <i>Aph. flos-aquae</i> , <i>Aph. klebahnii</i> , <i>Aph. gracile</i> , <i>Snowella lacustris</i> , <i>Linnococcus limneticus</i> , <i>Cuspidothrix issatschenkoi</i> , <i>Planktolyngbya limnetica</i> , <i>Pseudanabaena catenata</i> , <i>Raphidiopsis mediterranea</i> , <i>Planktothrix agardhii</i> , <i>C. raciborskii</i>	MC, NOD, STX	Stoyneva-Gärtner et al. (2017)
2015–2016	Turkey 18 selected waterbodies: 7 natural lakes, 8 reservoirs, 1 lagoon, 2 coastal and transitional waters	<i>Anabaena minderi</i> , <i>Anabaena recta</i> , <i>Anabaena</i> sp., <i>Anabaenopsis elenkii</i> , <i>Aphanizomenon</i> sp., <i>Aphanizomenon</i> spp., <i>Aph. flos-aquae</i> , <i>Chrysothrix ovalisporum</i> , <i>Cuspidothrix issatschenkoi</i> , <i>C. raciborskii</i> , <i>D. flos-aquae</i> , <i>D. mendotae</i> , <i>Microcystis</i> spp., <i>M. aeruginosa</i> , <i>Nodularia spumigena</i> , <i>Oscillatoria</i> sp., <i>Planktothrix</i> sp., <i>Planktothrix agardhii</i> , <i>Planktothrix rubescens</i> , <i>Sphaerospermopsis aphanizomenoides</i>	MC, CYN	Koker et al. (2017)

N/S not stated

Table 3 Classification of references accepted and presented in database

Period	Africa		Asia		Australia and New Zealand		Europe		North and Central America		South America		Total	
	Total	Poison.	Total	Poison.	Total	Poison.	Total	Poison.	Total	Poison.	Total	Poison.	Total	Poison.
...–1949	1	1	0	0	1	1	0	0	6	6	0	0	8	8
1950–1999	11	11	14	7	25	23	32	22	27	25	14	7	123	95
2000–2018	43	7	64	9	25	8	96	17	60	23	49	10	337	74
Total	55	19	78	16	51	32	128	39	93	54	63	17	468	177

poison. publications with reported poisoning cases, *total* total number of references (cyanotoxin distribution and reported poisoning cases)

toxins (Merel et al. 2013a). The first publications from the 1960s focussed on STX and ATX. In the 1980s, articles on NODs and MCs started to appear, while the first articles on CYN were published during the 1990s (Merel et al. 2013b). The vast majority of published cyanotoxin articles have focused on MCs (56%), then STXs (27%), followed by NODs and ATX (9%), CYN (7%) and other toxins (BMAA, lyngbyatoxin, aplysiatoxin less than 2%). These publications cover over 100 research areas, including toxicology (24%), ecology (19%), chemistry (18%), pharmacology (17%), water biology, molecular biology (13%), engineering, water resources (7%), the economy, public health and epidemiology (5%). A dozen authors are associated with 11% of the overall literature, and most of the articles (98%) were published in English. Taking into account the size of national populations, then productivity (if defined as simply the number of refereed publications) is high in the smaller countries of Western Europe, but is low in the USA, Japan and China. If the number of universities is also taken into account, then Australia and Finland have the highest publication rates. Based on the economic level of the country, African countries emerge ahead of USA or other European countries, only Finland and Australia remain among the most productive. With reference to citation and H-index per country, it appears that the publications from the countries with the highest cyanotoxin publication outputs are also the countries which have generated the papers of highest impact (Merel et al. 2013b).

Recent publication searches using the keyword phrase “cyanotoxins” were performed in several databases. The numbers of papers found in 2018 were Scopus database: 1231; Google Scholar: 1190; Science Direct: 286; PubMed: 94; Wiley Online Library: 54 results. The number of selected papers from this research was 468, dating from 1931 to February 2018 when this analysis of the published data began. However, a series of new papers has been published since February 2018 indicating the further appearance of cyanotoxins, for instance, in Ethiopia (Major et al. 2018), Brazil (Lorenzi et al. 2018; Walter et al. 2018),

USA (Beverdors et al. 2018), England (Turner et al. 2018) and Armenia (Minasyan et al. 2018).

Most of the research on cyanotoxins has been done on defining their chemistry, toxinology and toxicology, while a worldwide effort to map their occurrence and associated environmental health risks has been lacking (Carmichael 2008). Here we present the geographical distribution of the five most commonly found cyanotoxins (MCs, CYNs, ATXs, STXs, and NODs) throughout the world. All of the data are presented in separated maps, describing cyanotoxin occurrence on the different continents and subcontinents, as well as the most commonly observed cyanobacterial genera or species and the freshwater ecosystems in which they were found.

Africa

The dominant cyanotoxins reported from Africa were MCs (77%; 77 out of 100) which were found in 14 countries and in 76 freshwater ecosystems, predominantly lakes, reservoirs and ponds (30, 16, 11, respectively) (Fig. 3; APPENDIX S5). In addition to MCs, four other groups of cyanotoxins were also detected, but in negligible percentages: ATXs 9%, NODs 3%, CYNs 2%, and STX 1%. The highest number of waterbodies where ATXs were detected was in Kenya, than in Nigeria. STX was identified in only one African freshwater ecosystem (in Nigeria) together with MC and ATX, although cyanobacterial species known to be potential saxitoxin producers have been previously identified in Africa (APPENDIX S5). The most common genera identified (number of reports in parentheses) in freshwater ecosystems in Africa were *Microcystis* spp. (79), *Anabaena* spp. (35), *Oscillatoria* spp. (23), *Cylindrospermopsis* spp. (17) and *Planktothrix* spp. (13).

Asia

Cyanotoxins were found in 15 countries, in 131 freshwater ecosystems, predominantly lakes, ponds and reservoirs (67, 24, and 24, respectively) (Fig. 4; APPENDIX S2).

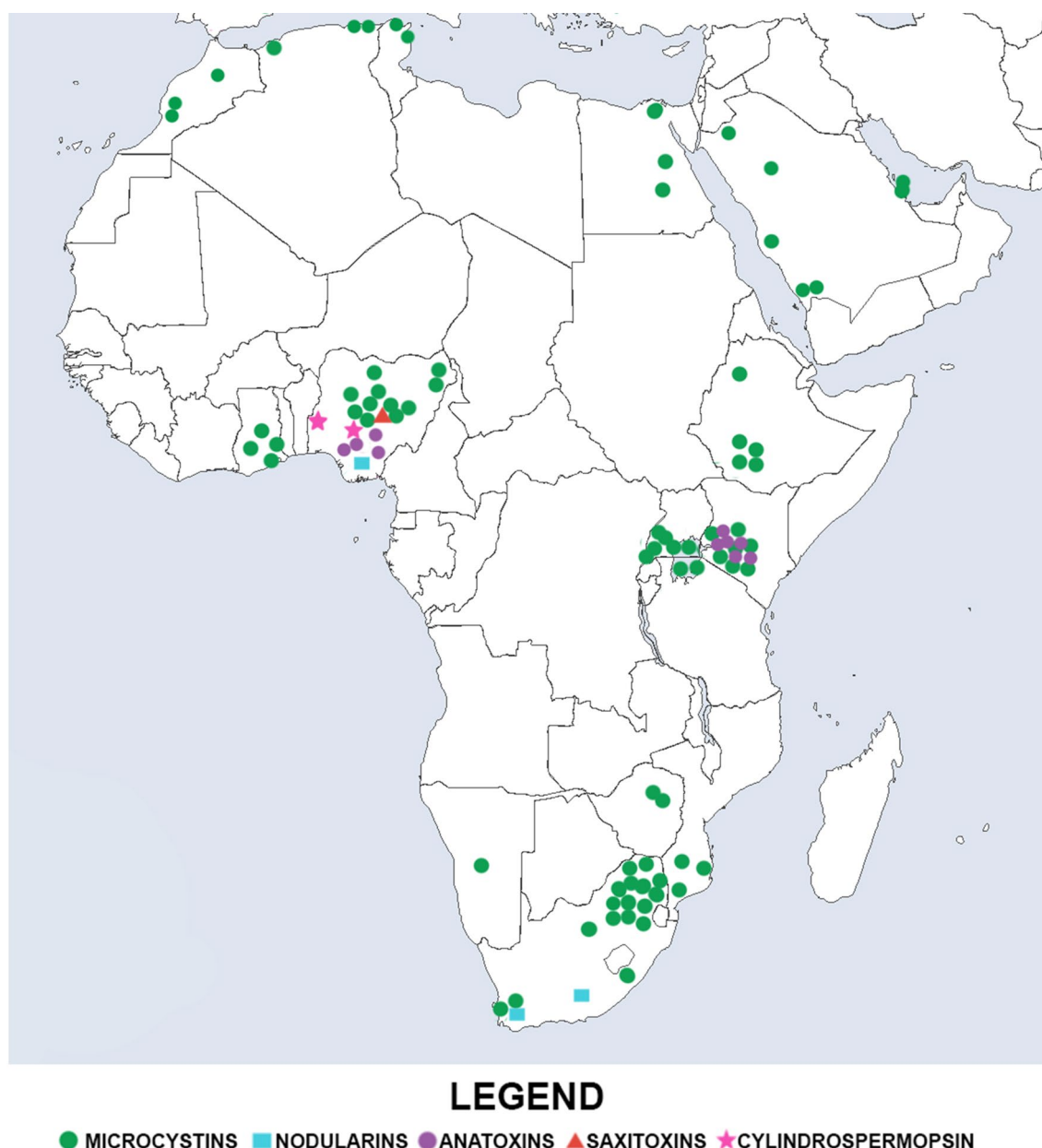


Fig. 3 Geographical distribution of the most commonly reported cyanotoxins in Africa

MCs (79%; 132 out of 168) were the most commonly found cyanotoxins in freshwater ecosystems in Asia. Cyanotoxins identified in Asia also have included CYNs (10%), ATXs (3%), NODs (3%), and STXs (1%). ATX was mostly reported in South Korea, but only once in China, Qatar, and Japan; CYN has been found mostly in Thailand, but also in Taiwan, Japan, Turkey, China and Saudi Arabia. NOD was found in Turkey and Taiwan, while STXs were detected only once in China and Russia. The most common genera identified (number of reports in parentheses) in freshwater ecosystems in Asia were *Microcystis*

spp. (162), *Anabaena* spp. (79), *Oscillatoria* spp. (52), *Aphanocapsa* spp. (33), and *Nostoc* spp. (30).

Australia and New Zealand

Cyanotoxins were found in Australia with New Zealand, in 106 freshwater ecosystems, predominantly lakes, rivers and ponds (66, 19, and 10, respectively) (Fig. 5; APPENDIX S6). MCs were the commonly found cyanotoxins (55%; 91 out of 166), with dominance in the freshwater ecosystems of

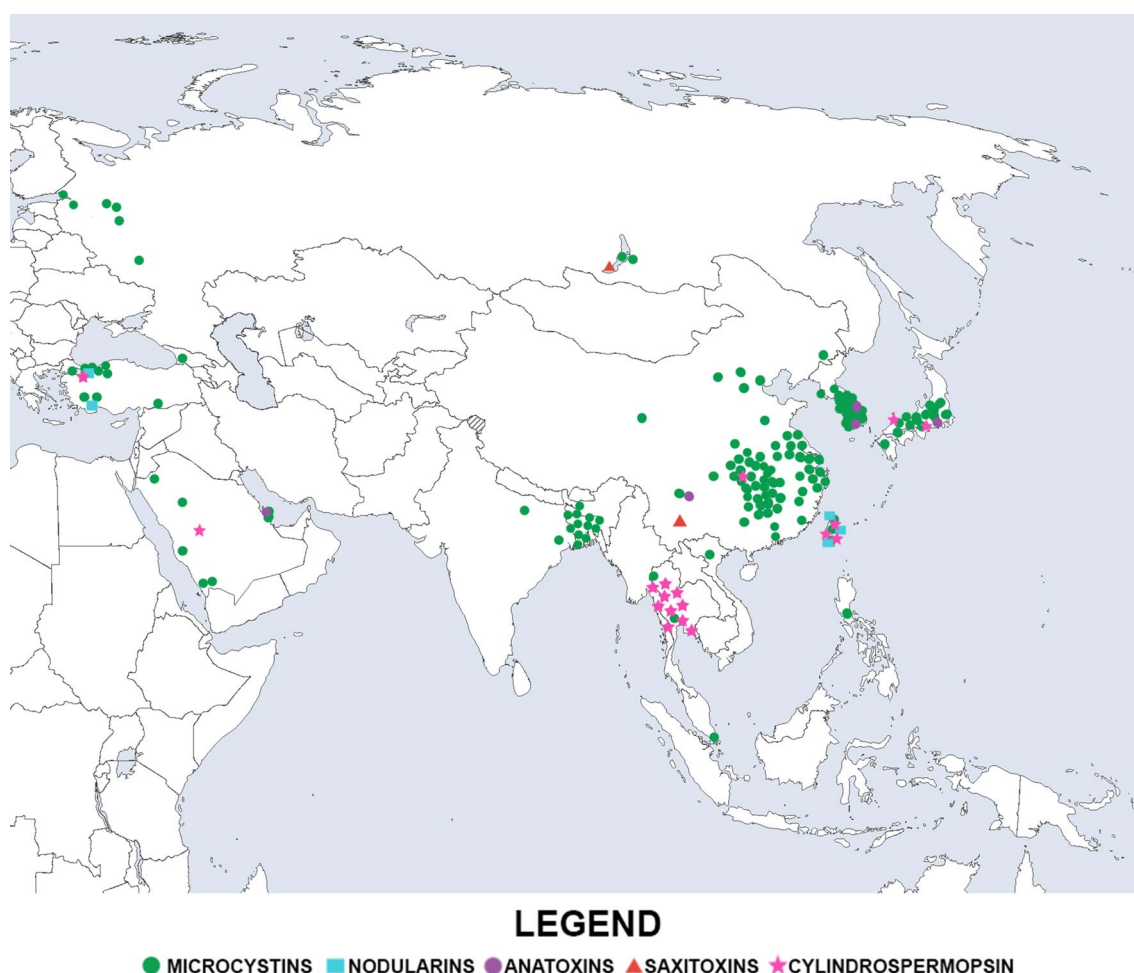


Fig. 4 Geographical distribution of the most commonly reported cyanotoxins in Asia

New Zealand. In addition to MCs, other detected cyanotoxins were: STXs (21%), CYNs (8%), ATXs (5%) and NOD (4%). The most common genera identified (number of reports in parentheses) in freshwater ecosystems in Australia were *Microcystis* spp. (72), *Anabaena* spp. (60), *Phormidium* spp. (13), *Nodularia* spp. (13) and *Cylindrospermopsis* spp. (7).

