Environ Monit Assess (2022) 194: 253
https://doi.org/10.1007/s10661-022-09875-z

Exposure to microcystin-LR in tropical reservoirs for water supply poses high risks for children and adults

Janaína Fagundes Malta · Adelaide Cassia Nardocci · Maria Tereza Pepe Razzolini · Vinicíus Diniz · Davi Gasparini Fernandes Cunha

Received: 13 October 2021 / Accepted: 17 February 2022 / Published online: 7 March 2022

Abstract While the presence of microcystin-LR (MC-LR) in raw water from eutrophic reservoirs poses human health concerns, the risks associated with the ingestion of MC-LR in drinking water are not fully elucidated. We used a time series of MC-LR in raw water from tropical urban reservoirs in Brazil to estimate the hazard quotients (HQs) for non-carcinogenic health effects and the potential ingestion of MC-LR through drinking water. We considered scenarios of MC-LR removal in the drinking water treatment plants (DWTPs) of two supply systems (Cascata and Guarapiranga). The former uses coagulation/flocculation/sedimentation/filtration/disinfection, while the latter has an additional step of membrane ultrafiltration, with contrasting expected MC-LR removal efficiencies. We considered reference values for infants (0.30 μg L^{-1}), children/adults (1.60 μg L^{-1}), or the population in general (1.0 μg L^{-1}). For most scenarios for Cascata, the 95% upper confidence level of the HQ indicated high risks of exposure for the population (HQ > 1), particularly for infants (HQ = 30.910). The water treatment in Cascata was associated to the potential exposure to MC-LR due to its limited removal capacity, with up to 263 days/year with MC-LR above threshold values. The Guarapiranga system had the lowest MC-LR in the raw water as well as higher expected removal efficiencies in the DWTP, resulting in negligible risks. We reinforce the importance of integrating raw water quality characteristics and treatment technologies to reduce the risks of exposure to MC-LR, especially for vulnerable population groups. Our results can serve as a starting point for risk management strategies to minimize cases of MC-LR intoxication in Brazil and other developing countries.

Keywords Cyanotoxins · Drinking supply reservoirs · Environmental monitoring · Hazard quotients · Public health · Risk assessment

J. F. Malta · D. G. F. Cunha (✉)
Department of Hydraulic and Sanitary Engineering, São Carlos School of Engineering, University of São Paulo, Av. Trabalhador São-Carlense, 400, Sao Carlos, SP 13566-590, Brazil
e-mail: davig@sc.usp.br

A. C. Nardocci · M. T. P. Razzolini
Department of Environmental Health, School of Public Health, University of São Paulo, Av. Dr Arnaldo 715, 1º andar, Sao Paulo, SP 01246-904, Brazil

A. C. Nardocci · M. T. P. Razzolini
Center for Research, Environmental Risk Assessment (NARA), Av. Dr Arnaldo 715, 1° andar, Sao Paulo, SP 01246-904, Brazil

V. Diniz
Institute of Chemistry, Department of Analytical Chemistry, University of Campinas, PO Box 6154, Campinas, SP 13084-971, Brazil

Introduction

Eutrophic reservoirs have gradually become a major concern regarding provision of drinking water and assurance of public health, more particularly in urban areas. Under specific environmental conditions (*e.g.*, organic matter availability, favorable light conditions, water column stratification, and high content of nutrients, such as phosphorus and nitrogen) (Cunha et al., 2018; Huisman et al., 2018; USEPA, 2019a, 2019b; Weber et al., 2020; WHO, 2015), harmful cyanobacterial blooms (HCBs) can be exacerbated. While these blooms have been a global concern (Huisman et al., 2018; Munoz et al., 2020; Sha et al., 2021), they can be more frequent in tropical and subtropical regions (Cunha et al., 2018), especially in developing countries where point and non-point water pollution sources are significant. While more detailed studies on HCBs are still lacking in South American countries (Dörr et al., 2010) in comparison to other regions (Chorus & Bartram, 2021; Massey et al., 2020), there have been growing reports showing the ubiquitous occurrence of cyanobacteria in Brazil (Barros et al., 2019; Moura et al., 2017; Walter et al., 2018), Argentina (Aguilera et al., 2018), Uruguay (Aubriot et al., 2020), and Chile (Almanza et al., 2016).

Cyanobacteria can produce cyanotoxins that severely affect both human health (Azevedo et al., 2002; Bernard et al., 2017) and wildlife (Wang et al., 2021). In the former case, cyanobacteria pose a significant threat to water supply and recreational uses. Accordingly, the effectiveness of drinking water treatment can be compromised due to taste and odor problems, aesthetic issues, and the presence of contaminants (*e.g.*, cyanotoxins) above safe levels in treated water (Devi et al., 2021; Kelly et al., 2019; Schreidah et al., 2020). Furthermore, the techniques to control and remove HCBs (*e.g.*, artificial mixing/aeration and algicides) are site specific and frequently cost-prohibitive (Vu et al., 2020). For example, in the USA, the economic losses were estimated at about US$4 billion per year associated with HCBs (Ho et al., 2019). In China, more than US$15.1 billion were spent to control HCBs in the Lake Taihu since 2007 (see Jiang et al., 2021).

The exposure of humans to cyanotoxins is usually related to the ingestion of contaminated drinking water (Funari & Testai, 2008; Pouria et al., 1998), and it has been reported worldwide (Gaget et al., 2017; Tamele & Vasconcelos, 2020; Vu et al., 2020; WHO, 2017). More specifically, 14 episodes of massive cyanotoxin poisoning in humans and animals were recorded in South America, with the highest number of episodes in Brazil and Argentina (Svirčev et al., 2019). In Brazil, one of the most serious poisoning events, known as the "Caruaru syndrome," caused 76 deaths in 1996 (Azevedo et al., 2002; Dixon et al., 2011). Accidental ingestion, inhalation, and skin contact can also occur during recreational activities (Giannuzzi et al., 2011; Menezes et al., 2017; Turner et al., 1990). The main concerns regarding the exposure to cyanotoxins are associated to the extensive list of negative implications to the human health after short-term (24 h or less) recreational or oral exposure, including skin irritations, allergic reactions, gastrointestinal illnesses, liver failure, and neurotoxic effects (Sarkar et al., 2019; Sotero-Santos et al., 2006; Zhang et al., 2010). However, long-term exposure to lower concentrations (*e.g.*, in ng L^{-1} or μg L^{-1} levels) of cyanotoxins can lead to chronic adverse effects or carcinogenic effects that are still not fully elucidated (He et al., 2017; Yi et al., 2019). The health care treatment costs due to the exposure to cyanotoxins also remain mostly uncharacterized, but some studies reported values between US$86 and US$12,605 as digestive illness costs per patient (in mild, moderate, or severe cases) (Kouakou & Poder, 2019).

The cyanotoxins can occur inside the cells (intracellular) or dissolved in the water (extracellular) as a result of the senescence of the cyanobacterial blooms or the cell lysis following water treatment processes (Pietsch et al., 2002; Teixeira & Rosa, 2006). Microcystin (MC) is one of the most common cyanotoxins related to cases of water contamination (Huisman et al., 2018). While more than 250 variants of MCs have been identified (Spoof & Catherine, 2017), MC-LR (leucine-arginine) has been studied worldwide as it is produced by a variety of cyanobacteria, including *Microcystis*, *Anabaena* (*Dolichospermum*), *Aphanizomenon*, *Cylindrospermopsis*, *Nostoc*, *Oscillatoria (Planktothrix*), and *Rivularia* (Rastogi et al., 2015). MC-LR is relatively stable and resistant to chemical hydrolysis or oxidation, with half-life ranging from 4 to 14 days (USEPA, 2015a).

The International Agency for Research on Cancer categorized MC-LR as a possible carcinogen to humans (group 2B) (IARC, 2010). Also, MC-LR is well known as a potent cyanotoxin reported by the majority of toxicological studies and frequently observed at up to μg L^{-1} levels during cyanobacterial blooms in aquatic systems (USEPA, 2015b). For example, Cunha et al. (2018) reported MC-LR yearly means ranging from <0.1 to 17 μg L^{-1} in six Brazilian reservoirs. Several countries included MC-LR in their risk management frameworks for water quality programs (Ibelings et al., 2014) and established guidelines to avoid or minimize intoxication episodes. The US Environmental Protection Agency (USEPA) established a 10-day health advisory dosage of MC-LR as a protective measure for non-carcinogenic effects of MC-LR in drinking water and recreational exposure (USEPA, 2015b). Although the health advisory dosage is not legally enforceable, it is used as an informal technical guidance for stakeholders of water systems and state agencies to protect public health (USEPA, 2015b).

