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Cyanobacteria and cyanotoxins in the World: Review

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Abstract
Water bodies of the world are gradually eutrophicated because of human interference in different ways like pesticide use, industrialization etc. The eutrophicated water is the good habitat for the luxuriant growth of algae and bloom forming cyanobacterial species. These blooms are harmful to animals and human being as they produce various toxic metabolites. Many studies have been done to elucidate the factors responsible for cyanobacterial bloom formation and their toxin production. As reported in these studies, factors favourable for cyanobacterial bloom formation are: light intensity, temperature, pH, nutrient in the form of phosphorus and water stability. But it is difficult to find out the factors responsible for cyanotoxin production. Some species of cyanobacteria have the ability to produce varieties of cyanotoxins. The cyanotoxins are neurotoxin, hepatotoxin, dermatotoxin, endotoxin and others. The effects of these toxins depend on the routes of exposure. So the drinking-water operators must beware about the growth pattern and species of cyanobacteria that dominate the bloom, the properties of the cyanotoxins (i.e., intracellular or extracellular), and the most effective treatment processes of these toxins.

Keywords: Cyanobacteria, cyanotoxins, world.

Introduction
Due to eutrophication and climatic changes (Markensten *et al.*, 2010; Paerl and Huisman, 2009) [47, 58] cyanobacterial blooms have increased in marine and freshwater ecosystems worldwide. These blooms severely disrupt the functioning of these ecosystems, affecting animals and human health. The photoautotropic cyanobacteria are found naturally in lakes, streams, ponds, and other surface waters (Paerl and Huisman, 2009) [58]. In suitable environmental conditions, they rapidly multiply in surface water causing "blooms". Carmichael (1992) [12] reported that the obligatory factors responsible for cyanobacterial bloom formation are light intensity, total sunlight duration, nutrient availability (especially phosphorus), water pH, increase in precipitation events and water column stability (whether water is calm or fast-flowing). Under favorable conditions of light and nutrient, some species of *Nostoc*, *Nodularia*, *Anabaena*, *Oscillatoria*, *Aphanizomenon*, *Microcystis*, *Anabeanopsis*, *Planktothrix*, *Cylindrospermopsis*, *Lyngbya*, *Rhaphidiopsis*, *Umezakia*, *Synechococcus*, *Hapalosiphon* and *Schizothrix* produce toxic secondary metabolites known as cyanotoxins (Dadheech *et al.*, 2001; Oberhaus *et al*., 2007; Briand *et al*., 2005; Codd *et al*., 1999; Agrawal *et al*., 2012) [24, 56, 10, 22, 1]. The blooms of BGA consume maximum oxygen and create anoxic condition. The toxins produced by these blooms are usually released into water (extracellular toxins) when the cells rupture or die (Bagchi, 1999) [5]. In most cases, cyanobacterial toxins such as anatoxin-a and the microcystin variants are found intracellularly (approximately 95%) in the cytoplasm and are retained within the cell. These toxins are found during the growth stage of the bloom (United States Environmental Protection Agency, 2012) [68]. However, *Cylindrospermopsis, Aphanizomenon* and *Umezakia* produce cylindrospermopsin, a significant amount of which may be naturally released in to the water by the live cyanobacterial cell; the ratio is about 50% intracellular and 50% extracellular (United States Environmental Protection Agency, 2012, Griffiths and Saker, 2003) [68, 32]. Extracellular toxins may be absorbed by clays, and organic materials dissolve in the water column, which is difficult to remove than the intracellular toxins (Griffiths and Saker, 2003) [32]. Westrick *et al.*, 2010 [71] have reported four classes of Cyanotoxins are reported i.e. microcystins, cyclindrospermopsin, anatoxin-a and saxitoxins. Microcystins are

type of hepatotoxin reported from genera *Microcystis*, *Anabaena*, *Planktothrix*, *Nostoc* and *Anabaenopsis* and this toxin is water soluble. (Westrick *et al.*, 2010) [71]. This review synthetizes the precise information on cyanotoxin and cyanoblooms produced by the species of cyanobacteria, and their prevalence in the world.