Europe

Based on the collected data, cyanotoxins were identified in 273 European freshwater ecosystems within 25 countries (Fig. 6; APPENDIX S1). The cyanotoxins were predominantly found in lakes (188). MCs were the most commonly detected cyanotoxins across European freshwater ecosystems (58%; 198 out of 341). CYN (18%) was found most often in waters of Poland and Germany, but also in Greece, Portugal, Spain, Italy, the Czech Republic, and Serbia, while STXs (10%) were identified in Poland, and also in Greece,

Serbia, Finland, Bulgaria, France, Portugal and Spain. ATXs (10%) were predominantly detected in lakes and rivers in Italy, then in Portugal, Denmark, Netherlands, France, Germany, Ireland, Bulgaria, the UK, Poland, Spain, Sweden, and Switzerland. The least represented cyanotoxins were NODs (1%), mostly found in freshwater ecosystems in Bulgaria, Finland and Greece. The most common genera identified (number of reports in parentheses) in freshwater ecosystems in Europe were *Microcystis* spp. (203), *Anabaena* spp. (130), *Planktothrix* spp. (85), *Aphanizomenon* spp. (71) and *Phormidium* spp. (28).

North America and Central America

Cyanotoxins were found in 4 countries in North and Central America, within 204 freshwater ecosystems, predominantly lakes (156) (Fig. 7; APPENDIX S4). MCs (57%; 135 out of 238) were the most frequently detected cyanotoxins in North and Central America. MCs were found in freshwater

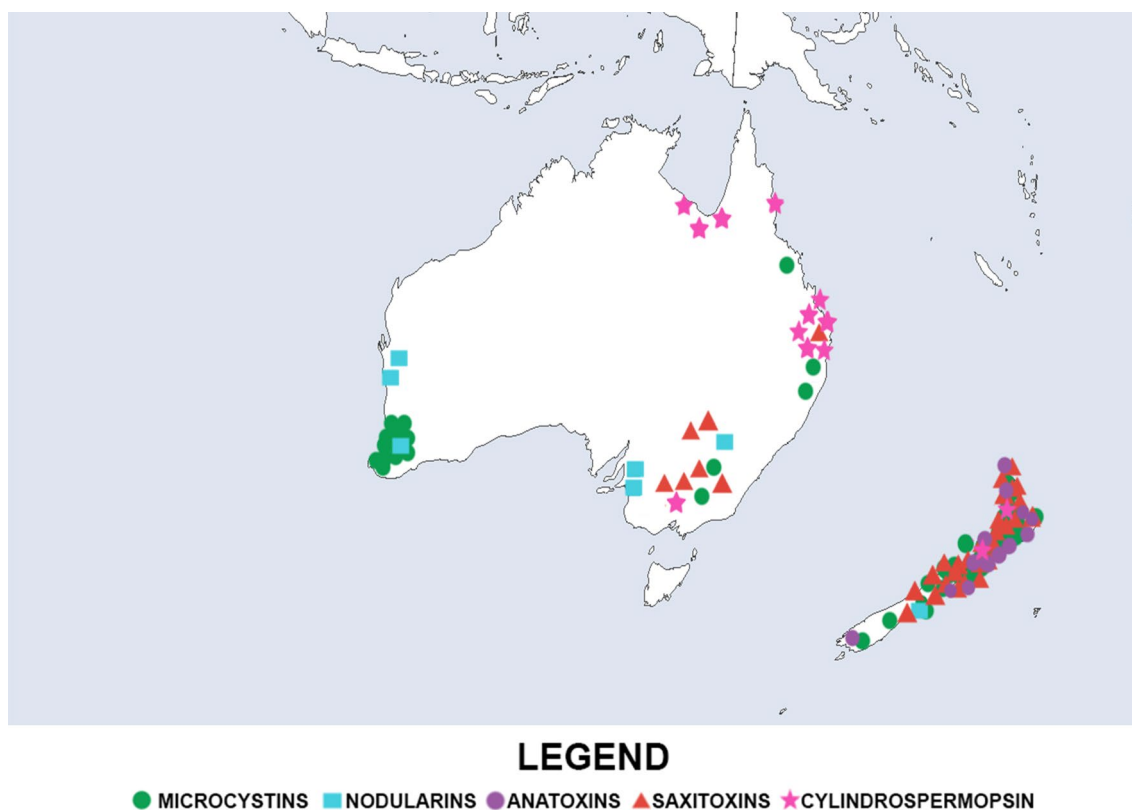


Fig. 5 Geographical distribution of the most commonly reported cyanotoxins in Australia and New Zealand

ecosystems in several USA States, in Mexico, Guatemala, and in Canada. ATXs, CYNs and STXs (15%, 4%, and 3%, respectively) were also detected in freshwater ecosystems. ATXs was mostly found in freshwater ecosystems in Washington and Nebraska, then singularly in Idaho, Oregon, Florida, California, Wisconsin, Milwaukee, Montana, and New York State, while STXs were detected in water reservoirs in Canada, Ohio, Alabama, Guatemala and Mexico. So far, NODs do not appear to have been reported in cyanobacterial blooms in North America. However, *Nodularia* blooms have been noted in lakes in western parts of North America and saline lakes on the American prairies (Galat et al. 1990; Reuter et al. 1993; Gerrath 2003; Oliva et al. 2009), suggesting that NODs could be found in the future. The most common genera identified (number of reports in parentheses) in freshwater ecosystems in North and Central America were *Microcystis* spp. (87), *Anabaena* spp. (69), *Aphanizomenon* spp. (19), *Lyngbya* spp. (9) and *Cylindrospermopsis* spp. (22).

South America

In South America, cyanotoxins were found in 6 countries, in 79 freshwater ecosystems, predominantly reservoirs (22) and lakes (13) (Fig. 8; APPENDIX S3). MCs were the most

commonly found cyanotoxins in South America (63%; 66 out of 105), with the highest distribution in Brazil, but also in Argentina, Chile, and Uruguay. STXs were predominantly reported from Brazil (13%). Furthermore, a few findings of ATXs (7%) were also detected only in Brazil, while CYN (3%) was found only in this South American country. There are apparently no reports of NOD presence in freshwater ecosystems in South America, although *Nodularia* sp. has been detected in Brazil and Uruguay (Oliva et al. 2009). The most common genera identified (number of reports in parentheses) in freshwater ecosystems in South America were *Microcystis* spp. (66), *Anabaena* spp. (24), *Cylindrospermopsis* spp. (22), *Aphanizomenon* spp. (10) and *Pseudanabaena* spp. (6).

Summary and interpretation of reported cyanotoxin distribution data throughout the world

This extensive literature review on the presence of the most commonly reported cyanotoxins in various freshwater ecosystems worldwide has included six continents, and 66 countries, mostly European (38%). The assessment was performed on 869 freshwater ecosystems, mostly lakes

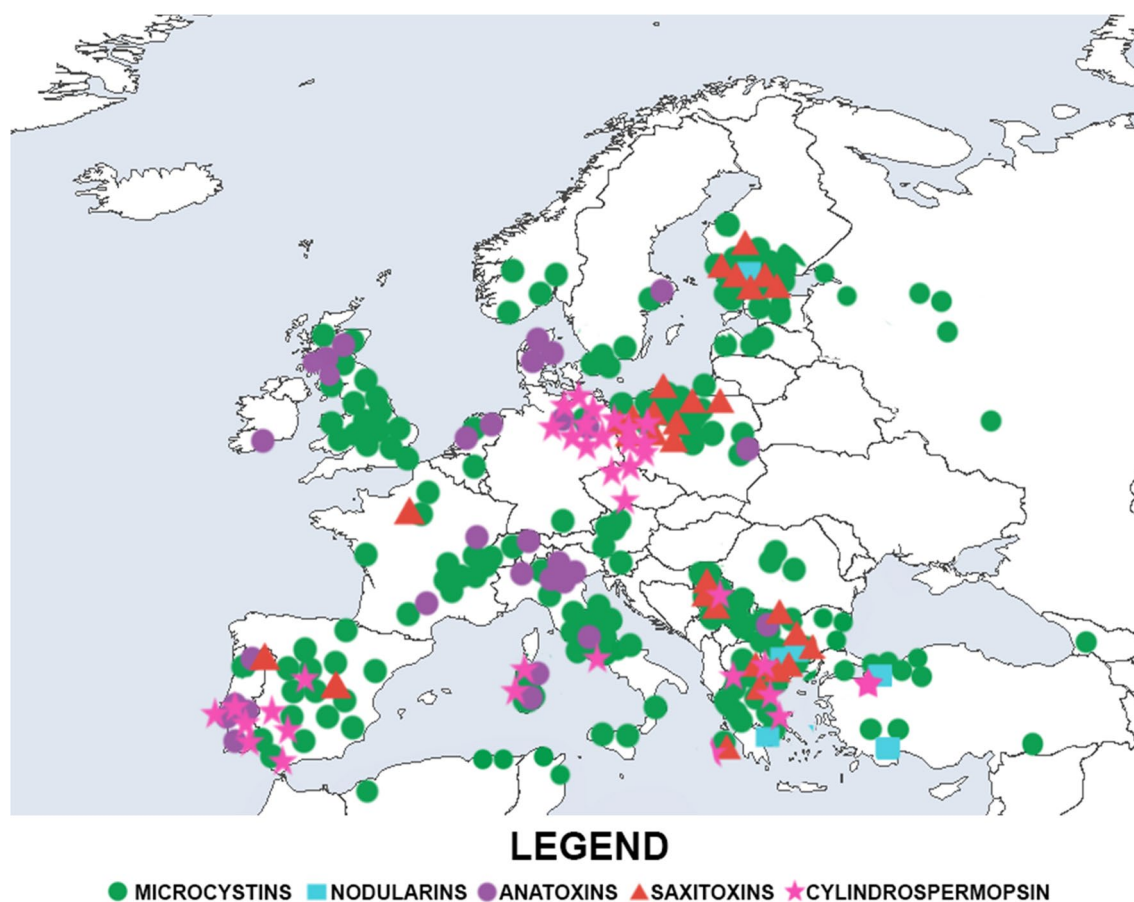


Fig. 6 Geographical distribution of the most commonly reported cyanotoxins in Europe

(60%; 520 out of 869 freshwater ecosystems), then reservoirs (13%), ponds (8%), and rivers (8%). The remaining freshwater ecosystems were either not specified or belonged to some other type of freshwater ecosystem. There were a total of 1017 inputs in the database, which relates to the number of reported investigations in each ecosystem at one point in time (see supplementary tables S1–S6). The most commonly reported cyanobacterial genera, globally, were *Microcystis* spp. (669 reportings), then *Anabaena* spp. (397), *Aphanizomenon* spp. (100), *Planktothrix* spp. (98) and *Oscillatoria* spp. (75). It should be noted that some previous *Oscillatoria* species are now classified in the *Planktothrix* genus. These most widely reported genera contain multiple species known to be potentially toxic.

The total number of recorded cyanotoxin investigations in the database was 1118, and the commonly identified cyanotoxins were MCs (63%; 699 out of 1118), while the other reported cyanotoxins were CYNs, ATXs, STXs, and NODs (10%, 9%, 8%, 2%, respectively) (Fig. 9).

The distribution of reported cyanotoxins in each continent is presented in Table 4. MCs appear to be the most widespread group of cyanotoxins in each continent. CYNs

are most often reported in Europe, then in Asia, Australia and New Zealand, and ATXs in North and Central America. STXs are mostly reported in Australia and New Zealand, as well as NODs.

There are some differences in the occurrence of cyanotoxin groups which could be attributed to the particular characteristics of each continent, resulting from geographic location and climate, the freshwater ecosystems investigated and presence of different cyanobacterial species. However, the target of most previous studies has been the MCs. Therefore, it is feasible that the number of ecosystems containing other cyanotoxins has been underestimated.