The most restrictive health advisory dosage of MC-LR (0.30 μg L^{-1}) was established for children under 6 years old and other sensitive populations (*e.g.*, pregnant women, nursing mothers, or individuals under dialysis treatment with impaired liver function or other health ailments). For people older than 6, such dosage was set as 1.60 μg L^{-1} (USEPA, 2015a; Yeager & Carpenter, 2019). The World Health Organization (WHO) proposed a tolerable daily intake (TDI) of 0.04 μg of MC-LR per kg of body weight (WHO, 2003, 2017). This value was based on the no-observed-adverse-effect level (40.00 μg of MC-LR per kg of body weight) established for mice in a 13-week study (Fawell et al., 1999). It should be noted that this TDI includes both intracellular and dissolved MC-LR, being valid for chronic (long-term) exposure (Szlag et al., 2015). In Brazil, the upper limit for MC-LR concentration in drinking water was established as 1.00 μg L^{-1}, the same value recommended by the WHO (Brasil, 2017, 2021; WHO, 2017).

Due to the physical and chemical properties of the MC-LR molecules (*i.e.*, water-solubility, cyclic structure, and stability under sunlight and neutral pH) (Akcaalan et al., 2006; Morón-lópez et al., 2017; Zhang et al., 2010), conventional drinking water treatment processes (*i.e.*, coagulation, flocculation, sedimentation or dissolved air flotation, rapid sand filtration, and disinfection) usually provide limited removal of dissolved MC-LR (USEPA, 2015a). If not dissolved, the expected intracellular MC-LR removal efficiencies in drinking water treatment plants (DWTPs) can reach relatively high percentages (see Drikas et al., 2001; Lahti et al., 2001; Hoeger et al., 2004; Mkhonto et al., 2020), especially if cyanobacterial cells are kept intact. However, if the DWTPs operation leads to cell lysis (increasing the dissolved MC-LR concentrations), additional processes (*e.g.*, adsorption, chemical oxidation, biodegradation, or membrane filtration) can be necessary (USEPA, 2015b). These advanced processes can further increase the overall removal efficiency even in the presence of dissolved MC-LR (Almuhtaram et al., 2018; He et al., 2016; Shang et al., 2018).

Since 2004, the WHO recommended the adoption of water safety plans (WSPs) by water suppliers, which include a model of risk analysis, assessment and management applied to all water supply components (*i.e.*, from the raw water sources to the consumers of finished water). Thus, the WSPs can assist in the identification of hazards (*i.e.*, physical, biological, chemical, or radiological agents that can cause harm to public health) and hazardous events (*i.e.*, events that introduce hazards to, or fail to remove hazards from the water supply system) to help the assessment of risks (*i.e.*, the probability that harm will be caused). This might allow minimizing adverse events and evaluating how water treatment processes contribute to health risk reduction (Codd et al., 2020; WHO, 2009). In this context, there is a gap of information in developing countries like Brazil regarding cyanotoxins and the potential health risks associated with oral exposure due to the insufficient capacity of water treatment technologies to reach acceptable limits in finished water.

To the best of our knowledge, no previous study performed a preliminary risk assessment related to the exposure to MC-LR via ingestion of contaminated drinking water in Brazil. Since conventional DWTPs are common in the country and can present limited capacity to perform MC-LR abatement from raw water, the present study considered different scenarios for intracellular and dissolved MC-LR removal in two Brazilian water supply systems (Cascata and Guarapiranga) with contrasting treatment technologies in their DWTP. For the exposure scenarios, we estimated the hazard quotients (HQs) values for non-carcinogenic health effects, the probabilities of exceeding the thresholds values (using both USEPA and WHO references), and the minimum number of days of potential ingestion of MC-LR per year through drinking water when the cyanotoxin was potentially above the acceptable thresholds. As the occurrence of cyanotoxins becomes more and more frequent worldwide (Brasil et al., 2016; Huisman et al., 2018; Amorim et al., 2021), the contributions made here have broad applicability for management strategies to mitigate the hazards posed by MC-LR, especially in developing countries where ensuring the provision of safe drinking water is still a challenge.

Material and methods

Study area and MC-LR dataset

We considered a dataset of 8 years (2011–2018) of MC-LR in raw water sources of two water supply systems in the São Paulo State (Brazil) with contrasting sizes, Cascata and Guarapiranga (Fig. 1). The raw water for the former system came from the Cascata Reservoir (surface area < 1 km^2), while the latter system was supplied by two reservoirs: Guarapiranga (27 km^2) and Billings-Taquacetuba (127 km^2) (Fig. 1). The DWTP of the Cascata system has a conventional process with a treatment capacity of about 0.1 $m^3\ s^{-1}$. The Guarapiranga system has the same conventional process but followed by a membrane ultrafiltration unit. This DWTP has a treatment capacity of 15.0 $m^3\ s^{-1}$ and supplies people living in the west and south zones of the city of São Paulo. Additional characteristics of each system are presented in Table 1 and Table S1. The MC-LR data were publicly available from different sources: São Paulo State Inland Water Quality Reports (CETESB, 2014, 2015, 2016, 2017, 2018, 2019a, 2020), CETESB Monitoring Network — Infoáguas System (CETESB, 2019b), Integrated Water Resources Management System (SIGRH-SP)

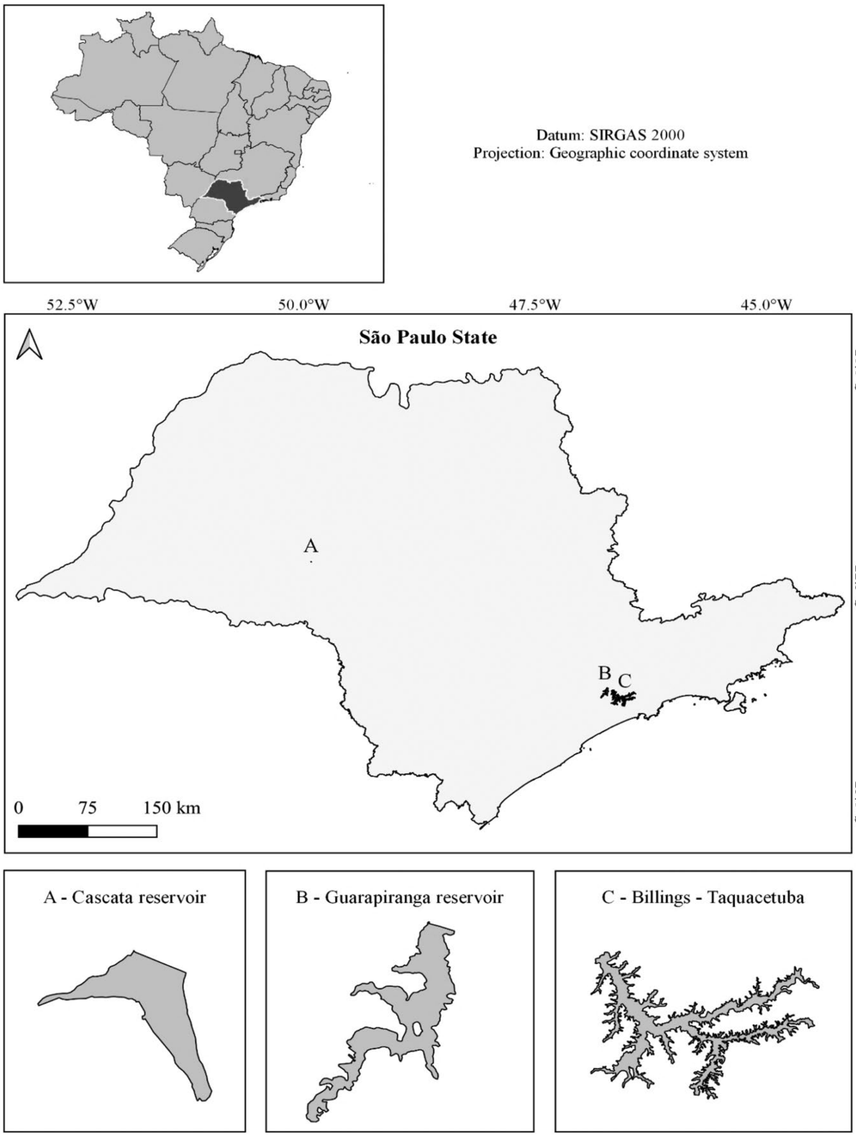

Fig. 1 Location of the study area (São Paulo State, Brazil) and the water supply systems: Cascata (**A**) and Guarapiranga (**B** and **C**)

Table 1 Main characteristics of the Cascata and Guarapiranga water supply systems

Water supply system[a]	City	Reservoir (Fig. 1)	Surface area (km^2)	Geographic coordinates	Drinking water production in the DWTP[b] ($m^3\ s^{-1}$)	Water treatment processes
Cascata	Marília	Cascata Reservoir (A)	< 1	23°14′06.7″S 46°23′34.8″W	0.1	Conventional[c]
Guarapiranga	Itapecerica da Serra	Guarapiranga Reservoir (B)	27	23°37′22.6″S 46°23′34.8″W	15.0	Conventional[c] + advanced treatment (ultrafiltration)
	Taboão da Serra São Paulo	Billings-Taquacetuba (C)	127	23°49′50″S 46°37′50″W		

[a]Adapted from SABESP (2019a, 2019b)

[b]Drinking Water Treatment Plant

[c]Coagulation, flocculation, sedimentation, filtration, disinfection, and fluoridation

(São Paulo, 2016), Information System for Monitoring Water Quality for Human Consumption (SISAGUA — Ministry of Health) (Brasil, 2019), and Sustainability Reports and Operational Information of the Sanitation Company of the State of São Paulo (SABESP) (SABESP, 2019a). The MC-LR concentrations are reported in micrograms per liter in these sources and were quantified by the respective institutions using one of the following methods: USEPA method 544 (liquid chromatography couple with tandem mass spectrometry) or 546 (enzyme-linked immunosorbent assays) (USEPA, 2012). Cyanobacterial development is common in both Cascata and Guarapiranga reservoirs, with frequent blooms of *Microcystis* spp., *Woronichinia* spp., and *Aphanocapsa* spp. (CETESB, 2019a).

