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Cyanobacteria and Cyanotoxins: Information for Drinking Water Systems

Summary

This fact sheet provides public water systems (PWSs) basic information on human health effects, analytical screening tools, and the effectiveness of various treatment processes to remove or inactivate the three most commonly occurring cyanotoxins in water bodies that are a source of drinking water throughout most of the U.S. and are listed on EPA's third drinking water Candidate Contaminant List: microcystin-LR, anatoxin-a, and cylindrospermopsin. Other cyanotoxins such as saxitoxins and anatoxin-a(S) also occur in U.S. water bodies that are a source of drinking water, but they are generally thought to be less common. Therefore, this fact sheet does not address these other well-known toxins produced by cyanobacteria such as the paralytic shellfish toxins (Saxitoxin family), anatoxin-a(S), the lyngbyatoxins, or taste and odor contaminants caused by the cyanobacteria.

Background

The Safe Drinking Water Act (SDWA) protects public health by regulating the nation's public drinking water supply and its sources: rivers, lakes, reservoirs, springs, and ground water wells. The SDWA requires EPA to publish a list of unregulated contaminants that are known or expected to occur in public water systems in the U.S. that may pose a risk in drinking water. This list is known as the Contaminant Candidate List (CCL). For more information on the CCL program visit http://water.epa.gov/scitech/drinkingwater/dws/ccl/

The cyanotoxins included in the most recent CCL are produced by several species of cyanobacteria (cyanobacteria are known as blue-green algae). The most widespread of the cyanotoxins are the peptide toxins in the class called microcystins. There are at least 80 known microcystins, including Microcystin-LR, which is generally considered one of the most toxic. More than a dozen countries have developed regulations or guidelines for microcystins in drinking water and recreational waters. Most of the drinking water guidelines are based on the World Health Organization provisional value for drinking waters of 1.0 µg/L microcystin-LR. No federal regulatory guidelines for cyanobacteria or their toxins in drinking water or recreational waters exist at this time in the U.S. At the moment of this publication, EPA is in the process of developing drinking water health advisories for microcystin-LR and cylindrospermopsin. There are currently a few states that have established cyanotoxin monitoring guidelines and cyanotoxin threshold levels for PWSs. PWSs are responsible for following those guidelines/thresholds and for undertaking any follow-up action required by their state.

Causes of cyanobacterial harmful algal blooms

Cyanobacteria are photosynthetic bacteria that share some properties with algae and are found naturally in lakes, streams, ponds, and other surface waters. Similar to other types of algae, when

conditions are favorable, cyanobacteria can rapidly multiply in surface water and cause "blooms." Several types of cyanobacteria, for example *Anabaena flos-aquae,* have gas-filled cavities that allow them to float to the surface or to different levels below the surface, depending on light conditions and nutrient levels. This can cause the cyanobacteria to concentrate on the water surface, causing a pea-soup green color or blue-green "scum." Some cyanobacteria like *Planktothrix* agardhii, can be found in bottom sediments and float to the surface when mobilized by storm events or other sediment disturbances. Other cyanobacteria blooms may remain dispersed through the water column (*Cylindrospermopsis* sp.) leading to a generalized discoloration of the water.

Conditions that enhance growth of cyanobacterial harmful algal blooms

Factors that affect cyanobacterial bloom formation and persistence include light intensity and total sunlight duration, nutrient availability (especially phosphorus), water temperature, pH, an increase in precipitation events, water flow (whether water is calm or fast-flowing), and water column stability. Although bloom conditions in much of the US are more favorable during the late summer, the interrelationship of these factors causes large seasonal and year-to-year fluctuations in the cyanobacteria levels. Some toxin-producing strains can occur early in the summer season while others are only found during late summer.

Effects of cyanobacterial harmful algal blooms

Cyanobacterial blooms can be harmful to the environment, animals, and human health. The bloom decay consumes oxygen, creating hypoxic conditions which result in plant and animal die-off. Under favorable conditions of light and nutrients, some species of cyanobacteria produce toxic secondary metabolites, known as cyanotoxins. Common toxin-producing cyanobacteria are listed in Table 1. The conditions that cause cyanobacteria to produce cyanotoxins are not well understood. Some species with the ability to produce toxins may not produce them under all conditions. These species are often members of the common bloom-forming genera. Both non-toxic and toxic varieties of most of the common toxin-producing cyanobacteria exist, and it is impossible to tell if a species is toxic or not toxic by looking at it. Also, even when toxin-producing cyanobacteria are present, they may not actually produce toxins. Furthermore, some species of cyanobacteria can produce multiple types and variants of cyanotoxins. Molecular tests are available to determine if the cyanobacteria, *Microcystis* for example, carry the toxin gene; quantitative cyanotoxin analysis is needed to determine if the cyanobacteria are actually producing the toxin. Water contaminated with cyanobacteria can occur without associated taste and odor problems.