Results

Cyanobacterial Blooms

Cyanobacterial blooms causes foul odour and taste of water and thereby deteriorating the water quality (Churro *et al.*, 2012) [18]. Cyanobacteria are widely distributed in all natural ecosystems such as land, soil, fresh water, oceans, estuarine salt lakes, salt marshes, and also in hypersaline salt pans (Fogg *et al.*, 1973) [31]. These organisms respond to eutrophication by the development of massive populations, in the form of blooms, scums and mats (Fogg *et al.*, 1973; Sutcliffe & Jones, 1992) [31, 66]. Since, cyanobacterial bloom can present a range of amenity like change in water quality, production of toxin and ultimately hazards to human and animal health, the mass populations of blooms; scums etc. have attracted the attention of environment agencies, water authorities, human and animal health organizations, (NRA, 1990; NSWBGATF, 1992; Ferguson *et al.*, 1996) [54, 55, 30]. Under favorable conditions of light intensity, nutrient availability (especially phosphorus), temperature, pH and water stability, cyanobacteria can grow rapidly in surface water and cause bloom (Carmichael, 1992; Humbert *et al.*, 2010; Dadheech *et al.*, 2001; Rolland *et al.*, 2010) [12, 36, 62, 24, 61]. In temperate regions, cyanobacterial bloom occur in summer as temperature and light intensity are high, and nutrient removal and water column are stable (Sivonen, 1996) [64]. However, in tropical regions where such conditions prevail throughout the year, blooms can occur at any time and last for a few weeks at a time (Mowe *et al.*, 2014) [51]

Majority of blooms (77%) in Asia and (66%) Africa (Figure 1) is caused by *Microcystis* sp., generally *Microcystis aeruginosa* (Mowe *et al.*, 2014) [51]. This species is dominant in all blooms of India, Turkey, Sri Lanka, Japan, Korea, Thailand, Saudi Arabia and Indonesia (Sangolkar *et al.*, 2009; Albay *et al.*, 2003; Jayatissa *et al.*, 2006; Ueno *et al.*, 1997; Codd *et al.*, 2005a; Mohamed, 2008) [63, 3, 37, 67, 21, 49]. The other bloom forming genera in Asia are *Anabaena*, *Cylindrospermopsis*, *Aphanizomenon*, *Nodularia*, *Synechococcus*, *Oscillatoria* and *Plankthotrix* (Jewel *et al.*, 2003; Codd *et al.*, 2005a; Chorus, 2012; Mowe *et al.*, 2014) [38, 21, 17, 51], *Plankthotrix zahidii* in Vietnam (Ngueyen *et al.*, 2007) [53], *Trichodesmium* formed bloom in India (Desikachary, 1959) [25]. In Africa, the most prevalent genera are *Anabaena* and *Cylindrospermopsis* (Codd *et al.*, 2005a; Mowe *et al.*, 2014) [21, 51], genera *Aphanizomenon*, *Oscillatoria*, *Lyngbya* and *Anabaenopsis* in Kenya, Nigeria, Zimbabwe and Uganda (Kotut *et al.*, 2010; Chia *et al.*, 2009; Kunz, 2011; Poste *et al.*, 2013, Mowe *et al.*, 2014) [40, 16, 42, 59, 51], *Phormidium*, *Nostoc* and *Plectonema* in Nile River blooms of Egypt (Mohamed *et al.*, 2006) [50].