The MC-LR concentrations were initially compared year-by-year using the Mann–Whitney test ($\alpha = 0.05$), as the data had non-normal distribution (Shapiro–Wilk test ($p < 0.05$)). The statistical procedures were performed with Origin 9.0®.

Scenarios of MC-LR removal by the water treatment processes

Eleven studies (Chorus & Bartram, 1999; Drikas et al., 2001; Lahti et al., 2001; Gijsbertsen-Abrahamse et al., 2006; Teixeira & Rosa, 2006; Daly et al., 2007; Zamyadi et al., 2012; Merel et al., 2013a; Swanepoel et al., 2017; Shang et al., 2018; Mkhonto et al., 2020) were previously screened for assessing the expected efficiencies of intracellular and extracellular MC-LR removal by conventional and advanced water treatment processes (*i.e.*, with ultrafiltration unit). In our study, these previously reported removal percentages were used to calculate the expected MC-LR concentrations in the treated water. The MC-LR removal efficiency depends on treatment technology, microcystin form (*i.e.*, dissolved or intracellular), hydraulic aspects (*e.g.*, water residence time), as well as design and operational parameters in the DWTP (Teixeira et al., 2020). Due to these variations, in our subsequent analyses, we assumed that the optimistic scenarios would have the best conditions for removing MC-LR, while the pessimistic scenarios would have unfavorable conditions for the MC-LR abatement. Thus, eight scenarios were considered to evaluate the expected concentrations of MC-LR after water treatment in both Cascata (C) and Guarapiranga (G) systems. Considering the MC-LR form (*i.e.*, intracellular (I) or dissolved (D)), the optimistic scenarios (O) assumed the following removal efficiencies: 95% (COI), 15% (COD), 99% (GOI), and 92% (GOD) and for the pessimistic scenarios (P): 64% (CPI), 0% (CPD), 96% (GPI) and 90% (GPD) (Table 2).

The values of mean, median, and 95% upper confidence interval (UCL95%) for the expected MC-LR concentrations in drinking water were estimated through the ProUCL5.1 Software (USEPA, 2015c). The assumed MC-LR concentrations in finished water following each scenario were used to estimate the probability of exceeding the reference values (*e.g.*, USEPA and WHO guidelines, see more information below) considering an empirical distribution (*i.e.*, the cumulative distribution function that generated the data points). The data were organized in the ascending order and the probability of no compliance with the guidelines was obtained according to Eq. 1.

Table 2 Intracellular and dissolved MC-LR removal efficiencies considered for each scenario

System	Scenario	MC-LR form in the water	Abbreviation	Assumed removal efficiency[a] (%)
Cascata	Optimistic	Intracellular	COI	95
		Dissolved	COD	15
	Pessimist	Intracellular	CPI	64
		Dissolved	CPD	0
Guarapiranga	Optimistic	Intracellular	GOI	99
		Dissolved	GOD	92
	Pessimist	Intracellular	GPI	96
		Dissolved	GPD	90

[a]Based on the following studies: Chorus and Bartram (1999); Drikas et al. (2001); Lahti et al. (2001); Gijsbertsen-Abrahamse et al. (2006); Teixeira and Rosa (2006); Daly et al. (2007); Zamyadi et al., (2012); Merel et al. (2013a); Swanepoel et al. (2017); Shang et al. (2018);Mkhonto et al. (2020)

The minimum number of days per year that MC-LR concentrations in drinking water were expected to be above the reference values was estimated by multiplying the probability (Eq. 1) by the number of days in 1 year (*i.e.*, 365 days).

$$\text{Probability}(\%) = \frac{N_{\text{above}}}{N_{\text{total}}} 100 \quad (1)$$

N_{above}: total number of samples with MC-LR concentrations equal or above the reference values.

N_{total}: total number of samples.

Risk assessment

Due to the limited information to assess the carcinogenic potential of MCs in general (USEPA, 2015b), the MC-LR non-carcinogenic risk (*i.e.*, chronic effects) for each drinking water exposure scenario was determined based on current scientific evidence (USEPA, 2015a). The HQ for non-carcinogenic health effects for each scenario was estimated by the ratio between the expected MC-LR concentration in drinking water and the reference values that represent the tolerable concentrations (Eq. 2).

$$\text{HQ} = \frac{C_{\text{dw}}}{RfC} \quad (2)$$

HQ: hazard quotient; C_{dw}: expected concentration of MC-LR (μg L^{-1}) in drinking water for each scenario (see Table 2); *RfC*: reference concentration of MC-LR (μg L^{-1}) in drinking water. $\text{HQ} \leq 1$ indicates that the exposure does not result in significant adverse non-carcinogenic effects, while HQ ˃ 1 indicates potential adverse health effects. The specific HQ values indicate the potential to cause adverse effects on health, but not the value of the risk (USEPA, 2014).

The HQ values were estimated using different sources for the reference concentrations (RfC). The first one was based on the WHO guideline for drinking water (1.00 μg L^{-1}), which is the same adopted by Brazilian legislation (Brasil, 2017, 2021). The second one was based on the 10-day health advisory established by USEPA (2015a) for children above 6 years old and adults (hereafter referred to as "children and adults") (1.60 μg L^{-1}) and for bottle-fed infants and young children of pre-school ("infants") (0.30 μg L^{-1}). These values are based on both body weight and drinking water intake by each age interval. The values of mean, median, and UCL95% of HQ in drinking water were estimated through the ProUCL5.1 Software (USEPA, 2015c, 2015d). The UCL95% values for HQs were calculated because they are considered more conservative and appropriate for estimating long-term risks than mean values (USEPA, 2015c).

Results

MC-LR in raw water in the Cascata and Guarapiranga systems

Our dataset from 2011 to 2018 had cases of MC-LR higher than 1.00 μg L^{-1} in the raw water from both Cascata and Guarapiranga systems, but especially

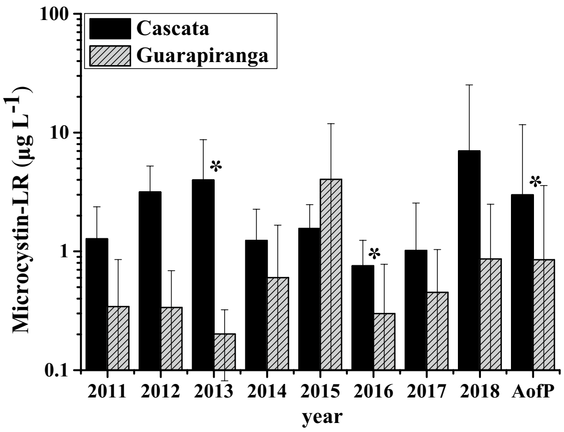

Fig. 2 Microcystin-LR (MC-LR) concentrations (µg L^{-1}) in the Guarapiranga and Cascata systems. Data range from 2011 to 2018, including an average of the whole period (AofP). Error bars are the calculated standard deviations. The symbol asterisk indicates significant statistical differences (Mann–Whitney test, $p < 0.05$) between the systems

from the former. Considering the full dataset, the yearly mean MC-LR concentrations in the Cascata system were higher in comparison to the Guarapiranga system, with significant statistical differences for the years 2013 and 2016 (Fig. 2).

Evaluation of the scenarios of MC-LR removal by the water treatment processes

Due to the different treatment processes, the expected residual MC-LR concentrations in the finished water varied between the Cascata and Guarapiranga systems (Table S3) for both intracellular and extracellular MC-LR. The Guarapiranga system showed lower probabilities of exceeding the RfC at all considered scenarios in comparison to the Cascata system. The most restrictive RfC (0.30 µg L^{-1}) showed the highest probabilities to be exceeded in the considered scenarios (Table 3; Tables S4 and S5; Fig. S1).

For the Cascata system, the dissolved MC-LR had a probability of exceeding the RfC for infants higher than 69% regardless of the scenario, potentially leading to at least 252 days of exposure to concentrations above the threshold value of 0.30 µg L^{-1} per year (Table 3). Also in Cascata, children and adults exhibited a significant potential exposure to dissolved MC-LR for a minimum of 142 and 172 days per year, considering the thresholds from USEPA (1.60 µg L^{-1}) and WHO (1.00 µg L^{-1}), respectively. If the MC-LR remained in the intracellular form (scenario COI), the probability of exceeding the RfC was at least 11.5 times lower (for infants) than the one for the dissolved form (scenario COD) in the optimistic scenario. In addition, for the pessimistic scenario, the probability of exceeding the RfC was 1.4 times (for infants) and 5.5 times (for children and adults) lower in comparison to the probabilities for the dissolved MC-LR (Table 3). The exposure scenarios for the Guarapiranga system indicated that the probabilities of exceeding the RfC were always below 6% (*i.e.*, 22 days of exposure per year) for all RfC considered and regardless of the MC-LR form (dissolved or intracellular).