In most cases, the cyanobacterial toxins naturally exist intracellularly (in the cytoplasm) and are retained within the cell. Anatoxin-a and the microcystin variants are found intracellularly approximately 95% of the time during the growth stage of the bloom. For those species, when the cell dies or the cell membrane ruptures the toxins are released into the water (extracellular toxins). However, in other species, cylindrospermopsin for example, a significant amount of the toxin may be naturally released to the water by the live cyanobacterial cell; the reported ratio is about 50% intracellular and 50% extracellular. Extracellular toxins may adsorb to clays and organic material in the water column and are generally more difficult to remove than the intracellular toxins.

Health effects caused by cyanotoxins

Exposure to cyanobacteria and their toxins could be by ingestion of drinking water contaminated with cyanotoxins and through direct contact, inhalation and/or ingestion during recreational activities. The acute recreational exposure to cyanobacterial blooms and their cyanotoxins can result in a wide range of symptoms in humans (Table 1) including fever, headaches, muscle and joint pain, blisters, stomach cramps, diarrhea, vomiting, mouth ulcers, and allergic reactions. Such effects can occur within minutes to days after exposure. In severe cases, seizures, liver failure, respiratory arrest, and (rarely) death may occur. The cyanotoxins include neurotoxins (affect the nervous system), hepatotoxins (affect the liver), and dermatoxins (affect the skin). However, there have been new studies of effects in other systems, including hematological, kidney, cardiac, reproductive, and gastrointestinal effects. There is evidence that long-term exposure to low levels of microcystins and cylindrospermopsin may promote cell proliferation and the growth of tumors. However, more information is needed to determine the carcinogenicity of both microcystins and cylindrospermopsin.

Table 1. Cyanotoxins on the Contaminant Candidate List (CCL)

Cyanotoxin	Number of Known Variants or Analogues	Primary Organ Affected	Health Effects[1]	Most Common Cyanobacteria Producing Toxin[2]
Microcystin-LR	80~90	Liver	Abdominal pain Vomiting and diarrhea Liver inflammation and hemorrhage Acute pneumonia Acute dermatitis Kidney damage Potential tumor growth promotion	*Microcystis* *Anabaena* *Planktothrix* *Anabaenopsis* *Aphanizomenon*
Cylindrospermopsin	3	Liver		*Cylindrospermopsis* *Aphanizomenon* *Anabaena* *Lyngbya* *Rhaphidiopsis* *Umezakia*
Anatoxin-a group[3]	2-6	Nervous System	Tingling, burning, numbness, drowsiness, incoherent speech, salivation, respiratory paralysis leading to death	*Anabaena* *Planktothrix* *Aphanizomenon* *Cylindrospermopsis* *Oscillatoria*

[1]Source: *Harmful Algal Research and Response National Environmental Science Strategy (HARRNESS)*
[2]Not all species of the listed genera produce toxin; in addition, listed genera are not equally as important in producing cyanotoxins.
[3]The anatoxin-a group does not include the organophosphate toxin anatoxin-a(S) as it is a separate group. In the US, the most common member is thought to be anatoxin-a, and thus this toxin is listed specifically.

There have been many documented reports of dog, bird and livestock deaths throughout the world as the result of consumption of surface water with cyanobacterial blooms. In 1996, one hundred and sixteen patients at a renal dialysis clinic in Caruaru, Brazil were affected and experienced headache, eye pain, blurred vision, nausea and vomiting when they were exposed intravenously to water containing a mixture of microcystin and cylindrospermopsin (Carmichael et al., 2001). Subsequently, 100 of the affected patients developed acute liver failure and, of

these, 76 died. Analyses of blood, sera, and liver samples from the patients revealed only the microcystin toxin.

Analytical methods

Table 2 describes the methods available for cyanotoxin measurement in freshwater. Commercially available Enzyme-Linked Immunosorbent Assay (ELISA) test kits are one of the more commonly utilized cyanotoxin testing methods, since they do not require expensive equipment or extensive training to run. Semi-quantitative field screening ELISA kits are available for the presence or absence of cyanotoxins. If cyanotoxins are detected by a field screening kit, repeat analysis is recommended using either a quantitative ELISA test or one of the other analytical methods identified in Table 2.