According to Mowe *et al.*, (2014) [51], *Cylindrospermopsis* is the dominant bloom-forming genus in tropical America (South America) and formed 47% of the bloom. In second position, genus *Microcystis* formed bloom in South and Central America (35%). Other bloom-forming genera are *Anabaena*, *Lyngbya*, *Plankthotrix*, *Aphanizomenon* and *Oscillatoria* in Brasilia, Guatemala, Uruguay, Cuba, Argentina (Codd *et al.*, 2005a; Rejmánkova *et al.*, 2011; Lagos *et al.*, 1999; Fabre *et al.*, 2010; Bonilla *et al.*, 2012) [21, 60, 43, 28, 8], *Raphidiopsis* in Brasilia and Argentina (Vieira *et al.*, 2003; Echeniques and Aguilera, 2009) [70, 27], *Cuspidothrix* in bloom of Uruguay (Codd *et al.*, 2005a) [21]. Dominant bloom-forming genera in North America are *Microcystis* (*Microcystis aeruginosa)* and *Anabaena* (Codd *et al.*, 2005a) [21], *Cylindrospermopsis* and *Plankthotrix* in United States and Canada (Chorus, 2012) [17], *Aphanizomenon* in Canada (Chorus, 2012) [17] and *Anabaenopsis* in United States (Manganelli *et al.*, 2012) [46].

Codd *et al*. (2005a) [21] reported that *Nodularia* and *Microcystis* were the dominant bloom-forming genus in Australia and New Zealand, *Cylindrospermopsis raciborskii* is in tropical Australia, accounting for 87.5% of blooms (Mowe *et al.*, 2014) [51], *Anabaena*, *Aphanizomenon*, *Oscillatoria*, *Nostoc*, *Plankthotrix* and *Scytonema* in Australia and New Zealand (Codd *et al.*, 2005a; Wood *et al*., 2011; Smith *et al*., 2011) [21, 65, 72, 65].

In Europe, cyanobacteria bloom is dominated by *Microcystis* and *Planthotrix* (Briand *et al*., 2008; Sabart *et al*., 2010) [9, 62], *Anabaena* and *Aphanizomenon* in Europe, *Nodularia* in Denmark and Poland; *Cylindrospermopsis* in Greece and Portugal; *Phormidium* in France; *Oscillatoria* in Italy and Switzerland; and *Woronichinia* in Netherlands (Chorus, 2012; Codd *et al*., 2005a; Manganelli *et al*., 2012) [17, 21, 46].

Cyanotoxins

Some species of cyanobacteria have the ability to produce toxins. The difficulty is that, potential toxin producing cyanobacterial strains may be present, but they may not be producing toxin in all season (Leitao and Coute, 2005; Westrick *et al*., 2010, Sabart *et al*., 2010) [44, 71, 62]. Visual identification by a trained taxonomist or molecular analysis is needed for proper identification of toxin producing cyanobacteria (Dittmann *et al*., 1997). In each case, quantitative cyanotoxin analysis is necessary to know whether the cyanobacteria are actually producing the toxin. Toxic bloom forming cyanobacteria are *Nostoc*, *Nodularia*, *Anabaena*, *Oscillatoria*, *Aphanizomenon* and *Microcystis* species which are found in freshwater, brackish and marine waters, associated with planktonic and benthic producer cells (Table 1), throughout the world (Carmichael, 1992, 1997; Codd, 1995, 1998; Sivonen, 1996; Dadheech *et al*., 2001) [12, 14, 19, 20, 64, 24]. Other toxin producing species are *Anabeanopsis*, *Planktothrix*, *Cylindrospermopsis*, *Lyngbya*, *Rhaphidiopsis*, *Umezakia*, *Synechococcus*, *Hapalosiphon* and *Schizothrix* (United States Environmental Protection Agency, 2012; Oberhaus *et al.*, 2007; Briand *et al*., 2005; Codd *et al*., 1999; Agrawal *et al*., 2012) [68, 56, 10, 22, 1]. The cyanotoxins are neurotoxins (affect the nervous system), hepatotoxins (affect the liver), and dermatoxins (affect the skin) (Bagchi, 1999) [5]. Toxin production varies between species within a single genus, and between laboratory isolates of a particular species (Codd *et al*., 1999) [22]. Cyanotoxins are: microcystin, cylindrospermopsin, nodularin, anatoxin-a, saxitoxin, lyngbyatoxin, aplysiatoxin, endotoxin and other LPS (Table1). *Oscillatoria* and *Anabaena* both produce four (4) types of toxins. *Microcystis*, *Lyngbya*, *Aphanizomenon* and *Cylindrospermospsis* produce three (3) types and the rest species produce one type of toxin (Figure 1).