Historical overview of cyanotoxins poisonings episodes

Although the chemical structures of most cyanotoxins have only been known for the last 30–40 years, the first reported cases of likely and demonstrated cyanobacteria-associated poisonings involving humans and animals are much older (Francis 1878; Metcalf and Codd 2012). Several reports

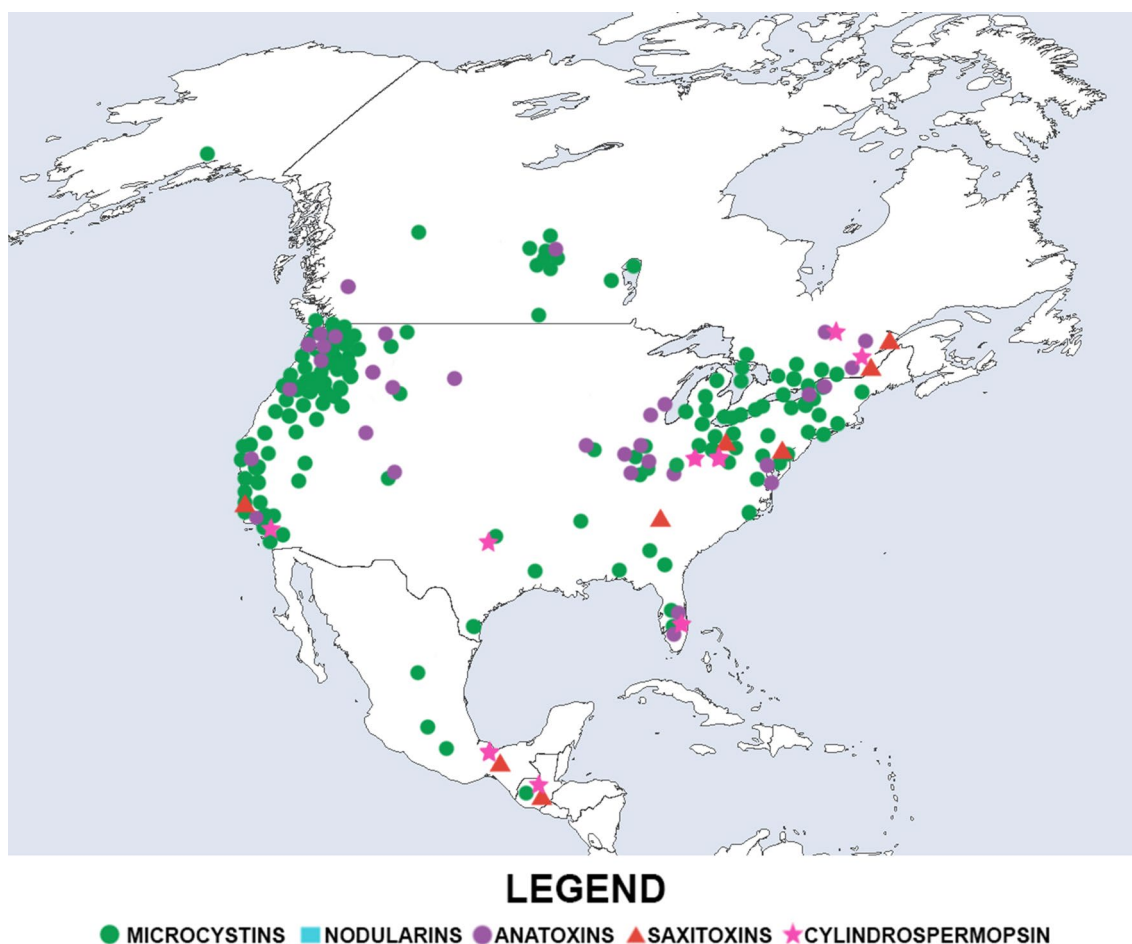


Fig. 7 Geographical distribution of the most commonly reported cyanotoxins in North and Central America

describing noxious effects of toxic cyanobacteria originate from the 1930s and the number of poisoning reports has been steadily increasing ever since.

Various toxic cyanobacterial metabolites are produced by cyanobacterial strains with the potential to cause ecotoxicological problems and health issues (Metcalf and Codd 2012). Routes of exposure to toxic cyanobacterial blooms may be via ingestion of contaminated drinking water (Falconer 1996); contaminated fish (Ferrão-Filho 2009) or shellfish (Eriksson et al. 1989); food and dietary supplements (Codd et al. 1999; Gilroy et al. 2000; Lawrence et al. 2001; Hoeger and Dietrich 2004); recreational use of lakes and rivers (Pilotto et al. 1997); inhalation of aerosols (Wood and Dietrich 2011; Metcalf et al. 2015); irrigation of agricultural products with contaminated water (Codd et al. 1999; McElhiney et al. 2001); terrestrial food chains (Metcalf et al. 2012); inhalation of terrestrial cyanobacterial crust particles (Metcalf et al. 2012); and haemodialysis (Azevedo et al. 2002).

MCs and ATXs have been the cyanotoxins most often associated with human and animal intoxications, due to

their implications in the majority of cyanotoxin occurrences reported so far, and to their wide distribution (see “[Distribution of cyanotoxins on a global scale](#)”). Cases of human and animal illnesses after exposure to toxic cyanobacteria through drinking and recreational waters have been documented worldwide (Table 5), with gastroenteritis being the most common outcome but also with hay fever-like symptoms and dermal irritation having been recorded. Hepatotoxicosis and neurotoxicity are the most common syndromes caused by swallowed or inhaled cyanobacteria. Potential consequences of cyanotoxin exposure range from mere nuisances to serious health problems in humans and animals, including fatal outcomes (Jochimsen et al. 1998; Pouria et al. 1998).

Individual poisonings in humans have been caused largely associated with recreational activities in rivers and lakes affected with cyanobacterial blooms (Table 5). Furthermore, cyanotoxins can also be aerosolized and continue to exist after a bloom has dissipated, causing chronic impact on humans (e.g. Backer et al. 2008). While the reported animal deaths have usually occurred shortly after the ingestion of



Fig. 8 Geographical distribution of the most commonly reported cyanotoxins in South America

cyanobacterial scums, progressive injury with delayed mortality has also been seen in animal poisoning by *Microcystis aeruginosa* (Table 5). The other main cause of livestock and pet deaths due to cyanotoxins has been from acute neurotoxicity leading to respiratory failure.

There have been some notable reviews on cyanobacterial occurrences and their toxin production; however, many of them are 10 or more years old (Codd et al. 1999; Chorus et al. 2000; Funari and Testai 2008; Bláha et al. 2009).

Highlights of the review from Codd et al. (1999) were cyanotoxin exposure media and routes, and Chorus et al. (2000) emphasized the importance of monitoring, precautionary measures, legislative actions and health effects. Chorus et al. (2000) and Bláha et al. (2009) dealt with documented cases of human illnesses attributed to cyanotoxins, citing 383 and 126 documents, respectively, but reporting only 14, and 19 poisoning cases, respectively. More recent papers such as Rastogi et al. (2015) have

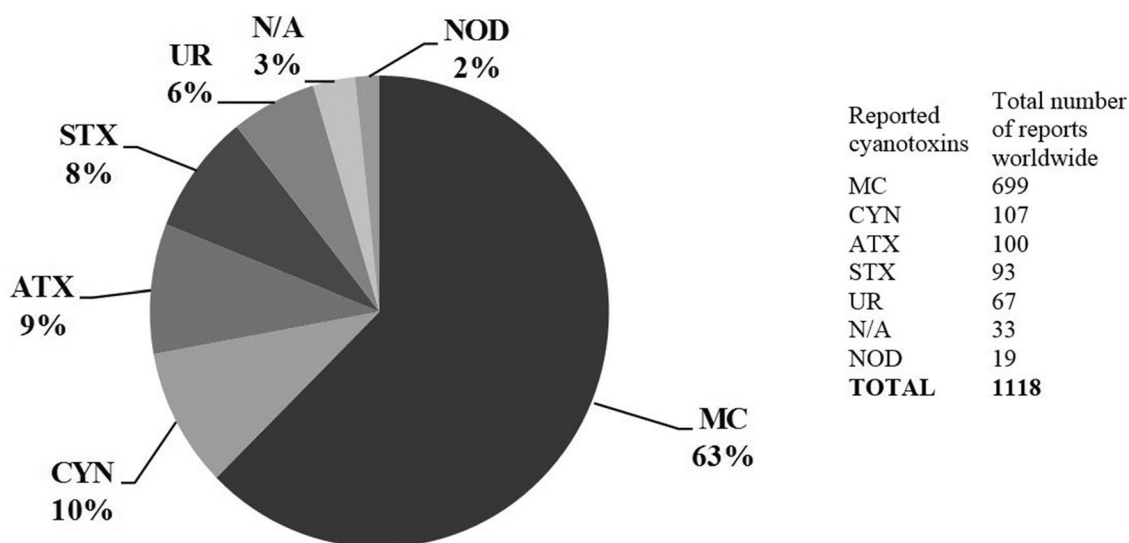


Fig. 9 Global distribution of reported cyanotoxins

Table 4 Summary of reported cyanotoxin identifications per continent

Cyanotoxins	Africa	Asia	Australia and New Zealand	Europe	North and Central America	South America	Globe
MCs	77%	79%	55%	58%	57%	63%	699 (63%)
CYNs	2%	10%	8%	18%	4%	3%	107 (10%)
ATXs	9%	3%	5%	10%	15%	7%	100 (9%)
STXs	1%	3%	21%	10%	3%	13%	93 (8%)
NODs	3%	1%	4%	1%	0%	0%	19 (2%)
UR	4%	3%	5%	1%	14%	11%	67 (6%)
N/A	4%	1%	2%	0%	8%	3%	33 (3%)
Total number of cyanotoxins reported	100	168	166	341	238	105	1118

The data are presented as absolute numbers and relative values (percentages), respectively

ATX anatoxin-a, CYN cylindrospermopsin, MC microcystins, NOD nodularin, STX saxitoxins, N/A toxic cyanobacterial metabolites not analysed, UR unknown reasons (group of cyanotoxins was not specified)

warned about cyanobacterial blooming events. Buratti et al. (2017) and Funari and Testai (2008) presented several cases of intoxication focusing on human health. Svirčev et al. (2017c) described 33 cases of human poisonings associated with cyanobacteria and their toxins in 11 countries, with a special emphasis on epidemiological research. Merel et al. (2013a) reviewed the current state of knowledge on cyanobacterial blooms and cyanotoxins, as well as their economic impact, research needs, mechanisms of cyanotoxin production and removal methods. Another paper from Merel et al. (2013b) on the spatial and thematic distribution of research on cyanotoxins showed that 90% of the research on cyanotoxins had originated from only ten countries. The present review paper focuses on the occurrence of cyanotoxins worldwide and presents

a more detailed overview of the animal and human poisoning incidents (Table 5).

The oldest known report of possible human poisoning by cyanotoxins was documented by General Zhu Ge-Liang, about 1000 years ago, concerning the deaths of soldiers who drank green water from a river in southern China (Chorus and Bartram 1999). The first known case of a widespread human poisoning (5000–8000 persons) may have been in 1931, Charleston, West Virginia, where precipitation, filtration and chlorination treatment were ineffective against cyanobacterial blooms (Miller and Tisdale 1931). Also, cyanotoxin episodes from Australia in 1979 are known, where 149 people were hospitalized (Metcalf and Codd 2004). In Brazil in 1988, 2000 persons, of whom which 88 died, manifested gastrointestinal symptoms after drinking

Table 5 Human and animal poisonings associated with cyanobacteria

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
Drinking water					
1878	Lake Alexandrina, Australia	<i>Nodularia spumigena</i>	NOD-like cyanotoxins	Several livestock deaths (within hours); livestock stupor; unconsciousness; convulsions; liver damage	Francis (1878)
1931	Elk River, Kanawha River, WV, USA	<i>Anabaena flos-aquae</i>	N/A	Animals: fish deaths Humans: gastrointestinal illness among thousands (9000) of people receiving drinking water from rivers	Veldee (1931)
1931	Ohio River, USA	<i>M. aeruginosa</i>	N/A	5000–8000 persons: gastroenteritis; abdominal pain; vomiting. Drinking water treatment by precipitation, filtration and chlorination was not sufficient to remove the toxins or toxic principles	Tisdale (1931)
1931	Charleston, WV, USA	<i>Cyanobacteria species</i>	N/A	The drinking water treatment process used (precipitation, filtration, chlorination) was ineffective against this bloom. Serious human poisoning	Miller and Tisdale (1931)
1942	Reservoir Vaal Dam, South Africa	<i>M. flos-aquae</i>	N/A	Poisoning of animals (horses, mules, donkeys, dogs, hares, poultry and waterbirds)	Steyn (1943)
1960–1965	Salisbury (now Harare), Zimbabwe, Africa	<i>M. aeruginosa</i>	N/A	Gastroenteritis; skin rashes; itching and sore eyes in children. Drinking water supply without proper drinking water purification process	Zilberg (1966)
1968	USA	Mass development of cyanobacteria, <i>M. aeruginosa</i>	N/A	Numerous cases of human gastrointestinal illness after exposure to mass developments of cyanobacteria	Schwimmer and Schwimmer (1968)
1973–1974	Reservoir Hartbeespoort Dam, Africa	<i>M. aeruginosa</i>	MC	Affected animals: cattle deaths	Toerien et al. (1976)
1974–1975	Earthen dam on a farm in Broomehill district, Australia	<i>Nodularia spumigena</i>	N/A	Sheep died and showed haemorrhage and diffuse liver necrosis after drinking water	Main et al. (1977)

Table 5 (continued)

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
1974	Belgrano Park Pond (Santa Fe City), Argentina	<i>M. aeruginosa</i>	N/A	Massive fish deaths Humans: gastrointestinal disorders, dermatitis, otitis and conjunctivitis in bathers and swimmers were associated with the bloom	Apesteguia et al. (1974)
1974–1994	Alpine Lakes, Switzerland	<i>Phormidium limosa</i> , <i>Phormidium tenuis</i> , <i>Tychonema</i> sp., <i>Pseudanabaena catenata</i> , <i>P. autumnale</i>	UR	Cattle deaths, liver damage	Mez et al. (1996)
1977–1996	Haining city, China	<i>Microcystis</i>	MC	Humans: colorectal cancer, deaths	Zhou et al. (2002)
1979	Barakologadi Game Reserve, Odi district of Bophuthatswana, South Africa	<i>M. aeruginosa</i>	N/A Suspected <i>Microcystis</i> poisoning	3 (of 4) white rhinoceroses died: acute hepatotoxicity Hepatomegaly with haemorrhage and severe liver necrosis, numerous echymoses and petechiae in the subcutaneous tissue and subserosa of the thorax, abdomen and diaphragm	Soll and Williams (1985)
1979	Reservoir on Palm Island Solomon Dam Palm Island, Australia	<i>C. raciborskii</i> (300,000 cells per ml), <i>Anabaena circinalis</i>	CYN	149 persons: gastroenteritis; vomiting; headache; liver, kidney and intestine damage. Treating bloom in a drinking water reservoir with copper sulphate led to liberation of toxins	Byth (1980), Bourke et al. (1983), Hawkins et al. (1985), Hawkins (1986), Ohtani et al. (1992), Hawkins and Griffiths (1993), Griffiths and Saker (2003)
1980	Vaal Dam, Africa	<i>M. aeruginosa</i>	MC	Affected animals: cattle deaths	Scott et al. (1981)
1981	Reservoir Malpas Dam, Armidale, Australia	<i>M. aeruginosa</i>	MC	Humans: liver damage. Cyanobacterial cells passing through water treatment process leading to re-growth in the open post-treatment drinking water tanks	Falconer et al. (1983), Botes et al. (1985)
1981–1984	Haimen city, China	<i>Oscillatoria agardhii</i> , <i>Anabaena</i> sp., <i>A. flos-aquae</i>	MC	Humans: primary liver cancer	Yu (1989), Ueno et al. (1996)
1985	USA	Mass developments of cyanobacteria	N/A	Humans: nausea; vomiting; diarrhoea; fever and eye; ear and throat infections	Carmichael (1994)

Table 5 (continued)