More precise, more quantitative ELISA test kits are available for microcystin-LR, microcystins/nodularins (ADDA), saxitoxin, and cylindrospermopsin. In addition, a rapid receptor-binding assay kit is available for the detection of anatoxin-a. Although they provide rapid results, ELISA kits generally have limitations in specificity and are not congener specific. In addition, some cross-reactivity may occur. The microcystins/nodularins (ADDA) kit is based on the ADDA structure within the microcystin molecule and is designed to detect over 80 microcystin congeners identified to date (but cannot distinguish between congeners).

Methods that utilize liquid chromatography combined with mass spectrometry (LC/MS) can precisely and accurately identify specific microcystin congeners for which standards are available; LC/MS methods have also been designed to minimize matrix interference. At this time there are only standards for a limited number of the known microcystin congeners. If congener-specific information is needed, an LC/MS method should be considered. HPLC-PDA methods are less specific than LC/MS methods and the quantitation is more problematic due to a less specificity and to sample matrix interference. However, when analytical toxin standards are available for confirmation, they could provide a measure of resolution of the congeners present.

Sample handling considerations

Samples must be handled properly to ensure reliable results. Detailed procedures are typically specified in the particular analytical methods/SOPs. Water systems should obtain and follow sample collection and handling procedures established by the laboratory performing the analysis. Laboratories establishing such procedures may wish to consult the USGS sampling protocol Guidelines for design and sampling for cyanobacterial toxin and taste-and-odor studies in lakes and reservoirs (2008)

Among the most important sample handling considerations are the following:

- Collection – Bottle type, volume, and preservative used depend on the laboratory doing the analysis. Generally, samples should be collected and stored in amber glass containers to avoid potential cyanotoxin adsorption associated with plastic containers and to minimize exposure to sunlight.

Table 2. Methods Available for Cyanotoxin Detection*

Freshwater Cyanotoxins			
Methods	**Anatoxins**	**Cylindrospermopsins**	**Microcystins**
Biological Assays			
Mouse	Yes	Yes	Yes
Protein Phosphatase Inhibition Assays (PPIA)	No	No	Yes
Neurochemical	Yes	No	No
Enzyme-Linked Immunosorbent Assays (ELISA)	No	Yes	Yes
Chromatographic Methods ***Gas Chromatography***			
Gas Chromatography with Flame Ionization Detection (GC/FID)	Yes	No	No
Gas Chromatography with Mass Spectrometry (GC/MS)	Yes	No	No
Liquid Chromatography			
Liquid Chromatography / Ultraviolet-Visible Detection (LC/UV or LC/PDA)	Yes	Yes	Yes
Liquid Chromatography/Fluorescence (LC/FL)	Yes	No	No
Liquid Chromatography Combined with Mass Spectrometry			
Liquid Chromatography Ion Trap Mass Spectrometry (LC/IT MS)	Yes	Yes	Yes
Liquid Chromatography Time-of-Flight Mass Spectrometry (LC/TOF MS)	Yes	Yes	Yes
Liquid Chromatography Single Quadrupole Mass Spectrometry (LC/MS)	Yes	Yes	Yes
Liquid Chromatography Triple Quadrupole Mass Spectrometry (LC/MS/MS)	Yes	Yes	Yes

*Adapted from Analytical Methods for Cyanotoxin Detection and Impacts on Data Interpretation, presentation by Keith Loftin, Jennifer Graham, Barry Rosen (U.S. Geological Survey) and Ann St. Amand (Phycotech) at the 2010 National Water Quality Monitoring Conference, Workshop. Guidelines for Design, Sampling, Analysis and Interpretation for Cyanobacterial Toxin Studies at Denver, CO on April 26, 2010.

- Quenching – samples (particularly "finished" drinking water samples) that have been exposed to any treatment chemicals should be quenched immediately upon sampling. Sodium thiosulfate or ascorbic acid are commonly used as quenching agents.
- Chilling – samples should be cooled immediately after collection; during shipping; and pending analysis at the laboratory. Depending on the analytical method being used, sample freezing (taking precautions to avoid breakage) may be appropriate to extend holding times.

Sample analysis considerations

When measuring "total" cyanotoxins (both intracellular and dissolved (extracellular) toxins), rupturing cyanobacterial cells (lysing) is generally employed to break the cell wall and release the toxins into solution. Freeze/thaw cycling (traditionally carried out over three or more cycles) represents the most common lysing technique, though some analytical methods rely on other approaches. Lysing is particularly important for samples collected prior to the PWS filter effluent. For a well-designed, well-operated PWS lysing would not be expected to have a significant impact on finished water (post-filtration) samples as cyanobacteria cells should not be present at significant levels in the finished water. Some analysts elect to confirm the effectiveness of raw-water lysing (or to judge the need for finished-water lysing) using microscopic examination for intact algal cells.