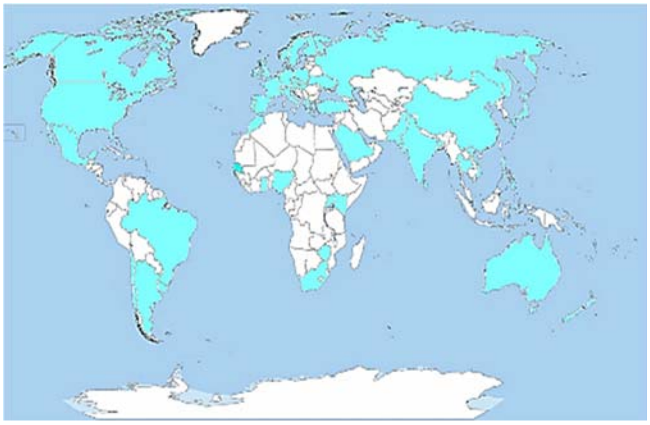

Fig 1: Blue color part in the world map represent studies on cyanobloom and cyanotoxin

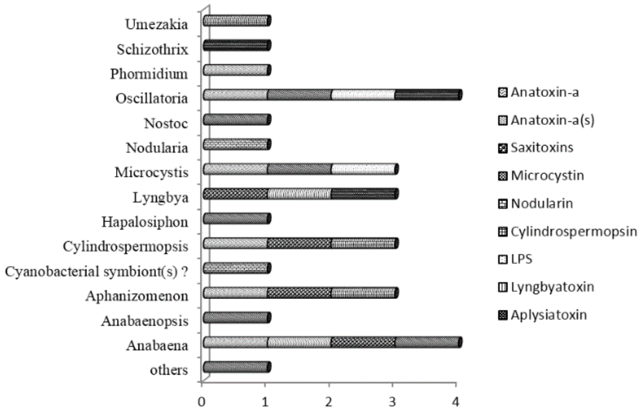

Fig 2: Cyanotoxins producing genera and the types of toxins

Table 1: Sources and types of cyanobacterial toxins

	Toxin	Producer genera	Habitats
Neurotoxins	Anatoxin-a	*Anabaena, Oscillatoria*	F, B
		Microcystis, Phormidium	F
		Cylindrospermum, Aphanizomenon	F, B
	Anatoxin-a(s)	*Anabaena*	F
	Saxitoxins	*Aphanizomenon, Anabaena, Lyngbya, Cylindrospermopsis*	F
Hepatotoxins	Microcystin	*Microcystis, Anabaena*	F, B
		Oscillatoria, Nostoc	F, B
		Anabaenopsis, others	F
		Hapalosiphon, others	T
	Nodularin	*Nodularia*	B, F
		Cyanobacterial symbiont(s) ?	M
	Cylindrospermopsin	*Cylindrospermopsis*	F
		Aphanizomenon	F
		Umezakia	B
Endotoxins and others	LPS	*Microcystis, Oscillatoria*	F
	Lyngbyatoxin	*Lyngbya*	M
	Aplysiatoxin	*Lyngbya, Oscillatoria*	M
		Schizothrix	M

F, freshwater ; B, brackish waters ; M, marine; T, terrestrial.

Basing on the survey of literature (Table 1), it is noted that the most frequently occurring toxin worldwide is microcystin. Cyclindospermopsin is another type of hepatotoxin and is water soluble reported from genera *Cylindrospermopsis*, *Anabaena*, *Umezakia* and *Aphanizomenon*. Carmichael (2011) [15] noticed that microcystins were detected in 80% of 677 freshwater sources in USA and Canada. In Africa, after microcystins, there are anatoxin-a, saxitoxin and LPS (Oudra *et al*., 2002; Van Halderen *et al*., 1995, Ballot *et al*., 2014) [57, 69, 7]. Anatoxin-a is detected in Kenya by Ballot *et al*. (2005) [6] and in Nigeria, saxitoxin, anatoxin-a, anatoxin-a(s) and cylindropermopsin types of cyanotoxins are identified (Mowe *et al*., 2014) [51]. In Asia, anatoxin-a and LPS are found in Saudi Arabia, Japan and Singapore (Maske *et al*., 2010; Ahmed *et al*., 2008; Hadas *et al*., 2000; Jayatissa *et al*., 2006, Chorus, 2012, Manganelli *et al*., 2012) [48, 2, 33, 37, 17, 46]. Anatoxin-a and saxitoxin are found in European countries (Chorus, 2012; Manganelli *et al*., 2012; Codd *et al*., 2005a; Lopes and Vasconcelos, 2011) [17, 46, 21, 45].