Table 3 Probability of exceedance (%) of different MC-LR thresholds and the minimum number of days per year during which the MC-LR exposure through drinking water can exceed the reference concentration values

	USEPA health advisory dosage of MC-LR				WHO guideline value	
System/ scenarios	Infants[a]		Children and adults[b]		Population (all ages)[c]	
	Probability of exceeding (%)	Min (days)	Probability of exceeding (%)	Min (days)	Probability of exceeding (%)	Min (days)
COI	6	22	3	11	3	11
COD	69	252	39	142	47	172
CPI	53	193	8	30	19	69
CPD	72	263	44	161	50	183
GOI	0	0	0	0	0	0
GOD	5	18	1	4	2	7
GPI	2	7	0	0	0	0
GPD	6	22	2	7	2	7

[a]Ten-day health advisory dosage (0.30 µg L^{-1})

[b]Ten-day health advisory dosage (1.60 µg L^{-1})

[c]WHO (1.00 µg L^{-1})

Risk assessment

For the Guarapiranga system, all scenarios evaluated had HQ < 1 (Table 4). However, for the Cascata system, the pessimistic scenario for intracellular MC-LR (CPI) and both scenarios for dissolved MC-LR (COD and CPD) resulted in HQ > 1 for infants, regardless of the statistical parameter considered (mean, median, or UCL95%) (Table 4). Overall, considering the other RfC (*i.e.*, 1.6 µg L^{-1} and 1.0 µg L^{-1}), most scenarios for Cascata also resulted in HQ > 1 considering mean and UCL95% (but not median) values. Therefore, the potential non-carcinogenic risk posed to the population exposed to MC-LR in drinking water from Cascata was very high, especially for infants whose UCL95% values ranged from 1.550 to 30.910 from optimistic to pessimistic scenarios.

Discussion

Our dataset showed relatively high levels of MC-LR in the raw water from both the Cascata and Guarapiranga systems during the period analyzed. Tropical urban reservoirs in general have been experiencing increased nutrient pollution in the last decades (Forde et al., 2019) mainly due to anthropogenic influences of unplanned urban growth, untreated sewage disposal, and riparian vegetation removal associated with the worsening effects of climate change. In the tropical reservoirs of São Paulo State, higher MC-LR yields seem to be stimulated by nutrient enrichment (mainly phosphorus), lower wind velocities, and higher air temperatures (Cunha et al., 2018). Previous studies in Cascata and Guarapiranga have already reported increasing trophic status in both systems associated to high concentrations of nutrients and chlorophyll (Moschini-Carlos et al., 2009; Oliver & Ribeiro, 2016; Sonobe et al., 2019). Besides water quality deterioration due to untreated sewage and urban runoff (Fontana et al., 2014; Bicudo & Bicudo, 2017), our dataset suggested that the cyanobacterial community in both waterbodies (Cascata and Guarapiranga) has been consistently producing MC-LR and therefore increasing the risks of human intoxication.

Conventional water treatment processes like the one in the Cascata system are widely used in Brazil and can remove intracellular MC-LR (unless cells are lysed or damaged). However, they usually have limited effectiveness for removing dissolved MC-LR (Drikas et al., 2001; Ewerts et al., 2013; Mkhonto et al., 2020). Furthermore, increasing dissolved MC-LR in the water can be caused by the chloride disinfection step in DWTPs, leading to damages to cells' integrity by chemical oxidation (Merel et al., 2013b; Zamyadi et al., 2013).

Due to the difficulty of ensuring the removal of intact cyanobacterial cells, additional separation technologies, such as adsorption or membrane filtration, can be considered to further eliminate the residual

Table 4 HQ estimated considering USEPA health advisory dosage of MC-LR and WHO values. HQ ≥ 1.00 (highlighted in bold) represents risks of adverse health effect; HQ ≤ 1.00, no adverse health effect is expected

	USEPA health advisory dosage of MC-LR						WHO guideline value		
System/ scenarios	Infants[a]			Children and adults[b]			Population (all ages)[c]		
	Mean	Median	UCL 95%	Mean	Median	UCL 95%	Mean	Median	UCL 95%
COI	0.503	0.150	**1.550**	0.094	0.028	0.291	0.151	0.045	0.465
COD	**8.487**	**2.583**	**15.743**	**1.591**	0.484	**2.952**	**2.546**	0.775	**4.723**
CPI	**3.593**	**1.100**	**11.127**	0.674	0.206	**2.086**	**1.078**	0.330	**3.338**
CPD	**9.980**	**3.050**	**30.910**	**1.871**	0.572	**5.796**	**2.994**	0.915	**9.273**
GOI	0.029	0.007	0.064	0.005	0.001	0.012	0.009	0.002	0.019
GOD	0.224	0.043	0.510	0.042	0.008	0.096	0.067	0.013	0.153
GPI	0.112	0.020	0.254	0.021	0.004	0.048	0.034	0.006	0.076
GPD	0.280	0.053	0.637	0.053	0.010	0.119	0.084	0.016	0.191

[a]Ten-day health advisory dosage (0.30 µg L^{-1})

[b]Ten-day health advisory dosage (1.60 µg L^{-1})

[c]WHO (1.00 µg L^{-1})

dissolved toxin (Antoniou et al., 2014; Dixon et al., 2011). The use of powdered or granular activated carbon can be an interesting alternative to remove MC-LR due to its efficiency and low cost (Villars et al., 2020). Notwithstanding, special attention has to be taken to the characteristics of the activated carbon and water to ensure an efficient removal (Park et al., 2020). Gijsbertsen-Abrahamse et al. (2006) reported no damage to cells during the membrane ultra/nanofiltration. However, the control of operational parameters in membrane filtration is essential to avoid the rapid increase of transmembrane pressure throughout the filtration process (Newcombe et al., 2021).

In our study, the HQs were high for the Cascata system (Table 4). For this reservoir, the UCL95% of the HQs varied from 1.550 to 30.910 (infants), 0.291 to 5.796 (children and adults), and 0.465 to 9.273 (population from all ages), indicating potential risks of MC-LR exposure for all considered ages. In addition, special attention should be given for infants since, regardless of the scenario considered, the UCL95% values of the HQs were always > 1. These results are similar to those observed in a study performed in conventional DWTPs in Quebec (Canada) and for alternative water treatment technologies (*i.e.*, riverbank filtration) in Kubani (Nigeria) (Uche et al., 2017). Uche et al. (2017) also observed that although the conventional DWTP could remove 98% of MC-LR from the raw water, the HQs varied between 1.6 and 4.1 for adults and infants. The alternative treatment in turn was able to remove around 36% of MC-LR, resulting in HQs from 2.5 to 4.6.

Advanced treatment units (*e.g.*, ozonation, membrane filtration) are especially important when targeting the dissolved form of MC-LR (Pietsch et al., 2002). More conventional processes such as coagulation, flocculation and filtration, are usually not able to remove MC-LR (Munoz et al., 2020), especially if it is in the dissolved form (Weir et al., 2020). These observations were reinforced in our study as the HQs for the dissolved MC-LR were greater in comparison to the values for the intracellular form. Our results indicated that the water treatment technology used in the Cascata system was probably inappropriate in face of the relatively high MC-LR concentrations in the raw water, leading to HQ values frequently > 1 for most scenarios considered. On the other hand, the expected higher efficiencies of the membrane ultrafiltration units coupled with the already lower MC-LR concentrations in the raw water in Guarapiranga were associated to lower HQs and therefore safer drinking water for all scenarios considered (Table 4). These observations are probably associated to the low-pressure membranes (*i.e.*, < 5 bar) in Guarapiranga. Ultrafiltration membranes are able to retain particles with diameter as small as 1 nm (Obotey Ezugbe & Rathilal, 2020), whereas the dimension of MC-LR molecules are usually around 1.4–2.9 nm (Abbas et al., 2020; Zhang et al., 2011). Thus, the presence of an ultrafiltration unit, such as observed in Guarapiranga, probably lead to high removal of MC-LR, reducing the HQs. On the other hand, our results highlighted the need of higher removal efficiencies in the DWTP of the Cascata system, since this system had higher MC-LR concentrations in the raw water and therefore greater risks for the supplied population (Table 4).