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
1987	Eastern Transvaal, South Africa	<i>M. aeruginosa</i>	MC	Affected animals; deaths of 47 cattle	Scott (1989)
1988	Itaparica Dam reservoir, Brazil	<i>Microcystis</i> sp., <i>Anabaena</i> sp.	UR	Humans: 2000 cases of gastroenteritis; diarrhoea; including 88 deaths, occurred in a 42-day period. People became sick after drinking boiled water from the dam	Teixeira et al. (1993)
1988	Lake Richmond, VA, USA	<i>A. flos-aquae</i> , <i>Aphanizomenon flos-aquae</i> , <i>Microcystis</i>	ATX-a(S)	Livestock, birds, dogs, fish	Mahmood et al. (1988)
1989	Reservoir Bloemhof Dam, Sandveld Nature Reserve (Free State), South Africa	<i>M. aeruginosa</i>	MC	Affected animals; seven giraffe deaths	Theron (1990a)
1989	Reservoir Klipdrif Dam, South Africa	<i>M. aeruginosa</i>	MC	Affected animals; livestock	Theron (1990b)
1990–1991	Darling River, Australia	<i>Microcystis</i> , <i>Anabaena circinalis</i>	STX, NSTX	Livestock, deaths. Copper sulphate was applied to lyse the organisms and to control taste and odour formation	Humpage et al. (1994)
1990 and 1991	Loch Insh, Scotland, UK	<i>Oscillatoria</i> sp.	ATX-a	Dog, deaths	Edwards et al. (1992)
1991–1992	Australia	<i>Anabaena</i> sp.	UR	Humans: 26 cases (aged 1–64 years) with skin diseases and multiple systemic symptoms associated with exposure (some via drinking water) to river water which was stored in open tanks	El Saadi and Cameron (1993)
1992	Dams and waterholes property in the McKinley Shire Dam, northern Queensland, Australia	Heavy growth of <i>C. raciborskii</i>	CYN	Cattle: weakness, hepatotoxicity. Death of three cows and ten calves	Thomas et al. (1998)
1981, 1982, 1983, 1985	Lake Black, Kootenai Country Idaho, ID, USA	<i>A. flos-aquae</i>	ATX-a	Dogs, cattle, deer deaths	Kann and Falter (1987)
1992–1995	Reservoir Cascade, Valley, ID, USA	<i>Anabaena spiroides</i> , <i>M. aeruginosa</i>	MC	23 cattle deaths	Jacoby and Kann (2007)
1992–1995	Lake American, WA, USA	<i>A. flos-aquae</i>	ATX-a	11 animal poisonings, 5 cat deaths	Jacoby and Kann (2007)
1992–1995	Lake Clear, WA, USA	<i>A. flos-aquae</i>	ATX-a	Several dog deaths	Jacoby and Kann (2007)
1992–1995	Lake Steilacoom, WA, USA	<i>Anabaena</i> sp., <i>A. flos-aqua</i> , <i>M. aeruginosa</i>	MC	Dog death	Jacoby and Kann (2007)

Table 5 (continued)

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
1993–1996	Tsitsikamma-Kareedouw district, South Cape, Africa	<i>Anabaena</i> spp., <i>Oscillatoria</i> spp.	MC	Affected animals; deaths of 290 dairy livestock and induced-photosensitivity in a further 70 7 cases of stock and animal deaths were recorded in this region	Harding (1997)
1994	Kavlingean River, outlet of Lake Vombsjön, Sweden	<i>Planktothrix agardhii</i> , <i>Microcystis</i>	MC	Humans: 121 of 304 people (and dogs, cats, and cattle); vomiting; diarrhoea; nausea; gastroenteritis; fevers; abdominal and muscular pain	Annadotter et al. (1996, 2001)
1994	Lake Ringsjön, Sweden	<i>Gloeotrichia echinulata</i>	UR	One family: after swimming, pruritic skin rashes	Cronberg (1999)
1994	Lake Zeekoevlei, near Cape Town, South Africa	<i>M. aeruginosa</i> , <i>Nodularia spumigena</i>	NOD, MC	Livestock: hepatotoxicity	Van Halderen et al. (1995)
1994–1995	High alpine lakes in Switzerland, Europe	<i>Phormidium limosum</i> (formerly <i>Oscillatoria limosa</i>), <i>Oscillatoria tenuis</i>	MC, ATX-a	Cattle: hepatotoxicity; neurotoxicity; over 100 cattle deaths	Mez et al. (1997)
1994–1995	Jiangsu Province, Nanhu/Shanghai, Fusui China, Asia	<i>M. aeruginosa</i> , <i>P. agardhii</i> , <i>Anabaena</i> sp., <i>O. tenuis</i> , <i>Lyngbya</i>	MC	Humans: primary liver cancer (100 of 10 ⁵)	Yu (1989), Yu et al. (1989), Ueno et al. (1996)
1998	Erfenis Dam earth-fill type dam, Free State, South Africa	<i>Anabaena</i> spp.	UR	Affected animals; deaths of livestock	Van Ginkel and Hohls (1999)
1999–2008	Reservoirs for drinking water supply Central Serbia, Serbia	<i>M. aeruginosa</i> , <i>M. flos-aquae</i> , <i>Aphanizomenon flos-aquae</i> , <i>Anabaena flos-aquae</i> , <i>A. spiroides</i> , <i>Planktothrix agardhii</i>	N/A	Humans: high incidence of primary liver cancer and 12 other cancers (brain; bronchus and lung; heart, mediastinum, and pleura; ovary; testis; kidney; stomach; small intestine; colorectum; retroperitoneum and peritoneum; leukaemia; and malignant melanoma of skin)	Svirčev et al. (2009), Drobac et al. (2011), Svirčev et al. (2013b, 2014a)
1999	Lake Ömerli dam, Istanbul, Turkey	<i>M. aeruginosa</i> , <i>Gomphosphaeria</i> sp.	MC-LR equiv.	Several thousand fish died after <i>M. aeruginosa</i> bloom	Albay et al. (2003a)
2000	Orange River, South Africa	<i>Cylindrospermopsis raciborskii</i> , <i>Anabaena</i> sp., <i>Oscillatoria</i> sp.	N/A	Fish-kills along the river. First reported incident of <i>C. raciborskii</i> in South Africa	Harding and Paxton (2001)

Table 5 (continued)

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
2000–2010	Portugal (eight Alentejo Reservoirs)	<i>M. aeruginosa</i> , <i>Aphanizomenon</i> spp., <i>Oscillatoria</i> sp.	N/A	Humans: high liver enzymes activities (GGT, AST, ALT), liver, colon and rectum cancer incidence	Bellem et al. (2013), Bellem (2014)
2001	Lake Bogoria, Kenya, Africa	<i>Phormidium terebriformis</i> , <i>O. willeyi</i> , <i>Spirulina subsalsa</i> , <i>Synechococcus bigranulatus</i>	MC-LR MC-RR MC-LF MC-YR ATX-a	Mass mortalities of lesser flamingos	Krienitz et al. (2003)
2002	Pond Mymensingh, Bangladesh	<i>Aph. flos-aquae</i> , <i>M. aeruginosa</i> , <i>M. botrys</i>	N/A	Mass mortality of fish in the pond.	Jewel et al. (2003)
2003	Pond in Central Queensland, Australia	<i>C. raciborskii</i>	CYN	Humans: skin rashes and eye inflammation 10 cattle deaths	Shaw et al. (2004)
2004	Lake Big Momela, Tanzania, Africa	<i>Arthrospira fusiformis</i> (dominant)	UR Mouse bioassay	Deaths of lesser flamingos (15 and 50 individuals per day during the study period)	Lugomela et al. (2006)
2004	Lake Manyara, Tanzania, Africa	other cyanobacterial species than <i>Arthrospira Pseudobaena</i> sp., <i>Phormidium</i> sp., <i>Oscillatoria</i> sp., <i>Aphanocapsa</i> sp. and others	UR Mouse bioassay	The deaths of lesser flamingos	Lugomela et al. (2006)
2005	Lake Oubeira, Algeria	<i>Microcystis</i> spp.	MC-LR MC-YR MC-RR MC	Mortality of freshwater terrapin, <i>Emys orbicularis</i> and <i>Mauremys leprosa</i>	Nasri et al. (2008)
2005–2009	Three Gorges Reservoir Region (two lakes and four wells), China	N/A	MC	Humans: liver damage (elevated liver enzyme activities: AST, ALP)	Li et al. (2011)
2005–2010	Lake Kotokel, Russia	<i>Aphanocapsa holsatica</i> , <i>Microcystis</i> spp., <i>A. lemmermanni</i>	MC-LR MC-RR MC-YR	Wildlife mortality and large fish mortality	Belykh et al. (2011)
2007	Constructed water impoundment Nhlanguzane Dam, Kruger National Park, South Africa	<i>M. aeruginosa</i>	MC	Bio-poisoning incidents in wild animals. Mortalities of mega herbivores	Oberholster et al. (2009)
2009	Reservoir Piedras Moras, Argentina	<i>Anabaena spiroides</i> , <i>M. aeruginosa</i>	MC	Several animal species mortality, mainly wild birds	Mancini et al. (2010)

Table 5 (continued)

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
2009	Lake William, Lake Roxton and Lake Champlain's Missisquoi Bay, Canada	Cyanobacterial cells	MC	Humans who received contaminated drinking water had an increase in muscle pain, and gastrointestinal, skin and ear symptoms; gastrointestinal symptoms were also associated with recreational contact	Lévesque et al. (2014)
2010	Lake Middle Foy, MT, USA	N/S	MC	Dog: lethargic and anorexic, severe depression and vomiting; liver failure	Rankin et al. (2013)
2011	Lake Milford, KS, USA	<i>M. aeruginosa</i>	MC-LR	Dogs: hepatotoxicity, gastroenteritis and fulminant liver failure	Van der Merwe et al. (2012)
2013	Reservoir Vrutci, Užice, Serbia	<i>Planktotrix rubescens</i>	MC-LR dmMC-LR dmMC-RR MC-YR	Humans: Skin and eye irritations; digestive disorders; fever; chronic headaches; kidney and liver problems Animals: skin lesions; allergies; stomach pain; death of fish, ducks, rooster, hawk, ram, sheep, goat, cow, horse, badger	Svirčev et al. (2017b)
N/S	Qidong city, Jiangsu Province, Fusui County in Guangxi, Tongan County in Fujian Province, and Shunde city, Guangdong Province (south east China)	N/S	MC	Humans: primary liver cancer (PLC), deaths. Mortality rate of PLC in these counties was 30 deaths per 100,000	Yu (1995)
Recreational water contact					
1924	Lake Ontario, Canada	<i>Anabaena</i> related	N/A	Cattle and other animal deaths	Howard and Berry (1933)
1934–1935	Lake Muskego, Waukesha County, WI, USA	"Weedy lake"	UR	One man: after swimming, itching of eyes, nasal congestion, mild asthma	Heise (1949)
1936–1946	Lake North, Waukesha County, WI, USA	<i>Oscillatoriaceae</i>	UR	One man: after swimming, Nasal discharge; congestion; conjunctivitis; mild asthma	Heise (1949)
1944	Lake Okoboji, IA, USA	<i>A. flos-aquae</i>	N/A	Deaths of pigs	Yoo (1995), Backer et al. (2013)
1945	Lake Dauphin, Manitoba, Canada	N/S	N/A	Horse, calves, two pigs and a cat died within an hour	McLeod and Bondar (1952)

Table 5 (continued)

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
1945–1946	Lake Keesus, Waukesha County, WI, USA	<i>Oscillatoriaceae</i>	UR	One female: after swimming gross eyelid oedema, nasal congestion, generalized urticarial rash	Heise (1949)
1946	Yahara River below Lake Kegonsa, WI, USA	<i>Aph. flos-aquae</i>	N/A	Heavy fish mortality	Mackenthun et al. (1948)
1949–1952	Lake Carey, PA, USA	<i>Anabaena</i>	UR	One female after swimming: Seasonal erythematous papulo-vesicular rash, occasionally progressing to oozing and crusting. Rash limited to face, neck, shoulders, upper chest and extremities; rash never seen on areas covered by swimsuit	Cohen and Reif (1953)
1952	Lake Storm, IA, USA	<i>A. flos-aquae</i>	UR Bioassay	Deaths of gulls, ducks, coots, pheasants, squirrels, muskrats, dogs, cats, hogs, hawks, skunk, mink. Neurotoxicity signs: prostration and convulsions preceding death; milder cases displayed restlessness; weakness; dyspnoea and tonic spasms	Firkins (1953), Rose (1953)
1955	Laguna del Monte, Argentina	<i>Anabaena inaequalis</i> , <i>Anabaena circinalis</i> , <i>Polycystis flos-aquae</i>	N/A	Massive fish mortality	Ringuelet et al. (1955)
1959	Lake Katepwa, SK, Canada	<i>Microcystis</i>	N/A	One man, adult: after swimming, headache, nausea, gastrointestinal symptoms	Dillenberg and Dehnelt (1960)
1959	Lake Long, SK, Canada	<i>Microcystis</i> , <i>Anabaena</i>	N/A	Ten children: after swimming diarrhoea, vomiting. Two cows died after drinking from the lake 12–16 h previously, during a bloom, sickness of one cow	Dillenberg and Dehnelt (1960)

Table 5 (continued)