Anatoxin-a is a type of neurotoxin, produced by three genera *Anabaena*, *Planktothrix* and *Aphanizomenon* (Westrick *et al*., 2010) [71]. Saxitoxins are neurotoxins, found commonly in red tides caused by marine dinoflagellates blooms and acts as paralytic shellfish poisons causing animal death. This toxin is found in genera *Aphanizomenon*, *Anabaena*, *Lyngbya* and *Cyclindrospermopsis* (Westrick *et al*., 2010) [71]. Nodularin is reported from Finland, Poland and United Kingdom (Codd *et al*., 2005a) [21], while homoanatoxin-a is reported at Ireland (Codd *et al*., 2005) [21]. Anatoxin-a, saxitoxin, nodularin, homoanatoxin-a are found in Australia and New Zealand (Negri *et al*., 1995; Heresztyn and Nicholson, 1997; Churro *et al*., 2012) [52, 35, 18]. Studies on cyanotoxins of America (North and South) revealed the presence of anatoxin-a and saxitoxin (Campos *et al*., 1999; Azevedo *et al*., 2002; Carmichael, 1996 and 2011) [11, 4, 13, 15]. Nodularin, debromoaphysiatoxin and aplysiatoxin are found in United States, Canada and Brasilia (Carmichael, 2011) [15].

Exposure routes and effect of toxins on health

The presence of high levels of cyanotoxins in water (recreational and drinking water) may cause a diverse range of symptoms including fever, headaches, rashes, muscle and joint pain, mouth ulcers, blisters, diarrohea, stomach cramps, vomiting and allergic reactions in humans (United States Environmental Protection Agency, 2012; Codd *et al*., 2005b; Leitao and Coute, 2005, Kuiper-Goodman *et al*., 1999; Codd *et al*., 2005b) [68, 23, 44, 41], liver failure, respiratory arrest and rarely death may occur. Long-term exposure to microcystins and cylindrospermopsin promote growth of tumors, and cause cancer (Bagchi, 1999; Jones, 1993; Humbert *et al*., 2010) [5, 36, 62]. There are many reports of dog, bird and livestock deaths throughout the world as a result of consumption of surface water with cyanobacterial blooms (Carmichael, 2011; Harding and Paxton, 2001; Van Halderen *et al*., 1995) [15, 34, 69]. The most serious known episode associated to human exposure to cyanotoxins occurred in Brazil, where 56 out of 130 haemodialysed patients died after treatment with MC contaminated water (Azevedo *et al*., 2002) [4]. The toxins produced by the marine cyanobacteria cause diseases including paralytic shellfish poisoning (PSP), diarrheic shellfish poisoning (DSP), azaspiracid poisoning (AZP), neurotoxic shellfish poisoning (NSP) and ciguatera fish poisoning (CFP) (Humbert *et al*., 2010) [36, 62]. The currently perceived exposure routes are skin contact (dermal route), inhalation, haemodialysis and ingestion (oral route) (Figure 3 and table 2). More than one exposure route may also operate simultaneously (Codd *et al*., 1999; Leitao and Coute, 2005) [22, 44]