The USEPA health advisory dosage of MC-LR provides information on contaminants in drinking water that can cause adverse effects in humans. There are different health advisory dosages of MC-LR, such as 1-day health advisory, 10-day health advisory, drinking water equivalent level, and lifetime health advisory (USEPA, 2018). The health advisory period consists of the concentration of contaminants in drinking water that should not cause any non-carcinogenic effects for a specific period of exposure days. Therefore, for longer periods, lower RfC will be more appropriate (for example, benzene 10-day health advisory dosage is 200 μg L^{-1}, while lifetime health advisory dosage is 3 μg L^{-1}) (USEPA, 2018). Regarding MC-LR, USEPA considers the ten-day health advisory dosage of MC-LR based on the study from Heinze (1999). This health advisory dosage indicates that USEPA considers a maximum of 10 days of exposure to unsafe concentrations of MC-LR per year could be tolerable. This observation is interesting once even in the optimistic scenarios, populations supplied by Cascata may be exposed to MC-LR for more than 10 days per year (Table 3, maximum of 263 days) and, consequently, a more restrictive RfC should be used.

Although the 10-day health advisory dosage is not to be construed as legally enforceable federal standards, they describe technical guidance to assist federal, state, and local officials, as well as managers of public or community water systems, in protecting public health (USEPA, 2015a). In 2014, a 48-h "do not drink" advisory was issued for Toledo, USA, due to high concentration of MC-LR and, in 2007, up to 2 million inhabitants of Wuxi, China, were not supplied with drinking water due to a massive toxic bloom of *Microcystis* spp. (Huisman et al., 2018). These events reinforce the importance of a constant monitoring of cyanobacteria in water supply systems in addition to risk assessment.

Considering our scenarios for the Cascata system, the risks of non-carcinogenic health effects for infants were critical even when the more permissive MC-LR reference values were considered (Table 4). Drinking water is a significant source of potential exposure to toxic substances among infants. Infants present the highest rate of water intake relative to their body weight, since water is the primary liquid in their diet, mainly for those younger than 6 (Grandjean, 2004; Mokoena et al., 2016; Popkin et al., 2010). For children older than 6, other foods and liquids are introduced into their diet, decreasing relative water consumption and making it similar to the intake by adults (USEPA, 2015a). As for the MC-LR impacts on the infants' health, they are more vulnerable than adults because of different parameters related to toxicodynamic (*i.e.*, exposures can occur during periods of enhanced susceptibility) and/or toxicokinetic (*i.e.*, absorption, excretion, and metabolism) (USEPA, 2002; Weirich & Miller, 2014). A study conducted by Li et al. (2011) suggested that chronic exposure to MC-LR (MC-LR daily intake of 2.03 $\mu g\ L^{-1}$) was probably associated with liver damage in children from the Three Georges Reservoir Region, China. Although adults are thus less vulnerable to MC-LR intoxication, our study revealed that this part of the population could also be affected since HQ values > 1 were observed for most scenarios in Cascata, even for the optimistic one (COD, UCL95% of HQ $= 2.952$; Table 4).

Finally, our results evidenced two main perspectives to be considered in respect to drinking water quality to protect consumers' health in Brazil. The first one is related to the protection of the water sources, including the provision of gray infrastructure (*e.g.*, sewer networks and wastewater treatment plants). Also, remediating impacted water bodies through canopy cover restoration and other ecological engineering techniques (Palmer et al., 2014) can bring benefits to the raw water quality and even decrease treatment costs (Cunha et al., 2016). The second one follows a more reactive approach to update existing DWTPs or propose complementary/advanced treatment techniques to effectively remove MC-LR from raw water when necessary. Combining more conventional treatments with new technologies can be promising for the removal of total MC-LR, even its dissolved fraction (Şengül et al., 2018; Weir et al., 2020). Further studies are needed to fully understand the dynamics of MC-LR in water bodies, the mechanisms of human exposure, and the health effects due to long-term exposure to MC-LR. Our study can be a starting point for more complete risk analyses focusing on preventive actions to improve water treatment efficiency and avoid human health implications related to MC-LR intoxication that can be applied elsewhere. In addition, the use of HQ in public health management could help identifying priority areas and populations that should receive special attention from decision makers and health authorities.

Conclusions

To the best of our knowledge, the present study is one of the first to provide a preliminary risk assessment of MC-LR intoxication related to drinking water in Brazil. While such investigations are relatively common in other countries (mainly from North America, Oceania, and Europe), they are still scarce in Brazil, despite the frequent occurrence of HCBs in local eutrophic reservoirs. The assessment of the non-carcinogenic risks associated with the ingestion of MC-LR from drinking water was conducted in two water supply systems from the São Paulo state in Brazil: Cascata and Guarapiranga. As a limitation of our investigation, due to data availability constraints, we considered MC-LR removal efficiencies achieved by conventional and advanced DWTPs as reported in previous studies for the intracellular and dissolved forms.

We found that people of all ages potentially have high probability of being exposed to the studied cyanotoxin, and we reported high non-carcinogenic risks of MC-LR exposure for all scenarios in the Cascata system, even after drinking water treatment. These results reinforced the limited expected removal efficiency of conventional water treatment, especially regarding the dissolved form of MC-LR. On the other hand, the presence of an ultrafiltration step in DWTPs (as in Guarapiranga) probably reduces the exposure to unsafe MC-LR concentrations in drinking water to acceptable levels (HQ < 1). Although epidemiological information regarding human health long-term exposure to MC-LR concentrations remains unclear, the possible association of exposure to MC-LR with other adverse and genotoxic effects cannot be underestimated. Developing countries, such as Brazil, have been facing challenges related to the lack of investments in water supply systems and sanitation infrastructure in general due to economic, social, financial, technological, and political issues. Our research raises a critical perspective about how changes or deterioration in raw water quality associated with inappropriate technology in DWTPs can pose high risks for children and adults due to the consumption of contaminated water. In addition, the risks reported in our study emphasizes the necessity to develop strategies to avoid and reduce the exposure to MC-LR in drinking water, in order to prevent negative human health implications associated with eutrophic freshwaters.

Acknowledgements The authors are grateful to Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) for the scholarship to JF Malta and for the funding to DGF Cunha (PROEX/PPGSHS/EESC/USP). The authors also thank Murilo de Souza Ferreira for the help with the maps on the Arcgis®.

Funding CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico) funded this research (Grants #300899/2016-5 and #406855/2016–1).

Data availability The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Competing interests The authors declare no competing interests.

References

Abbas, T., Kajjumba, G. W., Ejjada, M., Masrura, S. U., Marti, E. J., Khan, E., & Jones-Lepp, T. L. (2020). Recent advancements in the removal of cyanotoxins from water using conventional and modified adsorbents—A contemporary review. *Water, 12*, 2756. https://doi.org/10.3390/w12102756

Aguilera, A., Haakonsson, S., Martin, M. V., Salerno, G. L., & Echenique, R. O. (2018). Bloom-forming cyanobacteria and cyanotoxins in Argentina: A growing health and environmental concern. *Limnologica, 69*, 103–114. https://doi.org/10.1016/j.limno.2017.10.006

Akcaalan, R., Young, F. M., Metcalf, J. S., Morrison, L. F., Albay, M., & Codd, G. A. (2006). Microcystin analysis in single filaments of Planktothrix spp. in laboratory cultures and environmental blooms. *Water Research, 40*, 1583–1590. https://doi.org/10.1016/j.watres.2006.02.020

Almanza, V., Parra, O., De M., Bicudo, C. E., Baeza, C., Beltran, J., Figueroa, R., & Urrutia, R. (2016). Occurrence of toxic blooms of Microcystis aeruginosa in a central Chilean (36° Lat. S) urban lake. *Revista Chilena de Historia Natural, 89*, 8. https://doi.org/10.1186/s40693-016-0057-7

Almuhtaram, H., Cui, Y., Zamyadi, A., & Hofmann, R. (2018). Cyanotoxins and cyanobacteria cell accumulations in drinking water treatment plants with a low risk of bloom formation at the source. *Toxins (basel)., 10*, 430. https://doi.org/10.3390/toxins10110430

Amorim, C. A., Moura, A., & do N. (2021). Ecological impacts of freshwater algal blooms on water quality, plankton biodiversity, structure, and ecosystem functioning. *Science of the Total Environment, 758*, 143605. https://doi.org/10.1016/j.scitotenv.2020.143605

Antoniou, M. G., de La Cruz, A. A., Pelaez, M. A., Han, C., He, X., Dionysiou, D. D., Song, W., O'Shea, K., Ho, L., Newcombe, G., Dixon, M. B., Teixeira, M. R., Triantis, T. M., Hiskia, A., Kaloudis, T., Balasubramanian, R., Pavagadhi, S., & Sharma, V. K. (2014). Practices that prevent the formation of cyanobacterial blooms in water resources and remove cyanotoxins during physical treatment of drinking water. In *Comprehensive water quality and purification*, (pp. 173–195). Elsevier. https://doi.org/10.1016/B978-0-12-382182-9.00032-3

Aubriot, L., Zabaleta, B., Bordet, F., Sienra, D., Risso, J., Achkar, M., & Somma, A. (2020). Assessing the origin of a massive cyanobacterial bloom in the Río de la Plata (2019): Towards an early warning system. *Water Research, 181*, 115944. https://doi.org/10.1016/j.watres.2020.115944