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
1959	Lake Echo, SK, Canada	<i>Microcystis</i> , <i>A. circinalis</i>	UR	One adult male: after swimming and ingestion of contaminated water abdominal cramps and pain, nausea, vomiting, painful diarrhoea, fever, severe headache, weakness, pain in limb muscles and joints	Dillenberg and Dehnelt (1960)
1968	USA	<i>Anabaena</i>	N/A	Allergy with skin papulovesicular eruptions in a young woman who swam in a lake containing a bloom	Schwimmer and Schwimmer (1968)
1969	Lake Gibson, FL, USA	<i>M. aeruginosa</i>	N/A	Death of German Shepard dog	Brown (1973), Backer et al. (2013)
1971	Lake in New South Wales, Australia	<i>A. circinalis</i>	MC	“Almost total” mortality of bees from 84 hives associated with the insects watering on the leeward edge of lake	May and McBarron (1973)
1973–1974	Belgrano Park Pond, Santa Fe City, Argentina	<i>M. aeruginosa</i> ; bloom contained up to 60,000 colonies/mL	UR	Humans: after swimming and bathing gastrointestinal symptoms, dermatitis, otitis, conjunctivitis	Pizzolon et al. (1999)
1976	Lake Roosevelt, WA, USA	<i>A. flos-aquae</i>	N/A	Deaths of four dogs, seven sick	Soltero and Nichols (1981)
1977	Reservoir Hebgen, MO, USA	<i>A. flos-aquae</i>	ATX	14 cattle deaths	Juday et al. (1977)
1979	Lake Wallenpaupack, PA, USA	Heavy bloom of <i>Anabaena</i>	N/A	Humans (whole family): hayfever-like symptoms (sneezing, nasal discharge, eye irritation); earache	Billings (1981)
1979	Lake Arrowhead, PA, USA	N/S	N/A	One female: after swimming chills, sore throat, fever, nausea, diarrhoea	Billings (1981)
1979	Lake Arrowhead, PA, USA	N/S	N/A	20–30 children, several adults: after swimming headache, stomach cramps, nausea, vomiting, diarrhoea, fever, rash, sore or inflamed throat	Billings (1981)

Table 5 (continued)

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
1979	Lake at Northern Monroe County, PA, USA	<i>Anabaena</i>	N/A	One man: hay fever-like symptoms Outbreak involving 12 children and one adult at a lake shore community; symptoms ranged from gastrointestinal involvement to hayfever-like	Billings (1981)
1980	Lake Pocono Highlands, PA, USA	<i>Anabaena</i> sp.	UR Hepatotoxin	Humans: after swimming eye irritation, earache, sore throat	Carmichael et al. (1985)
1980	Lake Lahonton, NV, USA	<i>Aph. flos-aquae</i>	UR LD ₅₀ = 500 mg kg ⁻¹ body weight (i.p. mouse)	Humans: several affected after swimming and water skiing: erythema, eye irritation, dizziness, nausea, stomach cramps, diarrhoea	Carmichael et al. (1985)
1980	Camp William Penn, PA, USA	<i>Anabaena</i> sp.	UR	Humans: 75–100 campers affected from contact with water: conjunctivitis, sore-red throat, headaches, diarrhoea, nausea	Carmichael et al. (1985)
1981	Lake Harveys, PA, USA	<i>A. flos-aquae</i>	UR Neurotoxins, hepatotoxins	Humans: skin irritation, nausea, dizziness, diarrhoea	Carmichael et al. (1985)
1981	Lake Black, ID, USA	<i>Nostoc commune</i>	ATX	Five cattle and two dogs died after drinking water from lake shore	Kann and Falter (1985)
1982	Lake Moses, WA, USA	<i>Anabaena flos-aquae</i>	N/A	2 dogs died	Edmondson (1991), Jacoby and Kann (2007)
1985	Lake Richmond, SD, USA	<i>Anabaena flos-aquae</i>	ATX-a(S)	9 dogs died	Mahmood et al. (1988)
1985		N/S	N/A	Humans: Nausea, vomiting, diarrhoea, fever and ear, nose and throat infections	Carmichael (1994)
1985	Lake Alberta, Canada	N/S	ATX-a	500 dead bats and estimated over 1000 deaths on the leeward side of a lake, and at least 24 dead mallards	Pybus et al. (1986)
1985	Lakes in Wisconsin (25 of 86 analysed), USA	N/S	UR hepatotoxin (mouse bioassay)	Several incidents over the years when wildlife and domestic deaths were attributed to cyanotoxin(s)	Sonzogni et al. (1988)
1986	Lakes in Wisconsin, USA	N/S	N/A	3 dogs died	Dadisman (1987)
1986	Lake Forsyth, New Zealand	<i>Nodularia spumigena</i>	UR	Numerous stock deaths	Connor (1977)

Table 5 (continued)

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
1987	Lake Ostra Krksundet, Finland	<i>O. agardhii</i>	UR	Fish and bird kills associated with cyanobacterial blooms	Lindholm et al. (1989)
1989	Reservoir Rudyard, England, Staffordshire, UK	<i>M. aeruginosa</i>	MC-LR	Humans: after canoeing with 360° rolls, 10 of 20 soldiers ill; gastroenteritis; sore throat; blistered mouth; vomiting; abdominal pain; fever; pulmonary consolidation; diarrhoea; abdominal tenderness and elevated temperature; oral, inhalation route and skin contact. 2 patients in intensive care	Turner et al. (1990)
1989	Rutland Water, England	<i>Microcystis</i> sp.	5 MCs	Deaths of 15 dogs and 20 sheep after drinking; vomiting; diarrhoea; liver damage, kidney problems. 5 MCs identified in sheep rumen. Major water storage reservoir supplying drinking water to a population of 450,000 developed a bloom of <i>Microcystis</i>	National Rivers Authority (1990), Codd and Beattie (1991), Lawton et al. (1995), Rose (2003)
1989	Japan (lake)	<i>M. aeruginosa</i>	MC	Humans: one person: rashes after swimming	National Rivers Authority (1990)
1989	Bowl Water, Kent, UK	<i>Microcystis</i> sp.	N/A	Humans: after fishing: blotchy skin on face and hands after handling water on three separate occasions	National Rivers Authority (1990)
1990	Unnamed lake, Tiel, The Netherlands	<i>A. flos-aquae</i>	ATX-a	Humans: after swimming: gastrointestinal symptoms	Van Hoof (1994)
1990	Lake Cargelligo, NSW, Australia	<i>A. circinalis</i>	N/A	Humans: after swimming and canoeing: hay fever-like reactions, rash, eye irritation and pneumonia Livestock deaths	Christopher et al. (1991)
1990	Murray River, Australia	<i>A. circinalis</i>	STX and related neurotoxins	Deaths of 1600 cattle and sheep	Humpage et al. (1993)
1990 s	Reservoir Canyon, UT, USA	<i>Cyanobacteria</i>	UR	Deaths of two dogs	Winterton (2011)
1991	Lake, OR, USA	<i>Anabaena</i>	UR	Deaths of three dogs	McAllister (1991)

Table 5 (continued)

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
1991	Darling-Barwon River system, NSW, Australia	<i>Anabaena</i> spp.	N/A	Humans: after sampling water: skin irritation After water skiing: skin rash, conjunctivitis, diarrhoea, respiratory difficulty By summer, the blooms and scum had grown to cover an 1200 km of the Darling River	NSW Blue-Green Algae Task Force (1992)
1991–1992	Murray River, SA, Australia	<i>A. circinalis</i>	UR	Humans: 11 affected after skiing: rash, itching, mouth blistering, eye irritation After oral ingestion: diarrhoea, vomiting, nausea, muscle weakness, sore throat, respiratory difficulty, headache	El Saadi and Cameron (1993)
1992	Darling River, Wilcannia, NSW, Australia	<i>Anabaena</i> sp.	UR	Humans: two teenagers, after swimming gastroenteritis and myalgia	Williamson and Corbett (1993)
1992	Loch Leven, Scotland	<i>M. aeruginosa</i> , <i>A. flos-aquae</i>	MC	Fish (trout): gill injury; fish deaths	Rodger et al. (1994)
1992	Loch Insh, Scotland	<i>Planktotrix</i> spp.	ATX-a	Dog deaths after ingestion of cyanobacterial mats; neurotoxicity	Gunn et al. (1992)
1992	Lochs Awe and Avich, UK	<i>Oscillatoria</i> spp.	ATX-a	2 dog deaths, 2 recoveries after ingestion of dried shoreline cyanobacterial crusts; symptoms of neurotoxin poisoning	Codd et al. (1992)
1992–1993	Lake American, USA	<i>A. flos-aquae</i>	ATX	11 animal poisonings, 5 cat fatalities	Jacoby and Kann (2007)
1992–1993	Lake Mokoan, Australia	<i>M. aeruginosa</i>	MC-LR	Hepatocyte necrosis of fish (carp) liver	Carbis and Rawlin (1997)
1993	Michigan Pond, MI, USA (during cold weather)	<i>Microcystis</i> sp.	MC	Poisoning in four yearling heifer cattle (one survived)	Fitzgerald and Poppenga (1993)
1993	Lake in Denmark	<i>Anabaena lemmermannii</i>	ATX-a(S) MC	Waterbird deaths	Henriksen et al. (1997), Onodera et al. (1997)
1994	Lake Zeekoevlei near Cape Town, South Africa	95% <i>Nodularia spumigena</i> , 5% <i>M. aeruginosa</i>	NOD	Dog poisoning: Lethargy; vomiting, loss of appetite. Death after 5 days	Harding et al. (1995)

Table 5 (continued)

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
1994	Dam in Australia	<i>A. circinalis</i>	STX	14 sheep immediately died next to a farm dam. Observed signs were trembling, recumbency and crawling; neurotoxicity	Negri et al. (1995)
1994	Lake Velence, Hungary	Heavy bloom of <i>M. aeruginosa</i>	MC	Humans: 100–150 children: skin and eye irritation	Habermehl et al. (1997), https://books.google.rs/books/about/Current_Approaches_to_Cyanotoxin_Risk_As.html?id=jk9TtwEACA&redir_esc=y
1994	Ciénaga Grande de Santa Marta, Colombia	<i>Anabaenopsis</i> sp.	N/A	Massive fish mortality (over 20 tons). The massive death phenomenon here reported appears to be the largest in recent years	Mancera and Vidal (1994)
1994	Lake Iznik, Turkey	<i>Anabaena</i> spp.	N/A	After the formation of blooms of <i>Anabaena</i> spp., dead fish were found on the lake shore	Albay (1996)
1995	New South Wales, Victoria and South Australia	<i>Microcystis</i> , <i>Nodularia</i> , <i>Anabaena</i> , <i>Aphanizomenon</i>	UR	Humans: 852 participants showed elevated incidence of gastrointestinal and respiratory problems; flu-like symptoms; blistered mouth; fever, eye and ear irritation; vomiting; diarrhoea	Pilotto et al. (1997)
1995	Shimike Pond in Hyogo Prefecture, Japan	<i>M. aeruginosa</i>	MC-RR, MC-LR	Duck deaths. The entry of untreated sewage following an earthquake	Matsunaga et al. (1999)
1995	Ponds near Liège, Belgium	<i>M. aeruginosa</i>	MC-LR MC-RR	Bird mortality	Wirsing et al. (1998)
1996	Lake Hollingworth, England	<i>Planktothrix agardhii</i>	MC	Humans: 11 sea cadets with facial rashes; asthmatic signs and dry sporadic cough with vomiting	Codd et al. (1999)
1996	Lake Tarawera, New Zealand	<i>A. circinalis</i>	UR	Humans: people waterskiing displayed symptoms of cyanotoxin exposure (intense rash on face, arms and torso); fish-kill	Wilding (2000)
1997	Lake Pakowki, Alberta, Canada	<i>M. aeruginosa</i>	MC-LR	Bird mortality	Park et al. (2001)

Table 5 (continued)

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
1997	Carmel River, CA, USA	Cyanobacteria	N/A	Death of one dog	Marks (1997)
1997	Lake Sammamish, WA, USA	<i>M. aeruginosa</i>	MC	Humans: Young children after swimming: gastrointestinal, rashes	Calvan (1997), Johnston and Jacoby (2003)
1997	Lake Sapanca, Turkey	<i>Planktothrix rubescens</i>	MC	Fish died after the development of a bloom of <i>P. rubescens</i> After this incident, it was decided to investigate the occurrence of cyanobacterial toxins	Albay et al. (2003b)
1998	Georgia Pond, USA	<i>Microcystis</i> sp.	MC	Deaths of 4 cattle	Frazier et al. (1998)
1998	Waikanae River, New Zealand	<i>Oscillatoria</i> sp.	ATX-a	Deaths of five dogs	Hamill (2001)
1999	Lake Champlain, New York, USA	N/S	ATX-a	Several dogs died	Boyer et al. (2004)
1999	Lake Planetario, Buenos Aires, Argentina	<i>M. aeruginosa</i>	MC	Urban recreational lake, fish and duck mortality	Ehrenhaus and Vigna (2006)
1999–2000	Mataura River, New Zealand	<i>Oscillatoria</i> sp.	ATX-a MC	Death of six dogs	Hamill (2001)
1999–2005	Lake Salton Sea, CA, USA	<i>Synechococcus</i> sp., <i>Oscillatoria</i> sp., <i>Gloeocapsa</i> sp., <i>Phormidium</i> sp., <i>Aphanolthece</i> sp., <i>Lyngbya</i> sp.	MC	Over 200,000 grebe mortalities	Carmichael and Li (2006)
1999–2002	South Queensland and Myall Lakes area of New South Wales (Australia), and north-east and central FL (USA)	N/S	MCs CYN ATX-a	Human: ear, eye, gastrointestinal, respiratory, cutaneous symptoms—epidemiological study	Stewart et al. (2006b)
2000	Mymensingh district (Lake Ishakha, Brahmaputra River, BAU Pond, pond at Mymensingh city, BFRI Pond, Sutiakhali Pond, Bailor Pond, Kalirbazar, Chattrapur Pond), Bangladesh	<i>A. crassa</i> , <i>A. spiroides</i> , <i>Aph. flos-aquae</i> , <i>Cyanodictyon imperfectum</i> , <i>M. aeruginosa</i> , <i>Aphanocapsa</i> sp., <i>M. botrys</i> , <i>M. flos-aquae</i> , <i>M. natans</i> , <i>M. wiesenbergii</i> , <i>Snowella litoralis</i>	MCs	Fish mortality and bad odours; humans: eye and skin irritation; allergic reactions	Affan et al. (2015)
2000	Drainage ditch Grimstad, Norway	N/S	MC	Acute cyanobacterial hepatotoxicosis in a wild roe deer (<i>Capreolus capreolus</i>)	Handeland and Østensvik (2010)
2000–2004	Lake Champlain, USA	N/S	ATX	Deaths of 2 dogs	Boyer (2008)
2001	Donaña Wetland National Park, Spain	N/S	MC	Mortality of several hundred greater flamingo chicks	Alonso-Andicoberry et al. (2002)

Table 5 (continued)