Cyanotoxin treatment and bloom management

Once cyanobacteria and/or their cyanotoxins are detected in the surface water supplying the water system, the treatment system operators can act to remove or inactivate them in a number of ways. Some treatment options are effective for some cyanotoxins, but not for others. Effective management strategies depend on understanding the growth patterns and species of cyanobacteria that dominates the bloom, the properties of the cyanotoxins (i.e., intracellular or extracellular), and appropriate treatment processes. For example, oxidation of microcystin depends on the chlorine done, pH and the temperature of the water. Applying the wrong treatment process at a specific state in treatment could damage cells and result in the release rather than removal of cyanotoxins.

Table 3 summarizes the effectiveness of different types of water treatment to remove intact cyanobacteria cells and treatment processes that are effective in removing extracellular dissolved toxins of several of the most important cyanobacteria. Drinking water operators are encouraged to monitor the treated water to guarantee the removal of cyanotoxins. For more information and resources on treatment processes for cyanotoxins please visit http://www2.epa.gov/nutrient-policy-data/control-and-treatment

To avoid the release of cyanotoxins into the water, drinking water operators can undertake different management strategies to deal with cyanobacteria blooms. For example, those drinking water utilities that have access to more than one intake can switch to an alternate one that is not as severely impacted by the bloom. Another management alternative is to adjust intake depth to avoid drawing contaminated water and cells into the treatment plant.

Pretreatment oxidation at the intake poses several concerns with respect to lysing cells and releasing toxins. Copper sulfate and ozone at the intake are not recommended because of the risk of lysing algal cells. Chlorination, in addition to lysing the cells, has the potential to produce disinfection by-products during water treatment. If pretreatment oxidation is needed, it is important to carefully evaluate the influent as successful pre-oxidation depends on the algal species, oxidant and dose. Potassium permanganate ($KMnO_4$) at low levels could be used to remove *Microcystis* cells. Inline powdered activated carbon (PAC) could also be used to remove any toxins that may have been released.

Table 3. Cyanotoxin Treatment Processes and Relative Effectiveness

Treatment Process	Relative Effectiveness
Intracellular Cyanotoxins Removal (Intact Cells)	
Pre-treatment oxidation	Oxidation often lyses cyanobacteria cells releasing the cyanotoxin to the water column. If oxidation is required to meet other treatment objectives, consider using lower doses of an oxidant less likely to lyse cells (potassium permanganate). If oxidation at higher doses must be used, sufficiently high doses should be used to not only lyse cells but also destroy total toxins present (see extracellular cyanotoxin removal).
Coagulation/ Sedimentation/ Filtration	Effective for the removal of intracellular toxins when cells accumulated in sludge are isolated from the plant and the sludge is not returned to the supply after sludge separation.
Membranes	Study data are limited; it is assumed that membranes would be effective for removal of intracellular cyanotoxins. Microfiltration and ultrafiltration are effective when cells are not allowed to accumulate on membranes for long periods of time.
Flotation	Flotation processes, such as Dissolved Air Flotation (DAF), are effective for removal of intracellular cyanotoxins since many of the toxin-forming cyanobacteria are buoyant.
Extracellular Cyanotoxins Removal (Dissolved)	
Membranes	Depends on the material, membrane pore size distribution, and water quality. Nanofiltration is generally effective in removing extracellular microcystin. Reverse osmosis filtration is generally applicable for removal of extracellular microcystin and cylindrospermopsin. Cell lysis is highly likely. Further research is needed to characterize performance.
Potassium Permanganate	Effective for oxidizing microcystins and anatoxins. Further research is needed for cylindrospermopsin.
Ozone	Very effective for oxidizing extracellular microcystin, anatoxin-a, and cylindrospermopsin.
Chloramines	Not effective.
Chlorine dioxide	Not effective with doses used in drinking water treatment.
Chlorination	Effective for oxidizing extracellular cyanotoxins as long as the pH is below 8; ineffective for anatoxin-a.
UV Radiation	Effective at degrading microcystin and cylindrospermopsin but at impractically high doses.
Activated Carbon	Powdered activated carbon (PAC): Effectiveness varies highly based on type of carbon and pore size. Wood-based activated carbons are generally the most effective at microcystin adsorption. Carbon is not as effective at adsorbing saxitoxin or taste and odor compounds. Doses in excess of 20mg/L may be needed for complete toxin removal. Granular activated carbon (GAC): Effective for microcystin but less effective for anatoxin-a and cylindrospermopsins.