Azevedo, S. M. F., Carmichael, W. W., Jochimsen, E. M., Rinehart, K. L., Lau, S., Shaw, G. R., & Eaglesham, G. K. (2002). Human intoxication by microcystins during renal dialysis treatment in Caruaru—Brazil. *Toxicology, 181–182*, 441–446. https://doi.org/10.1016/S0300-483X(02)00491-2

Barros, M. U. G., Wilson, A. E., Leitão, J. I. R., Pereira, S. P., Buley, R. P., Fernandez-Figueroa, E. G., & Capelo-Neto, J. (2019). Environmental factors associated with toxic cyanobacterial blooms across 20 drinking water reservoirs in a semi-arid region of Brazil. *Harmful Algae, 86*, 128–137. https://doi.org/10.1016/j.hal.2019.05.006

Bernard, C., Ballot, A., Thomazeau, S., Maloufi, S., Furey, A., Mankiewicz-Boczek, J., Pawlik-Skowrońska, B., Capelli, C., & Salmaso, N. (2017). Appendix 2: Cyanobacteria associated with the production of cyanotoxins. In *Handbook of cyanobacterial monitoring and cyanotoxin analysis*, (pp. 501–525). John Wiley & Sons, Ltd, Chichester, UK. https://doi.org/10.1002/9781119068761.app2

Bicudo, C. E., & de Campos Bicudo, D. (Eds.). (2017). *100 anos da represa Guarapiranga: lições e desafios*. Editora CRV. https://doi.org/10.24824/978854441690.7

Brasil. (2019). Sistema de Informação de Vigilância da Qualidade da Água para Consumo Humano - SISAGUA [WWW Document]. Ministério da Saúde. http://sisagua.saude.gov.br/sisagua/login.jsf. Accessed 1 June 2019.

Brasil, J., Attayde, J. L., Vasconcelos, F. R., Dantas, D. D. F., & Huszar, V. L. M. (2016). Drought-induced water-level reduction favors cyanobacteria blooms in tropical shallow lakes. *Hydrobiologia, 770*, 145–164. https://doi.org/10.1007/s10750-015-2578-5

Brasil, M., & da S. (2017). Portaria de Consolidação Nº5 [WWW Document]. 28 Setembro.

Brasil, M., & da S. (2021). Portaria GM/MS Nº 888, de 4 de Maio de 2021.

CETESB. (2014). Qualidade das Águas Interiores no Estado de São Paulo - 2013. São Paulo.

CETESB. (2015). Qualidade das Águas Interiores no Estado de São Paulo - 2014. São Paulo.

CETESB. (2016). Qualidade das Águas Interiores no Estado de São Paulo - 2015. São Paulo.

CETESB. (2018). Qualidade das Águas Interiores no Estado de São Paulo 2017. São Paulo.

CETESB. (2017). Qualidade das Águas Interiores no Estado de São Paulo - 2016. São Paulo.

CETESB. (2019a). Qualidade das Águas Interiores no Estado de São Paulo - 2018. São Paulo.

CETESB. (2019b). Infoáguas [WWW Document]. Cia. Ambient. do Estado São Paulo. https://sistemainfoaguas.cetesb.sp.gov.br/. Accessed 1 May 2019.

CETESB. (2020). Qualidade das Águas Interiores no Estado de São Paulo - 2019. São Paulo.

Chorus, I., & Welker, M. (2021). *Toxic cyanobacteria in water: a guide to their public health consequences, monitoring and management* (p. 858). Taylor & Francis. https://doi.org/10.1201/9781003081449

Chorus, I., & Bartram, J. (1999). Toxic cyanobacteria in water: A guide to their public health consequence monitoring and management. In *Freshwater biology*, (pp. 1–400). London. https://doi.org/10.1046/j.1365-2427.2003.01107.x

Codd, G. A., Testai, E., Funari, E., & Svirčev, Z. (2020). Cyanobacteria, cyanotoxins, and human health. In *Water treatment for purification from cyanobacteria and cyanotoxins*, (pp. 37–68). Wiley. https://doi.org/10.1002/9781118928677.ch2

Cunha, D. G. F., Dodds, W. K., & Loiselle, S. A. (2018). Factors related to water quality and thresholds for microcystin concentrations in subtropical Brazilian reservoirs. *Inland Waters, 8*(3), 368–380. https://doi.org/10.1080/20442041.2018.1492526

Cunha, D. G. F., Sabogal-Paz, L. P., & Dodds, W. K. (2016). Land use influence on raw surface water quality and treatment costs for drinking supply in São Paulo State (Brazil). *Ecological Engineering, 94*, 516–524. https://doi.org/10.1016/j.ecoleng.2016.06.063

Daly, R. I., Ho, L., & Brookes, J. D. (2007). Effect of chlorination on Microcystis aeruginosa cell integrity and subsequent microcystin release and degradation. *Environmental Science and Technology, 41*, 4447–4453. https://doi.org/10.1021/es070318s

Devi, A., Chiu, Y.-T., Hsueh, H.-T., & Lin, T.-F. (2021). Quantitative PCR based detection system for cyanobacterial geosmin/2-methylisoborneol (2-MIB) events in drinking water sources: Current status and challenges. *Water Research, 188*, 116478. https://doi.org/10.1016/j.watres.2020.116478

Dixon, M. B., Falconet, C., Ho, L., Chow, C. W. K., Neill, B. K. O., & Newcombe, G. (2011). Removal of cyanobacterial metabolites by nanofiltration from two treated waters. *Journal of Hazardous Materials, 188*, 288–295. https://doi.org/10.1016/j.jhazmat.2011.01.111

Dörr, F. A., Pinto, E., Soares, R. M., de Oliveira, F., & e Azevedo, S. M. (2010). Microcystins in South American aquatic ecosystems: Occurrence, toxicity and toxicological assays. *Toxicon, 56*, 1247–1256. https://doi.org/10.1016/j.toxicon.2010.03.018

Drikas, M., Chow, C. W. K., House, J., & Burch, M. D. (2001). Using coagulation, flocculation, and settling to remove toxic cyanobacteria. *Journal American Water Works Association, 93*, 100–111. https://doi.org/10.1002/j.1551-8833.2001.tb09130.x

Ewerts, H., Swanepoel, A., & Du Preez, H. (2013). Efficacy of conventional drinking water treatment processes in removing problem-causing phytoplankton and associated organic compounds. *Water SA, 39*, 739. https://doi.org/10.4314/wsa.v39i5.19

Fawell, J. K., Mitchell, R. E., Everett, D. J., & Hill, R. E. (1999). The toxicity of cyanobacterial toxins in the mouse: I Microcystin-LR. *Human and Experimental Toxicology, 18*, 162–167. https://doi.org/10.1177/096032719901800305

Forde, M., Izurieta, R., & Ôrmeci, B. (2019). Water quality in the Americas, water and health. The Inter-American Network of Academies of Sciences IANAS, México.

Fontana, L., Albuquerque, A. L. S., Brenner, M., Bonotto, D. M., Sabaris, T. P. P., Pires, M. A. F., Cotrim, M. E. B., & Bicudo, D. C. (2014). The eutrophication history of a tropical water supply reservoir in Brazil. *Journal of Paleolimnology, 51*, 29–43. https://doi.org/10.1007/s10933-013-9753-3

Funari, E., & Testai, E. (2008). Human health risk assessment related to cyanotoxins exposure. *Critical Reviews in Toxicology, 38*, 97–125. https://doi.org/10.1080/10408440701749454

Gaget, V., Humpage, A. R., Huang, Q., Monis, P., & Brookes, J. D. (2017). Benthic cyanobacteria: A source of cylindrospermopsin and microcystin in Australian drinking water reservoirs. *Water Research, 124*, 454–464. https://doi.org/10.1016/j.watres.2017.07.073

Giannuzzi, L., Sedan, D., Echenique, R., & Andrinolo, D. (2011). An acute case of intoxication with cyanobacteria and cyanotoxins in recreational water in Salto Grande Dam. *Argentina Marine Drugs, 9,* 2164–2175. https://doi.org/10.3390/md9112164.

Gijsbertsen-Abrahamse, A. J., Schmidt, W., Chorus, I., & Heijman, S. G. J. (2006). Removal of cyanotoxins by ultrafiltration and nanofiltration. *Journal of Membrane Science, 276,* 252–259. https://doi.org/10.1016/j.memsci.2005.09.053.

Grandjean, A. C. (2004). Water requirements, impinging factors, and recommended intakes. *Water, sanitation and health protection and the human environment* (pp. 25–34). World Health Organization.