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
2001	Central and Northwest Queensland, Australia	<i>C. raciborskii</i>	CYN	In two separate poisoning incidents 55 cows were lethargic and recumbent for 3 or 4 days antemortem, with hepatocyte degeneration and necrosis, nephrosis and multifocal cardiomyopathy. Cattle deaths	Shaw et al. (2002)
2002	Eel River, Humboldt County, CA, USA	<i>Anabaena</i> sp., <i>Lyngbya</i> sp., <i>Planktothrix</i> sp.	ATX-a	Deaths of 3 dogs	Puschner et al. (2008)
2002	Golf course Pond, Milwaukee, WI, USA	<i>A. flos-aquae</i>	ATX-a	Humans: 17-year-old developed nausea, vomiting, progressed to “shock” and “seizure”, acute heart failure; death occurred 48 h after exposure A companion boy who also swallowed some of the pond water while swimming later became sick with severe diarrhoea and abdominal pain but survived. 3 other boys who had not been fully submerged in the water, developed only unspecified minor symptoms Dog deaths	Behm (2003), Carmichael et al. (2004), Furey et al. (2005) Cadel-Six et al. (2007)
2002–2005	Tarn River, South France	<i>Oscillatoriales</i> , <i>Pseudanabaena</i> , <i>Geitlerinema</i> , <i>Oscillatoria</i>	ATX-a HomoATX-a		
2002–2006	Sassafras River, tidal estuary of Chesapeake Bay, USA	<i>Synechococcus</i> sp.	MC	Reported waterfowl deaths	Tango and Butler (2008)
2002–2003	Four Lakes (Lake Salajarvi, Lake Iso-Kukkanen, Lake Lapinjarvi, Lake Iso-Torava), Finland	<i>A. lemmermannii</i> , <i>Aphanizomenon</i> sp., <i>Aph. flos-aquae</i> , <i>M. aeruginosa</i> , <i>M. flos-aquae</i> , <i>M. wessenbergii</i>	STX MC	Humans: symptoms of fever, eye irritation, abdominal pains, and skin rash were reported in children aged 2–10 years after exposure to the water	Rapala et al. (2005)
2003	Lake Sompanen, Finland	N/S	STX	Humans: Seven young people: “extensive” generalized rash	Rapala et al. (2005)
2003	La Loue River (Jura region), France	<i>Lyngbya</i> sp., <i>Oscillatoria</i> sp., <i>Oscillatoria</i> cf. <i>limosa</i> , <i>Phormidium</i> sp., <i>Phormidium favosum</i> , <i>Pseudanabaena</i> sp.	ATX-a	Death of 2 dogs	Gugger et al. (2005)

Table 5 (continued)

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
2003	Reservoir Marechal Dutra, Brazil	<i>C. raciborskii</i> , <i>M. aeruginosa</i>	MC	Mass fish mortality	Chellappa et al. (2008)
2003–2004	Lake Rototi, New Zealand	<i>A. circinalis</i> , <i>A. lemmermannii</i> , <i>A. planktonica</i> , <i>M. aeruginosa</i> , <i>M. botrys</i>	MC	MC in rainbow trout muscle tissues and in freshwater mussels	Wood et al. (2006)
2003–2004	Lake Rotoehu, New Zealand	<i>Microcystis</i> spp., <i>M. panniformis</i> , <i>Anabaena</i> spp.	MC	MC in rainbow trout liver and muscle tissues	Wood et al. (2006)
2004	Donaña Wetland National Park, Spain	<i>M. aeruginosa</i>	MC-LR equiv.	Thousands of fish, at least 6000 birds (47 species), including endangered species such as the <i>Marmaronetta angustirostris</i> and <i>Oxyura leucocephala</i> , died within 2 weeks	Lopez-Rodas et al. (2008)
2004	Lake Kegonsa State Park, WI, USA	<i>Anabaena</i> , <i>Microcystis</i> , <i>Aphanizomenon</i>	UR	Death of Labrador dog	Novak and Sensenbrenner (2004), Williams (2004)
2004	Lake Buccaneer Bay's, NE, USA	<i>Anabaena</i> sp.	MC	Death of 2 dogs	Walker et al. (2008)
2004	Lake Neatahwanta, NY, USA	<i>Anabaena</i> sp.	ATX-a	Dog death	Goldberg (2004)
2004	Reservoir San Roque, Cordoba, Argentina	Cyanobacterial blooms	MC-RR (in liver, gills, and muscle of all exposed and wild fish)	The amount of MC-RR in muscle of <i>Odontesthes bonariensis</i> exceeded the value suggested by WHO to be safe	Cazenave et al. (2005)
2004	Lake Pawnee, NE, USA	N/S	MC	50 calls about skin rashes, lesions, blisters, vomiting, headaches, and diarrhoea after swimming or skiing; death of 5 dogs	Walker et al. (2008)
2005	Pond near Harlingen TX, USA	<i>M. aeruginosa</i>	MC-LR	Mortality of white shrimp in aquaculture ponds	Zimba et al. (2006)
2005	Hutt River, New Zealand	<i>Phormidium autumnale</i>	ATX-a HomoATX-a	At least five dogs died rapidly after contact with water	Wood et al. (2007)
2006	Lake Anderson, WA, USA	<i>Anabaena</i> , <i>Microcystis</i> , <i>Aphanizomenon</i>	ATX-a	Death of 2 dogs	Jacoby and Kann (2007)
2006	Lakes Chamo, Langano, Ziway, Tana and Koka, Ethiopia	<i>M. aeruginosa</i> , <i>Microcystis panniformis</i> , <i>A. spiroides</i> , <i>Cylindrospermopsis</i> spp.	MC	Deaths and illnesses of wild and domestic animals	Willén et al. (2011)

Table 5 (continued)

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
2007	Water impoundments in the Kruger National Park (South Africa) 4 dams (Nhlanguzani, Mpanamana, Makholola, and Sunset)	<i>M. aeruginosa</i>	MC	Wildlife mortalities around Nhlanguzani Dam (15 white rhinos, eight zebras, and five blue wildebeest) and Sunset Dam (one white rhino and six impala)	Masango et al. (2010)
2007	Reservoir Salto Grande Dam, Argentina	<i>Microcystis</i> spp.	MC	Humans: acute poisonings of a man; nausea; abdominal pain and fever; dyspnea and respiratory distress; atypical pneumonia and liver failure	Giannuzzi et al. (2011)
2008	Waitaki River, New Zealand	<i>Phormidium</i> sp.	MC-LR	Dog died soon after ingesting benthic "algal" mat material. First known instance of a benthic MC-producing species causing an animal death in New Zealand	Wood et al. (2010)
2009	Lake in Ortiz de Ocampo, La Rioja, Argentina	<i>M. aeruginosa</i>	UR neurotoxins, hepatotoxins	Deaths of 72 cows in 24 h	Claro et al. (2010)
2008–2009	Lake Vico, Italy	<i>Planktothrix rubescens</i>	MC	MC contamination in five fish species	Bruno et al. (2012)
2011	Lake Ilmeer, Netherlands	<i>Phormidium</i> sp.	HomoATX-a ATX-a	Dogs: neurotoxicity, death of three dogs	Faassen et al. (2012)
2011	Lake Amstelmeer, Netherlands	<i>M. aeruginosa</i>	MC-LR	Dogs: 3 dogs died	Lüring and Faassen (2013)
2011–2013	Lake Milford, KS, USA	<i>M. aeruginosa</i>	MC	Dog deaths; vomiting; inappetence; weakness; lethargy. Death of dogs Humans: human illnesses (eye and upper respiratory tract irritation, rash and gastrointestinal problems)	Van der Merwe et al. (2012), Sebbag et al. (2013), Trevino-Garrison et al. (2015)
2012–2013	Lake Aleksandrovac, Serbia	<i>C. raciborskii</i>	CYN	Fish-kill	Đorđević et al. (2015)
2014	Lake Vistonis, Greece	<i>Aph. favaloroi</i>	STX NSTX	Massive fish kill	Moustaka-Gouni et al. (2017)
2015	Carrasco Beach, Montevideo, Uruguay	Intense bloom; <i>Microcystis</i> (predominant)	MC [D-Leu1]MC-LR	Human family, after swimming: self-limited gastrointestinal symptoms, except for child who was admitted to hospital with extensive liver damage, diarrhoea, vomiting, fatigue, and jaundice. First known case of liver transplant after MC exposure.	Vidal et al. (2017)

Table 5 (continued)

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
2016	Reservoir Karla, Greece	<i>Anabaenopsis elenkinii</i> , <i>Planktothrix</i> spp., <i>C. raciborskii</i> , <i>Aph. javalarii</i>	MC STX CYN	91 immature Dalmatian pelicans found dead	Papadimitriou et al. (2018)
2017	Lake Tegel, Berlin, Germany	<i>Fontinalis antipyretica</i> with high amounts of <i>Tychonema</i> sp.	ATX	12 dogs showed signs of acute neurotoxicosis after swimming in or drinking from lake, several of the affected dogs died This is the first report of a dense population of <i>Tychonema</i> sp. in stands of <i>Fontinalis</i> resulting in high ATX contents	Fastner et al. (2018)
N/S	Australia	<i>M. aeruginosa</i>	MC	Sheep: hepatotoxicity; neurotoxicity	Jackson et al. (1986)
N/S	Finland	<i>N. spumigena</i>	NOD	Dogs: hepatotoxicity	Persson et al. (1984)
N/S	Finland	<i>P. agardhii</i>	MC	Waterfowl, fish, muskrats: hepatotoxicity	Eriksson et al. (1986)
N/S	Norway	<i>M. aeruginosa</i>	MC	Cattle: hepatotoxicity	Skulberg (1979)
N/S	Australia	<i>A. circinalis</i>	STX	Humans: Severe respiratory distress in water-skiers, inhaling water spray	Falconer (1996)
N/S	Darling River, Australia	<i>A. circinalis</i>	N/A	10,000 livestock died	Falconer (1998)
N/S	N/S (reservoir), UK	N/S	MC	One man: hepatic dysfunction in a 39-year-old who was windsurfing in a MC-contaminated reservoir	Probert et al. (1995)
Haemodialysis					
1996	Reservoir Tabocas (Caruaru's water source), northwest Brazil	<i>Aphanizomenon</i> sp., <i>Oscillatoria</i> sp., <i>Microcystis</i> , <i>Anabaena</i> , <i>Anabaenopsis</i> , <i>Cylindrospermopsis</i>	MC-LR MC-YR MC-AR CYN	Humans: 52 deaths out of 131 hemodialysis patients after receiving dialysis treatment using chlorinated water. Tinnitus; blindness; nausea; gastrointestinal disease; vomiting; liver damage; deaths	Jochimsen et al. (1998), Pouria et al. (1998), Carmichael et al. (2001), Azevedo et al. (2002)
2001	Rio de Janeiro, Brazil	<i>Anabaena</i> , <i>Microcystis</i>	MC	Humans: visual disturbance; tinnitus; nausea; vomiting; liver damage	Bláha et al. (2009)

Table 5 (continued)

Year	Location (source)	Cyanobacteria	Toxin(s)	Health outcomes	References
Terrestrial environments 2013–2014	Doha, Qatar	Terrestrial cyanobacterial species	MC ATX-a(S)	Four dogs showed signs of severe neurotoxicity after recreation in desert environments and consumption of rainwater accumulated in natural depressions	Metcalf et al. (2012), Chatziefthimiou et al. (2014)

ATX- α anatoxin-a, ATX- α (S) anatoxin-a(S), CYN cylindrospermopsin, MC microcystins, NOD nodularin, N/A not analysed cyanobacterial toxic metabolites, N/S not stated, NSTX neosaxitoxin, STX saxitoxins, UR unknown reasons (group of cyanotoxins was not specified)

water from a newly built dam reservoir contaminated with cyanotoxins (Teixeira et al. 1993; Metcalf and Codd 2004). An early case of MC poisoning occurred in northwest England in 1989, when a group of 20 army recruits was carrying out canoeing and swimming exercises in Rudyard Lake, where a *Microcystis* scum occurred. After being in contact with, and ingesting cyanotoxin-containing scum and water, 10 of 20 soldiers became ill, showing symptoms of gastroenteritis, sore throat, blistering in and around the mouth, vomiting, abdominal pain, fever, pulmonary consolidation and diarrhoea (Turner et al. 1990). Investigations have shown similar blooms in a number of other lakes, reservoirs, ponds and rivers throughout the world (Table 5), and as a result, most of those affected were temporarily closed for recreational use. In Australia, during the summer of 1989/1990, major blooms of *Anabaena*, *Microcystis* and *Nodularia* occurred in water storage reservoirs, rivers and natural lake systems. It was likely that the inhalation route was to some extent involved in the Rudyard and Hollingworth Lake incidents (Turner et al. 1990; Codd et al. 1999). While the toxicity of MCs via inhalation has not received as much attention as via oral exposure, available evidence indicates that nasal exposure in rodents has a toxicity close to that of intraperitoneal injection, and some 10–50 times greater than via oral administration (Fitzgeorge et al. 1994). In Wisconsin, USA, a case was reported where a teenage boy, who was diving in a golf course pond with heavy scums of toxic *Anabaena flos-aquae*, died; exposure to ATX-a was a likely cause (Carmichael et al. 2004). Additionally, in Australia, several cases have been reported of severe respiratory distress in water-skiers, who were inhaling water spray containing *A. circinalis*, a STX producer (Falconer 1996). A tragic case of cyanotoxin poisoning, including 52 human fatalities occurred in the town of Caruaru, Brazil in 1996, after intravenous exposure to large amounts of MCs through ineffectively treated water during haemodialysis (Jochimsen et al. 1998; Pouria et al. 1998; Carmichael et al. 2001; Azevedo et al. 2002). The lake supplying the haemodialysis clinic with raw water for treatment had a history of cyanobacterial bloom development and a bloom occurred at the time of the intoxications. MCs and CYN were present in the clinic water treatment system, while MCs were also detected in patient serum and liver tissue. Furthermore, histological inspection of liver tissue uncovered similar histopathological changes as previously seen in animals exposed to MCs. After this outbreak of this “Caruaru Syndrome”, cyanobacteria and their toxins were incorporated into new Brazilian regulations for drinking water quality. A recent European case involved 70,000 water-users in Serbia who were potentially exposed to MCs through their drinking water. In December 2013 an intensive bloom of *Planktothrix rubescens* was observed in the Vrutci Reservoir which served as the drinking water source for the city of Užice, Serbia. *Planktothrix* filaments

were soon noticed in the finished drinking water and the use of the tap water was restricted. While the MC-LR concentration in the finished water was below the WHO provisional guideline value ($1 \mu\text{g L}^{-1}$) several MCs were detected by LC–MS/MS (liquid chromatography with tandem mass spectrometric detection methods) in the reservoir biomass and demethylated MC-RR was also found in the tap water. A questionnaire and epidemiological studies indicated an elevated occurrence of digestive tract and skin diseases in the exposed population and a connection of symptoms to the exposure to cyanobacterial bloom material was deemed plausible (Svirčev et al. 2017b).