The standard drinking water treatment processes (coagulation, flocculation, sedimentation and filtration) can be effective in removing intracellular cyanotoxins. Coagulation, flocculation and dissolved air flotation (DAF) are more effective than sedimentation. Microfiltration and ultrafiltration are highly effective at removing intact cyanobacterial cells. During an active bloom, operators may need to alter process parameters to account for the increased loading of cyanobacteria. It may be necessary to backwash filters more frequently to prevent retained cells from releasing intracellular toxins.

Common treatment techniques for the removal of extracellular toxins include activated carbon, membrane filtration and chemical inactivation (Ultraviolet (UV), disinfectants and oxidants). Both powdered activated carbon (PAC) and granular activated carbon (GAC) have been effective in adsorbing microcystin and cylindrospermopsin, although microcystin variants may have different adsorption efficiencies. The performance of activated carbon depends on the concentration of the toxin and the dose and origin of the activated carbon. Jar tests are recommended to test the effectiveness of various PAC types, with the implementation of the carbon with the greatest capacity for removal of the target contaminants. GAC filters are effective in removing microcystins if they are properly replaced or regenerated. Nanofiltration and reverse osmosis may be effective in removing cylindrospermopsin and microcystin. However, site specific tests are recommended as removal efficiency depends on the membrane pore size distribution and water quality.

It is impractical to deliver ultraviolet (UV) radiation at the doses required to photolytically destroy microcystin, anatoxin-a, and cylindrospermopsin in a process setting. UV has been used along with a catalyst (titanium dioxide) to oxidatively decompose the toxins; however, the effectiveness of this process is largely dependent on the organic content of the water. Oxidants like chlorine, ozone and $KMnO_4$ can be used to inactivate microcystins but chlorine effectiveness is pH-dependent. Various cyanotoxins react differently to chlorine; for example, anatoxin-a is resistant to inactivation by chlorine. However, if the pH is below 8, chlorine is effective for inactivation of microcystin and cylindrospermopsin. Ozone can be a good oxidant for microcystins, but its efficacy may be affected by the presence of organic matter. Ozone can also be used as an oxidant for anatoxin-a and cylindrospermopsin; however, ozone is pH-dependent for the oxidation of anatoxin-a (pH 7 to 10) and for cylindrospermopsin (4 and 10). KMnO4 is effective in oxidizing microcystin and anatoxin-a (from pH 6 to 8), but is not very effective for cylindrospermopsin. Chloramines and chlorine dioxide are not effective treatments for microcystin, anatoxin-a or cylindrospermopsin.

Formation of disinfection by-products is another potential problem with the use of ozone, copper sulfate, and chlorine when there are high bromide concentrations in the water. However, results from studies on the impact of chlorination of cell-bound toxins and resulting disinfection by-products formation are contradictory. The majority of the findings suggest that pre-chlorination should ideally be avoided during blooms, unless adequate CT values[1] can be guaranteed to ensure efficient oxidation of broken cyanobacteria.

[1] A CT value is used in the calculation of disinfectant dosage for chlorination of drinking water. A CT value is the product of the concentration of a drinking water disinfectant and the contact time with the water being disinfected (typically expressed in units of mg-min/L).

Developing a contingency plan

Water supply managers should develop a contingency plan for cyanobacterial bloom occurrence. Most algal blooms are not toxic, and the plan should address how to determine the potential risk associated with each event. Elements of such a plan should include a Monitoring Program to determine when and where to sample; sampling frequency; sample volume; whether to sample for cyanobacterial cells or specific cyanotoxins or both; which analytical screening test to use; and conditions when it is necessary to send sample(s) to an identified laboratory for confirmation. Water supply managers should also develop a Management and Communication plan including what treatment option(s) to use to reduce the potential of cyanotoxins in the finish water or reaching the distribution system; and identifying the required communication steps to coordinate with the agencies involved the appropriate actions that must be taken, and the steps to inform consumers and the public. Chapter 6 (Situation Assessment, Planning and Management) from the WHO's *Toxic Cyanobacteria in Water: A guide to their public health consequences, monitoring and management* and the Incident Management Plans chapter from the *International guidance manual for the management of toxic cyanobacteria* (Water Quality Research Australia) could be used as resources to develop such plans.

For more information

Visit EPA's Cyanobacteria Harmful Algal Blooms (CyanoHABs) web page at http://www2.epa.gov/nutrient-policy-data/cyanobacterial-harmful-algal-blooms-cyanohabs.

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