He, J., Li, G., Chen, J., Lin, J., Zeng, C., Chen, J., Deng, J., & Xie, P. (2017). Prolonged exposure to low-dose microcystin induces nonalcoholic steatohepatitis in mice: A systems toxicology study. *Archives of Toxicology, 91*, 465–480. https://doi.org/10.1007/s00204-016-1681-3

He, X., Liu, Y., Conklin, A., Westrick, J., Weavers, L. K., Dionysiou, D. D., Lenhart, J. J., Mouser, P. J., Szlag, D., & Walker, H. W. (2016). Toxic cyanobacteria and drinking water: Impacts, detection, and treatment. *Harmful Algae, 54*, 174–193. https://doi.org/10.1016/j.hal.2016.01.001

Heinze, R. (1999). Toxicity of the cyanobacterial toxin microcystin-LR to rats after 28 days intake with the drinking water. *Environmental Toxicology, 14*, 57–60. https://doi.org/10.1002/(SICI)1522-7278(199902)14:1%3c57:AID-TOX9%3e3.0.CO;2-J

Ho, J. C., Michalak, A. M., & Pahlevan, N. (2019). Widespread global increase in intense lake phytoplankton blooms since the 1980s. *Nature, 574*, 667–670. https://doi.org/10.1038/s41586-019-1648-7

Hoeger, S. J., Shaw, G., Hitzfeld, B. C., & Dietrich, D. R. (2004). Occurrence and elimination of cyanobacterial toxins in two Australian drinking water treatment plants. *Toxicon, 43*, 639–649. https://doi.org/10.1016/j.toxicon.2004.02.019

Huisman, J., Codd, G. A., Paerl, H. W., Ibelings, B. W., Verspagen, J. M. H., & Visser, P. M. (2018). Cyanobacterial blooms. *Nature Reviews Microbiology, 16*, 471–483. https://doi.org/10.1038/s41579-018-0040-1

IARC. (2010). *Ingested nitrate and nitrite, and cyanobacterial peptide toxins*. IARC Press.

Ibelings, B. W., Backer, L. C., Kardinaal, W. E. A., & Chorus, I. (2014). Current approaches to cyanotoxin risk assessment and risk management around the globe. *Harmful Algae, 40*, 63–74. https://doi.org/10.1016/j.hal.2014.10.002

Jiang, P., Liu, X., Zhang, J., Te, S. H., Gin, K.Y.-H., Fan, Y. V., Klemeš, J. J., & Shoemaker, C. A. (2021). Cyanobacterial risk prevention under global warming using an extended Bayesian network. *Journal of Cleaner Production, 312*, 127729. https://doi.org/10.1016/j.jclepro.2021.127729

Kelly, N. E., Javed, A., Shimoda, Y., Zastepa, A., Watson, S., Mugalingam, S., & Arhonditsis, G. B. (2019). A Bayesian risk assessment framework for microcystin violations of drinking water and recreational standards in the Bay of Quinte, Lake Ontario. *Canada Water Research, 162,* 288–301. https://doi.org/10.1016/j.watres.2019.06.005.

Kouakou, C. R. C., & Poder, T. G. (2019). Economic impact of harmful algal blooms on human health: A systematic review. *Journal of Water and Health, 17*, 499–516. https://doi.org/10.2166/wh.2019.064

Lahti, K., Rapala, J., Kivimäki, A.-L., Kukkonen, J., Niemelä, M., & Sivonen, K. (2001). Occurrence of microcystins in raw water sources and treated drinking water of Finnish waterworks. *Water Science and Technology, 43*, 225–228. https://doi.org/10.2166/wst.2001.0744

Li, Y., Chen, J., Zhao, Q., Pu, C., Qiu, Z., Zhang, R., & Shu, W. (2011). A cross-sectional investigation of chronic exposure to microcystin in relationship to childhood liver damage in the Three Gorges Reservoir Region. *China. Environ. Health Perspect., 119*, 1483–1488. https://doi.org/10.1289/ehp.1002412

Massey, I. Y., Al osman, M., & Yang, F. (2020). An overview on cyanobacterial blooms and toxins production: Their occurrence and influencing factors. *Toxin Review,* 1–21. https://doi.org/10.1080/15569543.2020.1843060

Menezes, C., Churro, C., & Dias, E. (2017). Risk levels of toxic cyanobacteria in Portuguese recreational freshwaters. *Toxins (basel)., 9*, 327. https://doi.org/10.3390/toxins9100327

Merel, S., David, W., Chicana, R., Snyder, S., Baurès, E., & Thomas, O. (2013a). State of knowledge and concerns on cyanobacterial blooms. *Environment International, 59*, 303–327.

Merel, S., Walker, D., Chicana, R., Snyder, S., Baurès, E., & Thomas, O. (2013b). State of knowledge and concerns on cyanobacterial blooms and cyanotoxins. *Environment International, 59*, 303–327. https://doi.org/10.1016/j.envint.2013.06.013

Mkhonto, S., Ewerts, H., Swanepoel, A., & Snow, G. C. (2020). The efficacy of a recovered wash water plant in removing cyanobacteria cells and associated organic compounds. *Water Supply*. https://doi.org/10.2166/ws.2020.086

Mokoena, M. M., Mukhola, M. S., & Oknonkwo, O. J. (2016). Hazard assessment of microcystins from the household's drinking water. *Applied Ecology and Environmental Research, 14*, 695–710. https://doi.org/10.15666/aeer/1403_695710

Morón-lópez, J., Nieto-reyes, L., & El-shehawy, R. (2017). Assessment of the influence of key abiotic factors on the alternative microcystin degradation pathway (s) (mlr^-): A detailed comparison with the mlr route (mlr^+). *Science of the Total Environment, 599–600*, 1945–1953. https://doi.org/10.1016/j.scitotenv.2017.04.042

Moschini-Carlos, V., Bortoli, S., Pinto, E., Nishimura, P. Y., Gomes de Freitas, L., Pompêo, M. L., & Dörr, F. (2009). Cyanobacteria and cyanotoxins in the Billings Reservoir (São Paulo, SP, Brazil). *Limnetica, 28*, 273–282. https://doi.org/10.23818/limn.28.23

Moura, A. do N., Aragão-Tavares, N. K. C., & Amorim, C. A. (2017). Cyanobacterial blooms in freshwaters bodies in a semiarid region, northeastern Brazil: A review. *Journal of Limnology*, *77*. https://doi.org/10.4081/jlimnol.2017.1646

Munoz, M., Cirés, S., de Pedro, Z. M., Colina, J. Á., Velásquez-Figueroa, Y., Carmona-Jiménez, J., Caro-Borrero, A., Salazar, A., Santa María Fuster, M.-C., Contreras, D., Perona, E., Quesada, A., & Casas, J. A. (2020). Overview of toxic cyanobacteria and cyanotoxins in Ibero-American freshwaters: Challenges for risk management and opportunities for removal by advanced technologies. *Science of the Total Environment*, 143197. https://doi.org/10.1016/j.scitotenv.2020.143197

Newcombe, G., Ho, L., & Neto, J. C. (2021). Controlling cyanotoxin occurrence: Drinking-water treatment. In *Toxic Cyanobacteria in Water*, (pp. 591–639). CRC Press. https://doi.org/10.1201/9781003081449

Obotey Ezugbe, E., & Rathilal, S. (2020). Membrane technologies in wastewater treatment: A review. *Membranes (basel)., 10*, 89. https://doi.org/10.3390/membranes10050089

Oliver, S. L., & Ribeiro, H. (2016). Water supply, climate change and health risk factors: Example case of São Paulo—Brazil, 433–447. https://doi.org/10.1007/978-3-319-24660-4_25

Palmer, M. A., Filoso, S., & Fanelli, R. M. (2014). From ecosystems to ecosystem services: Stream restoration as ecological engineering. *Ecological Engineering, 65*, 62–70. https://doi.org/10.1016/j.ecoleng.2013.07.059

Park, J., Kang, J., Jung, S., Choi, J., Lee, S., Yargeau, V., & Kim, S. (2020). Investigating microcystin-LR adsorption mechanisms on mesoporous carbon, mesoporous silica, and their amino-functionalized form: Surface chemistry, pore structures, and molecular characteristics. *Chemosphere*, *246*. https://doi.org/10.1016/j.chemosphere.2020.125811

Pietsch, J., Bornmann, K., & Schmidt, W. (2002). Relevance of intra- and extracellular cyanotoxins for drinking water treatment paper presented in parts as a lecture at the annual meeting of the Water Chemical Society — A division of the German Chemical Society (Wasserchemische Gesellschaft — Fachgruppe. *Acta Hydrochimica Et Hydrobiologica, 30*, 7. https://doi.org/10.1002/1521-401X(200207)30:1%3c7::AID-AHEH7%3e3.0.CO;2-W

Popkin, B. M., D'Anci, K. E., & Rosenberg, I. H. (2010). Water, hydration, and health. *Nutrition Reviews, 68*, 439–458. https://doi.org/10.1111/j.1753-4887.2010.00304.x

Pouria, S., de Andrade, A., Barbosa, J., Cavalcanti, R., Barreto, V., Ward, C., Preiser, W., Poon, G. K., Neild, G., & Codd, G. (1998). Fatal microcystin intoxication in haemodialysis unit in Caruaru, Brazil. *Lancet, 352*, 21–26. https://doi.org/10.1016/S0140-6736(97)12285-1

Rastogi, R. P., Madamwar, D., & Incharoensakdi, A. (2015). Bloom dynamics of cyanobacteria and their toxins: Environmental health impacts and mitigation strategies. *Frontiers in Microbiology, 6*, 1–22. https://doi.org/10.3389/fmicb.2015.01254

SABESP. (2019a). Companhia de Saneamento Básico do Estado de São Paulo [WWW Document]. http://site.sabesp.com.br/site/Default.aspx. Accessed 28 May 2019.