The earliest known experimental investigation following (and confirming) a cyanobacterial poisoning episode involved that of animals and was performed by Francis (1878) at Lake Alexandrina, South Australia. In this study, Francis was able to reproduce the signs of pathology and the time course leading to the deaths of sheep after drinking scum containing *Nodularia spumigena* by orally dosing healthy sheep using the scum. The inference that the *Nodularia* scum contained a hepatotoxic factor was consistent with the discovery of NOD in such material over a hundred years later (Francis 1878; Codd et al. 2015b). Numerous cases of animal poisonings associated with cyanobacterial blooms, and including likely causality by cyanotoxins, have since been reported throughout the world. Most of these have been associated with *Microcystis* spp., *Anabaena* spp., *Aphanizomenon flos-aquae*, *Planktothrix* spp. and

Cylindrospermopsis spp. (e.g. Thomas et al. 1998; Saker et al. 1999; Shaw et al. 2002; Table 5). Some reports have referred to large numbers of affected animals, rapid disease progression (within minutes), and deaths (e.g. McLeod and Bondar 1952; Rose 1953; Codd et al. 1995; Table 5). Some of the biggest and most frequent episodes of animal intoxication with cyanotoxins appear to have occurred in Australia, where about 10,000 livestock died following a large bloom of *A. circinalis* in the Darling River (Falconer 1998). Some animals appear to be attracted to cyanobacteria in water, and to dried crusts and mats on shorelines (Codd et al. 1992; Stewart et al. 2008), including an apparent preference for *M. aeruginosa* scum over clean drinking water (Lopez-Rodas and Costas 1999). Livestock poisonings have even occurred under environmental conditions considered unfavorable for cyanobacterial blooms, such as cold temperatures and low nutrient concentrations, e.g. in a Michigan, USA, pond during cold weather (Fitzgerald and Poppenga 1993); and in a Georgia pond during mid-November (Frazier et al. 1998). However, most of the animal intoxications associated with cyanobacteria and cyanotoxins appear to have occurred during/after conditions favourable for cyanobacterial mass accumulation (Huisman et al. 2018), including higher temperature, elevated nutrient concentrations and low water flows. An early indication of these conditions and associated animal mortalities was provided by Kirkby (1672) who reported cattle, dog and poultry deaths between June and August at the Tuchomskie Lake in northern Poland, after

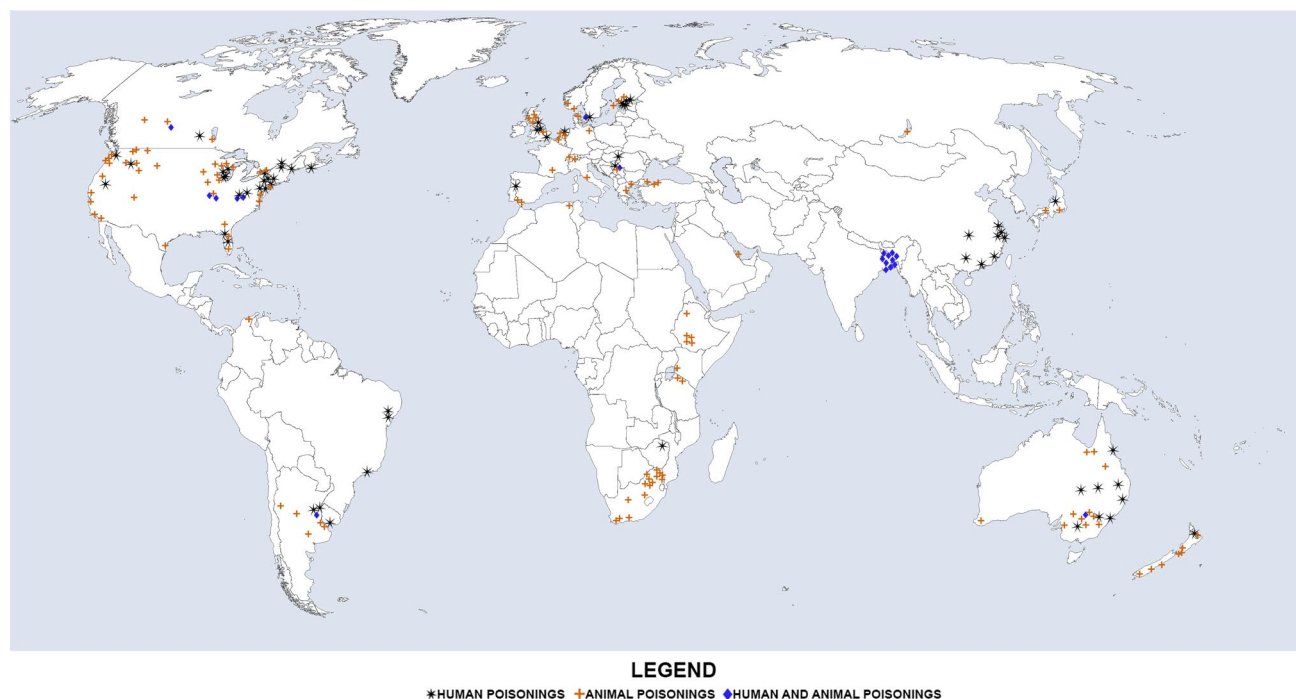


Fig. 10 Geographical distribution of human and animal poisonings associated with cyanobacteria or cyanotoxins

drinking when buoyant green biomass was concentrated along the shoreline by an onshore wind. Nutrient concentrations may also have been high in the lake since this was a fishery serving a nearby monastery (Kirkby 1672; Codd et al. 2015a). The incomplete historical record of cyanobacterial mass population and cyanotoxin occurrences in waterbodies is likely to be supplemented by the promising application of specific chemical and molecular genetic methods to dated profiles of sediments (e.g. Ceglowska et al. 2018).

The cyanotoxin poisoning cases have been assembled and assessed to gain more insight into their distribution, reasons for their occurrences, and from which areas of the world they have originated. The database is summarized and discussed in the next section.

Summary and interpretation of reported findings on cyanotoxin poisonings throughout the world

Based on the publications included in the database, there were 183 recorded cyanotoxin poisonings of humans and animals reported worldwide. Their distribution is shown in Fig. 10.

From the gathered data from each continent, it is evident that most poisoning cases were reported in North and Central America, followed by Europe and Australia/New Zealand (Figs. 10 and 11).

There were 20 poisoning cases (out of 179 ecosystems with intoxications worldwide) described in *Africa* which

accounted for 11% of the total number of poisonings reported globally (Fig. 11). Among them, humans were only known to have been exposed to cyanotoxins in one case, while the remainders were animal poisonings, with 19 cases resulting in deaths. The number of poisonings was much lower than the number of waterbodies found to contain cyanotoxins. The highest number of waterbodies found to contain cyanotoxins (24 and 17) was found in South Africa and Nigeria, where 58% of the poisonings were documented in South Africa, and none in Nigeria. Furthermore, three waterbodies from Algeria and Zimbabwe recorded one poisoning case in each waterbody (Fig. 3). In some ecosystems, several cyanotoxins were found, but the number of detected poisonings was small (APPENDIX S5). Most of the reported poisonings were associated with exposure to MCs (60%; 15 out of 25 cases of the cyanotoxins involved in poisonings in Africa). NODs and ATXs were also assumed to be responsible for cyanobacterial poisoning in Africa (8% and 4%, respectively). In 12% of the poisoning cases, there was a lack of information about the chemical nature of the cyanobacterial compounds and they were designated as UR (unknown reason). Furthermore, in 16% of the poisoning cases in Africa, analyses for cyanotoxins were not performed and they were designated as N/A (not analysed).

Compared to the number of waterbodies with cyanotoxin(s) detected in Asia (131), the number of poisonings described was very low (16) (APPENDIX S2). Poisoning cases were documented in China, Turkey, Japan, Bangladesh, Qatar and Russia. MCs appeared to be the most common cause of cyanobacterial poisoning in Asia (87%; 20 out of the 23 cyanotoxin cases involved in poisonings in

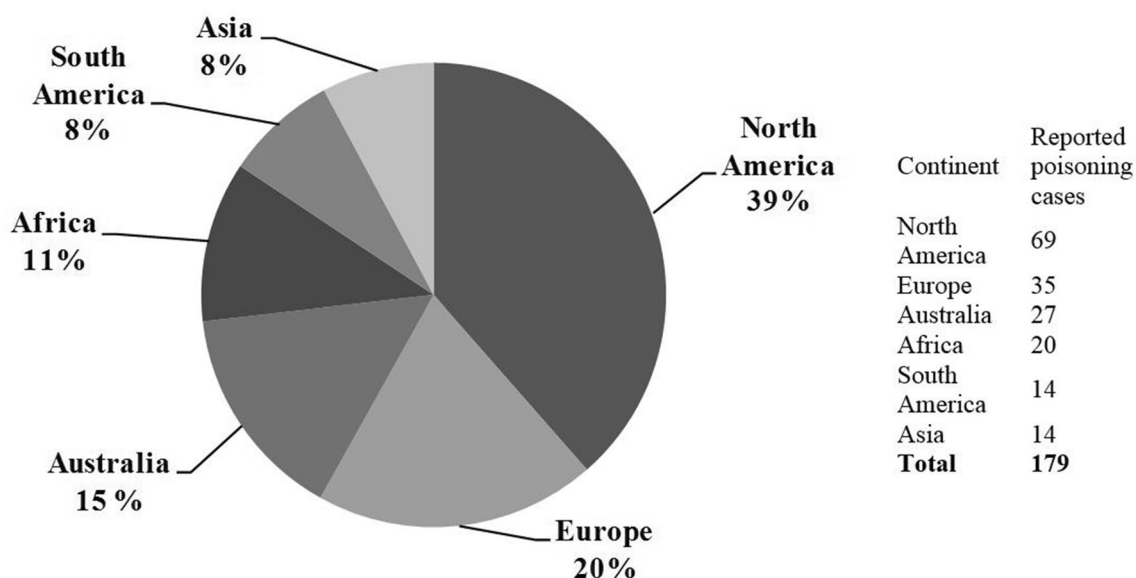


Fig. 11 Distribution of reported poisoning cases worldwide including identification of cyanotoxins

Asia), whilst the presence of ATXs was detected in 4% of the waterbodies examined. The remaining cases (9%) described in the reports and literature from Asia did not include necessary analyses for cyanotoxins (N/A). However, NODs, STXs and CYNs were detected in Asian waterbodies, suggesting that they may have already caused health problems in humans and animals in Asia and may do so in the future.

In Australia including New Zealand, 15% (27 out of 179 ecosystems with intoxications worldwide) of the total number of worldwide poisonings was reported (Fig. 11). As a likely cause of poisonings in Australia including New Zealand, members of all five of the most commonly recognized cyanotoxin types were detected, including MCs (29%; 8 out of 28 cases of cyanotoxins involved in poisonings in Australia including New Zealand), STXs (18%), CYN (11%), ATXs (11%) and NOD (4%). The data from Australia with New Zealand also show that 18% of the cyanotoxin episodes were apparently caused by uncharacterized cyanotoxins (UR), suggesting a lack of data regarding cyanotoxin detection in some acute cases. In comparison with size of the country, a high number of waterbodies with identified cyanotoxins have been reported from New Zealand: 87 (APPENDIX S6) with 8 associated poisoning incidents (Fig. 10). The finding of this high number probably reflects the relatively intensive cyanotoxin research in progress in New Zealand.

In comparison with the rest of the world, much of the research on cyanobacterial blooms and cyanotoxins has been done in **Europe**, which has undoubtedly contributed to a relatively detailed understanding of cyanotoxin distribution throughout this continent. Most of the reported poisoning cases were detected in freshwater ecosystems in the UK, but also in Finland, the Netherlands, France, Greece, Norway,

Serbia, Spain, Sweden, Switzerland, Belgium, Denmark, Hungary and Italy. In Europe, all of the most commonly found types of cyanotoxins have been found to be associated with negative health effects in humans and animals. MCs were inferred to be responsible for poisoning in 32% (10 out of 31 cyanotoxins cases involved in poisonings in Europe) of the reported cases, the same as ATXs with 32%, while NOD and CYN were responsible for only 1 and 2 poisoning cases (3% and 6%), respectively. Only in 10% of the cases were the chemical structures of compounds, inferred to be responsible for the poisonings, not specified (UR), and in 3% of the cases appropriate toxicity tests were not applied (N/A).