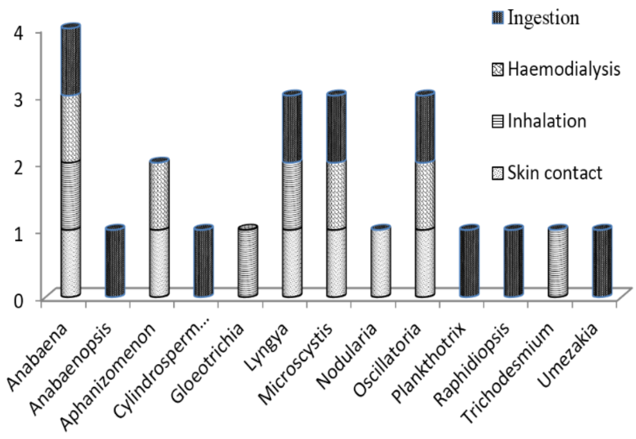

Fig 3: Exposure routes of organism to cyanobacteria

Cyanotoxin and Bloom Management

When cyanoblooms are detected in the surface water of water system, measures should be taken by the operators to remove or inactivate those blooms in a number of ways. For inactivation or removal the drinking water operators must know the growth patterns and species of cyanobacteria that dominate the bloom and whether the cyanotoxins produced are extracellular or intracellular. Three management strategies are recommended to minimize the consumer exposure to cyanotoxins. They are alternate water supply source, to adjust intake depth and water treatment. Chlorination, besides cell breaking, has the potential to disinfect the water and potassium permanganate ($KMnO_4$) has been confirmed to be effective in removing *Microcystis* cells with no release of toxin. It has been recommended that powdered activated carbon (PAC) also can be used to remove any toxin. Other than these strategies, the standard drinking water treatment processes (coagulation, flocculation, sedimentation and filtration), have also proved to be effective in removing intracellular cyanotoxins. Coagulation, flocculation and dissolved air flotation (DAF), are however reported, more effective than sedimentation (United States Environmental Protection Agency, 2012; Westrick *et al*., 2010) [68, 71]. Microfiltration and ultrafiltration are highly effective for removing intact cyanobacterial cells. When a bloom occurs and cells are carried through the filters, backwash should be conducted more frequently to reduce the risk of toxin release into the water (Falconer, 2005) [29].

Table 2: Exposure routes and health effects

Exposure routes	Genera	Health effects
Skin contact	*Oscillatoria* *Lyngbya* *Microcystis* *Nodularia* *Aphanizomenon* *Anabaena* *Gloeotrichia*	Rashes, blisters, Allergicreations: hayfever, asthma, conjonctivitis, ear and eye irritation, eye inflammation
Inhalation	*Trichodesmium* *Lyngbya* *Anabaena*	Liver lesions
Haemodialysis	*Aphanizomenon* *Anabaena* *Microcystis* *Oscillatoria* *Anabaenopsis*	Tender hepatomegaly, gastrointestinal bleeding sepsis and cardiovascular problems
Ingestion	*Cylindrospermo spsis* *Microcystis* *Anabaena* *Oscillatoria* *Lyngbya* *Plankthotrix* *Rhaphidiopsis* *Umezakia*	Gastroenteritis, hepatoenteritis, vomiting, headache, abdominal pain, tender hepatomegaly, lethargy, diarrhaea, acidosis, injury to the liver, kidneys lungs, adrenals and intestine

Conclusion

The occurrence of cyanoblooms is now-a-days much better documented. Among the major impacts we may point out the decrease in water transparency and oxygen levels, the production of off-flavours and the production of toxins. Among the most common toxins, microcystins, anatoxin-a, and saxitoxins are the most common in the world. The effect of these toxins depends on the route of exposure: skin contact (dermal route), inhalation, haemodialysis and ingestion (oral route). Such effects can occur within minutes to days or weeks after exposure. In some cases, liver failure, seizures, respiratory arrest, growth of tumors and cancer may be occur. Death cases are also noted in case of dog, bird and livestock. The marine cyanobacteria toxins cause many diseases including paralytic shellfish poisoning (PSP), ciguatera fish poisoning (CFP), azaspiracid poisoning (AZP), neurotoxic shellfish poisoning (NSP) and diarrheic shellfish poisoning (DSP).

Many procedures may be adopted for treatment of drinking water. However, the best method is protection of water source.

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