In comparison to the number of waterbodies with detected cyanotoxin(s) in North America and Central America (204), the number of poisonings described as related to cyanotoxins was the highest (39%; 69 cases out of 179) (Fig. 11; APPENDIX S4). Most of the poisoning cases were detected in the USA, with relatively few in Canada. Out of all poisonings, MCs were inferred to have caused 27% (18 out of 67), followed by 19% of the intoxications being attributed to ATXs. CYN was present in a very small proportion of the cases (1%) involving animal and human poisonings. NODs and STXs were not found in any of the cyanobacterial poisoning cases reported from North America. On the other hand, the presence of STXs (of cyanobacterial origin) and CYN was detected in numerous freshwater ecosystems; therefore, these cyanotoxins could become a possible threat to animal and human health in the future. In about 30% of the North and Central American human and animal health incidents, no analyses for particular cyanotoxins are available (N/A), a consequence, perhaps of the early reporting of such incidents before the availability modern analytical cyanotoxin methods. Thus, a high proportion of

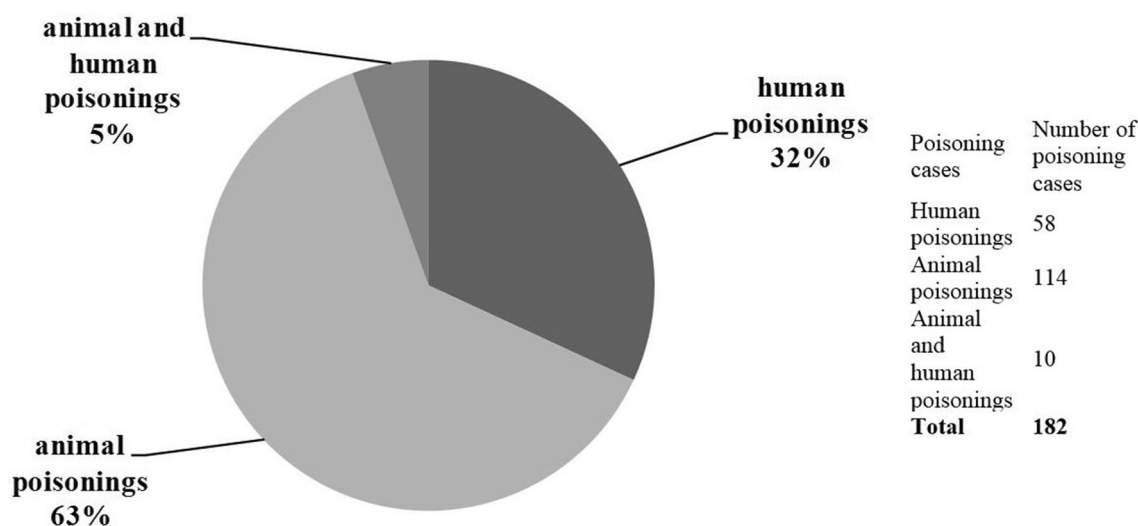


Fig. 12 Percentage ratio of reported cases of human and animal poisonings caused by or associated with cyanotoxins

the number of poisoning cases (22%) is classified as due to unknown reasons (UR).

Besides Asia, a low percentage of poisoning cases reported to be associated with cyanobacterial mass populations is apparent in South America (8%, 14 cases out of 179) (Fig. 11). The highest number of waterbodies with reported cyanotoxin episodes has been in Argentina (8 cases), with further cases in Brazil, Uruguay and Colombia (Fig. 10). MCs were inferred to be responsible for about half of the cyanobacterial poisonings in South America (53%; 8 out of 15), and CYN was present in a smaller percentage of the events (7%). About 20% of the reported intoxications cannot be attributed to particular toxins (UR) and no toxicity tests were performed (N/A) in a similar percentage of cases. Although both ATXs and cyanobacterial STXs were detected in freshwater environments in South America, so far, there appear to be no reports of poisoning caused by these cyanotoxins. However, in the future, STXs from cyanobacteria could raise concern regarding potential cyanotoxin poisoning, being the second most commonly found group of cyanotoxins in South America.

After examination of the data on poisonings associated with exposure to cyanobacterial mass populations (blooms, scums and mats), wildlife and domestic animals were found to have been the most common victims (63%; 114 out of 182) (Fig. 12). In 32% (58 out of 182) of poisoning cases, the exact cause was not determined (UR and N/A), but cyanobacterial blooms, scums and mats were reported. About half of these cases were reported from North America. Although a range of human illnesses, from mild to severe, have been reported, actual human deaths associated with exposure to cyanobacteria or cyanotoxins have been reported only from South America, North America and Asia, with six known incidents in total, while animal deaths (usually domestic animals, pets, and fish) were reported in about 100 separate cases throughout the world. More than one-third of the cases involving animal deaths were reported in North America.

In addition to the attraction to cyanobacterial mats and dried crusts, perhaps due to cyanobacterial taste and odour compounds, dogs appear to be particularly vulnerable to cyanotoxin poisoning: after swimming in cyanobacterial blooms and scum, the animals may concentrate and ingest the material by licking and cleaning their legs and coats (Codd et al. 1992). Furthermore, domestic dogs are very common victims of toxic cyanobacterial blooms because they will swim in, or drink contaminated water that people would otherwise avoid. Reports of early detection of cyanotoxicosis in dogs can provide an important alert to local and national environmental and public health authorities regarding potential human exposure to cyanotoxins (Backer et al. 2013). Humans appear to have been less often affected than animals (32%; 58 out of 182): usually after swimming or

after accidentally ingesting contaminated water that resulted in respiratory/gastrointestinal problems, while in 5% of the reports both humans and animals were affected.

The finding that MCs (42%; 79 out of 189) have been the cyanotoxins most commonly reported in-, and causally related to- cyanobacterial intoxications is not surprising since the cyanobacterial genera which produce these heptapeptides (e.g. Fig. 1) are also of worldwide distribution (Huisman et al. 2018). NOD has been least often causally implicated (2%) in the reported cases of cyanobacterial poisoning cases. 15% of all the poisoning cases were assigned due to UR and 17% due to N/A (APPENDIX S1 - S6). It is acknowledged that a large number of the cases regarding cyanobacterial poisoning were documented in the previous Century, when specific methods for cyanotoxin analysis were not widely available and before the development of modern methods with improved specificity and quantification, with lower minimum detection limits (Meriluoto et al. 2017). Insufficient veterinary training and awareness in the public health community necessary to recognize cyanotoxin poisonings, as well as limited access to validated, cost-effective diagnostic tests may also have contributed to lack of data of these important health events (Elder et al. 1993; Backer et al. 2013).

Despite improvements in the awareness of the symptoms and consequences of exposure to cyanobacterial mass populations and cyanotoxins, current and projected increases in cyanobacterial populations due to increasing anthropogenic pressures and climate change (Huisman et al. 2018) suggest that further reports of poisoning events will occur. Guidelines and regulations in developed countries can promote the regular and pro-active monitoring of freshwater cyanobacterial populations and (some) cyanotoxins, but the actual number of poisoning cases in countries with no such guidelines or regulations could be higher than hitherto reported. The gathered data suggest that future research should be orientated towards the creation of robust and precise, yet inexpensive and more widely available, analytical techniques for cyanotoxin detection, as well as toward better understanding of other potential toxic cyanobacterial compounds that could affect human and animal health, as well as the ecosystem as a whole. Also, further evaluation and analysis of cyanobacterial toxicity in both aquatic and terrestrial environments are of high importance.

Discussion on study limitations and recommendations for further investigations

Cyanobacteria in surface waters are well known for their ability to form toxic blooms, scums and mats which can jeopardize animal and human health (Carmichael 1992,

2008; Codd et al. 1999, 2005a, b; Huisman et al. 2018). The health concerns related to cyanotoxins in addition to the advances in science and technology over the last 25 years have expanded the number of studies in this field. This has further led to a dramatically increased state of knowledge of the cyanotoxins. However, some unavoidable limitations and influencing factors remain:

- **Publications:** the survey is based only on published reports with variable degrees of verification and expert peer review. The reports in general range from papers in refereed journals of international repute, to the “grey literature” of (usually non-refereed) technical and project reports. Since an oral tradition of recognizing cyanobacterial blooms or scums exists (e.g. Griffiths 1938), it is possible that associated health incidents have also occurred but without subsequent publication. The true extent of such events, both historically and today, may thus be greater than evidenced in the literature;
- **Motives for and circumstances applying to publishing reports of cyanotoxins and associated adverse health events:** these have changed versus time. Early investigations may have been mainly prompted by scientific curiosity and by the need to warn water users of perceived health hazards. However, the development of cyanobacterial risk management measures and a duty of care, whether including voluntary guidelines or legislation (Chorus 2012), have increasingly recommended, or specified, cyanotoxin analysis (mainly for MCs), among the measures to be applied in situation assessment. These developments may have inevitably contributed to the growing environmental database of cyanotoxin occurrence around the world;
- **Almost half of the publications (47%; 221 out of 468) originated from Europe (128 out of 468), North and Central America (93 out of 468). Furthermore, published research on cyanotoxins appears to be more limited in Asia (17%; 78 out of 468), South America (13%; 63 out of 468), Africa (12%; 55 out of 468) and Australia including New Zealand (11%; 51 out of 468). The centralization of publication in some of the wealthier countries of the world could be conditioned by the continuing, relatively high cost of equipment and reagents for the analysis of cyanotoxins. The lesser quantity of publications from Asia, South America, Africa, and Australia could be misleading; however, thus more global monitoring studies are needed to fully assess the spatial distribution of toxic cyanobacterial blooms, and particularly of cyanotoxins to help to formulate guidelines and regulations for their risk management;**
- **Analytical developments:** contributions to the global database have occurred during a period of rapid improvements in methods for the extraction, identification and quantification of cyanotoxins and of increases in the availability and dissemination of improved methods (Meriluoto and Codd 2005; Meriluoto et al. 2017). Thus, analyses of environmental samples using modern methods are yielding data which could not have been obtained in earlier studies at the same sites;
- **Infrastructure and financial support:** despite improvements in analytical techniques, access to specialist equipment, technical and interpretative skills (e.g. LC–MS/MS; Meriluoto et al. 2017) and high financial costs will undoubtedly continue to limit cyanotoxin monitoring activity in several countries. Also, the number of researchers and scientific projects dealing with cyanobacteria, i.e. the scientific tradition, varies from country to country, and this has an influence on the quality and quantity of the research;
- **Focus on MCs:** with their potency, persistence and demonstrated causative roles in animal and human intoxications, most cyanotoxin research effort and resources have centred on the toxicology, environmental occurrence and fates of MCs (Metcalf and Codd 2012; Merel et al. 2013a, b; Svirčev et al. 2017b). To what degree the considerably larger database of MC occurrences, versus those for the other cyanotoxins, is due to the greater effort expended on MC analyses is unclear;
- **Studies on cyanotoxins beyond MCs:** MCs have been the primary or only targets in many earlier studies and the number of ecosystems affected by other cyanotoxins may have been underestimated. Ecosystem studies targeting further cyanotoxins are necessary;
- **Continuing lack of validated analytical standards for cyanotoxins and cyanobacterial reference materials:** whilst the availability of analytical standards for cyanotoxins, rather than simply research reagents, to aid environmental identification and quantification has increased over past decades, significant gaps remain, e.g. for neurotoxins including ATX-a(S) and the non-proteinogenic amino acids. This limited availability influences the focus of analytical effort towards cyanotoxins for which standards are more readily available;
- **Focus on aquatic environments:** the widespread development of cyanobacteria in water resources used by humans and animals, plus the focus of research into waterborne intoxications involving cyanobacteria and their toxins, has led to an overwhelmingly aquatic database. However, cyanobacteria are also common inhabitants of terrestrial habitats, with mass populations occurring as, e.g. biocrusts and rock varnishes, in loess formations and in symbioses (Whitton 2012; Svirčev et al. 2013a). Few reports are available on cyanotoxins in terrestrial environments, although examples of MCs in cyanobacterial desert crusts in Qatar (Metcalf et al.

2012) raise the likelihood of human exposure to wind-blown cyanotoxins.

- It is necessary to point out that this survey was based on reports generated over many years. Over this period, the following influential factors have been developing: (a) understanding and recognition of signs of cyanobacterial poisoning; (b) reporting systems; (c) monitoring and analytical methods—extraction/recovery methods, sensitivity, specificity, applicability in the field, etc. These factors can lead to overestimates and to underestimates. Furthermore, the global distribution of cyanotoxins seems highly likely because (a) cyanobacteria are cosmopolitan; (b) the molecular phylogeny of cyanotoxin genes indicates that the production of MCs (and probably NODs) originated in ancestral cyanobacteria before the branching into the diverse taxa which exist today (Rantala et al. 2004). It should be emphasized that we do not know the true global extent of cyanotoxins and associated poisonings: we are only collating and evaluating the known and reported occurrences of these phenomena. Their true extents are likely to be greater.

Based on the findings from our investigations, the question remains: do blank areas on the maps indicate the absence of cyanobacterial blooms, cyanotoxins and associated intoxications, or an insufficiency of those who are able to recognize, investigate, interpret and report them? Future challenges regarding cyanotoxin distribution in the world should also include answering the question of whether the cyanotoxins are always species-specific or whether they may also be ecosystem-specific, taking horizontal gene transfer into consideration.

Conclusions

An initial database of cyanotoxin global distribution, with a historical overview of the reported associated intoxication cases, has been assembled and assessed. This could be the basis for future collections of reports worldwide. Most countries in which investigations into cyanotoxin occurrence were performed were European (25). MCs were the cyanotoxins detected in two-thirds of the investigated freshwater ecosystems. Lakes were the most abundant of the investigated freshwater ecosystems (520 from 869 freshwater ecosystems in total). The cyanobacterial genera most commonly found were *Microcystis* spp. (669), *Anabaena* spp. (397), *Aphanizomenon* spp. (100), *Planktothrix* spp. (98), and *Oscillatoria* spp. (75), all well known as actual or potential cyanotoxin producers.

References (72%; 337 out of 468) were mostly published after 2000, which is consistent with the unprecedented growth in the analysis, toxinology and ecotoxicology of cyanotoxins. 38% (177 out of 468) of the papers reported

on animal and/or human poisoning cases during the whole of the investigation period, with a lower percentage of references in recent decades (2000–2018; 21%; 70 out of 334) compared to that in the period from the 1950s until the end of the 1990s (77%; 92 out of 119).

Toxic cyanobacterial blooms have affected both animals and humans, with most reports of intoxications resulting in animal deaths. In freshwater ecosystems globally, MCs and ATX were the most commonly identified and causally inferred cyanotoxins in poisoning incidents in which cyanotoxin analyses were performed. All of the investigated types of cyanotoxins were found to have been present in poisoning episodes in Europe, whereas in Asia, this was only the case with MCs. However, almost half of the health incidents associated with exposure to cyanobacteria worldwide have not been accompanied by specific cyanotoxin analysis, indicating a continuing international need for improved awareness, and the sharing of technological capabilities for cyanotoxin identification and quantification.

Whilst some countries or regions have a high density of investigated cyanotoxin-poisoning events, large blank areas on the map, lacking data, are also apparent. The ubiquity of cyanobacteria, their common ability to produce cyanotoxins and the increasing anthropogenic demands upon water resources require further awareness-raising, research and technology transfer to provide a more comprehensive understanding of the distribution and negative impacts of cyanobacterial mass populations and cyanotoxins on freshwater ecosystems and water users.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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