SABESP. (2019b). Formulário de Referência 2019b. São Paulo.

São Paulo (2016). istema Integrado de Gerenciamento de Recursos Hídricos do Estado de São Paulo - SigRH [WWW Document]. Revisão e Atualização do Plano Bacia da UGRHI 02 - Paraíba do Sul. http://www.sigrh.sp.gov.br/public/uploads/documents/CBH-PS/14089/sintese-do-plano-de-bacia-ugrhi_02-01-08-17-completo.pdf. Accessed 4 June 2019.

Sarkar, S., Kimono, D., Albadrani, M., Seth, R. K., Busbee, P., Alghetaa, H., Porter, D. E., Scott, G. I., Brooks, B., Nagarkatti, M., Nagarkatti, P., & Chatterjee, S. (2019). Environmental microcystin targets the microbiome and increases the risk of intestinal inflammatory pathology via NOX2 in underlying murine model of Nonalcoholic Fatty Liver Disease. *Science and Reports, 9*, 8742. https://doi.org/10.1038/s41598-019-45009-1

Schreidah, C. M., Ratnayake, K., Senarath, K., & Karunarathne, A. (2020). Microcystins: Biogenesis, toxicity, analysis, and control. *Chemical Research in Toxicology, 33*, 2225–2246. https://doi.org/10.1021/acs.chemrestox.0c00164

Şengül, A. B., Ersan, G., & Tüfekçi, N. (2018). Removal of intra- and extracellular microcystin by submerged ultrafiltration (UF) membrane combined with coagulation/flocculation and powdered activated carbon (PAC) adsorption. *Journal of Hazardous Materials, 343*, 29–35. https://doi.org/10.1016/j.jhazmat.2017.09.018

Sha, J., Xiong, H., Li, C., Lu, Z., Zhang, J., Zhong, H., Zhang, W., & Yan, B. (2021). Harmful algal blooms and their eco-environmental indication. *Chemosphere, 274*, 129912. https://doi.org/10.1016/j.chemosphere.2021.129912

Shang, L., Feng, M., Xu, X., Liu, F., Ke, F., & Li, W. (2018). Co-occurrence of microcystins and taste-and-odor compounds in drinking water source and their removal in a full-scale drinking water treatment plant. *Toxins (basel)., 10*, 1–17. https://doi.org/10.3390/toxins10010026

Sonobe, H. G., Lamparelli, M. C., & Cunha, D. G. F. (2019). Avaliação espacial e temporal de aspectos sanitários de reservatórios com captação de água para abastecimento em SP com ênfase em cianobactérias e cianotoxinas. *Eng. Sanit. e Ambient., 24*, 909–918. https://doi.org/10.1590/s1413-41522019193351

Sotero-Santos, R. B., Silva, C. R. D. S. E., Verani, N. F., Nonaka, K. O., & Rocha, O. (2006). Toxicity of a cyanobacteria bloom in Barra Bonita Reservoir (Middle Tietê River, São Paulo, Brazil). *Ecotoxicology and Environmental Safety, 64*, 163–170. https://doi.org/10.1016/j.ecoenv.2005.03.011

Spoof, L., & Catherine, A. (2017). Appendix 3: Tables of microcystins and nodularins. In *Handbook of cyanobacterial monitoring and cyanotoxin analysis*, (pp. 526–537). John Wiley & Sons, Ltd, Chichester, UK. https://doi.org/10.1002/9781119068761.app3

Svirčev, Z., Lalić, D., Bojadžija Savić, G., Tokodi, N., Drobac Backović, D., Chen, L., Meriluoto, J., & Codd, G. A. (2019). Global geographical and historical overview of cyanotoxin distribution and cyanobacterial poisonings. *Archives of Toxicology, 93*, 2429–2481. https://doi.org/10.1007/s00204-019-02524-4

Swanepoel, A., Du Preez, H., & Cloete, N. (2017). The occurrence and removal of algae (including cyanobacteria) and their related organic compounds from source water in Vaalkop Dam with conventional and advanced drinking water treatment processes. *Water SA, 43*, 67. https://doi.org/10.4314/wsa.v43i1.10

Szlag, D., Sinclair, J., Southwell, B., & Westrick, J. (2015). Cyanobacteria and cyanotoxins occurrence and removal from five high-risk conventional treatment drinking water plants. *Toxins (basel)., 7*, 2198–2220. https://doi.org/10.3390/toxins7062198

Tamele, I. J., & Vasconcelos, V. (2020). Microcystin incidence in the drinking water of Mozambique: Challenges for public health protection. *Toxins (basel)., 12*, 368. https://doi.org/10.3390/toxins12060368

Teixeira, M. R., & Rosa, M. J. (2006). Comparing dissolved air flotation and conventional sedimentation to remove cyanobacterial cells of Microcystis aeruginosa. *Separation and Purification Technology, 52*, 84–94. https://doi.org/10.1016/j.seppur.2006.03.017

Teixeira, M. R., Rosa, M. J., Sorlini, S., Biasibetti, M., Christophoridis, C., & Edwards, C. (2020). Removal of cyanobacteria and cyanotoxins by conventional physical-chemical treatment. In *Water treatment for purification from cyanobacteria and cyanotoxins*, (pp. 69–97). Wiley. https://doi.org/10.1002/9781118928677.ch3

Turner, P. C., Gammie, A. J., Hollinrake, K., & Codd, G. A. (1990). Pneumonia associated with contact with cyanobacteria. *BMJ, 300*, 1440–1441. https://doi.org/10.1136/bmj.300.6737.1440

Uche, A. U., Edward, A. M., & Bahram, G. (2017). Risk assessment of cyanobacteria-toxins for small drinking water treatment plants with lake water intakes. *International Journal of Water Resource and Environmental Engineering, 9,* 121–126. https://doi.org/10.5897/IJWREE2016.0669.

USEPA. (2019a). Recommended human health recreational ambient water quality criteria or swimming advisories for microcystins and cylindrospermopsin documents. Washington, DC.
USEPA. (2019b). Cyanobacteria and cyanotoxins: Information for drinking water systems.
USEPA. (2018). Edition of the drinking water standards and health advisories tables. U.S. Environmental Protection Agency, Washington, DC.
USEPA. (2015a). *Health effects support document for the cyanobacterial toxin microcystins*. United States Environmental Protection Agency.
USEPA. (2015b). Drinking water health advisory for the cyanobacterial microcystin toxins. *U.S. Evironmental Protection Agency,* 75. https://doi.org/10.1590/S1980-57642009DN30100010
USEPA. (2015c). ProUCL 5.1.
USEPA. (2015d). ProUCL Version 5.1 - User guide: Statistical software for environmental applications for data sets with and without nondetect observations. Washington, DC.
USEPA. (2014). National Air Toxics Assessment, NATA Glossary of Terms.
USEPA. (2012). Environmental Technology Verification Program.
USEPA. (2002). Child-specific exposure factors handbook, Interim report, EPA-600-P-. ed. United States Environmental Protection Agency, Washington, DC.
Villars, K., Huang, Y., & Lenhart, J. J. (2020). Removal of the cyanotoxin microcystin-LR from drinking water using granular activated carbon. *Environmental Engineering Science*, *37*(9), 585–595. https://doi.org/10.1089/ees.2020.0017
Vu, H. P., Nguyen, L. N., Zdarta, J., Nga, T. T. V., & Nghiem, L. D. (2020). Blue-green algae in surface water: Problems and opportunities. *Current Pollution Reports, 6,* 105–122. https://doi.org/10.1007/s40726-020-00140-w.
Walter, J. M., Lopes, F. A. C., Lopes-Ferreira, M., Vidal, L. M., Leomil, L., Melo, F., de Azevedo, G. S., Oliveira, R. M. S., Medeiros, A. J., Melo, A. S. O., De Rezende, C. E., Tanuri, A., & Thompson, F. L. (2018). Occurrence of harmful cyanobacteria in drinking water from a severely drought-impacted semi-arid region. *Frontiers in Microbiology, 9*. https://doi.org/10.3389/fmicb.2018.00176
Wang, H., Xu, C., Liu, Y., Jeppesen, E., Svenning, J.-C., Wu, J., Zhang, W., Zhou, T., Wang, P., Nangombe, S., Ma, J., Duan, H., Fang, J., & Xie, P. (2021). From unusual suspect to serial killer: Cyanotoxins boosted by climate change may jeopardize African megafauna. *The Innovation*, 100092. https://doi.org/10.1016/j.xinn.2021.100092
Weber, S. J., Mishra, D. R., Wilde, S. B., & Kramer, E. (2020). Risks for cyanobacterial harmful algal blooms due to land management and climate interactions. *Science of the Total Environment, 703*, 134608. https://doi.org/10.1016/j.scitotenv.2019.134608
Weir, M. H., Wood, T. A., & Zimmer-Faust, A. (2020). Development of methods to estimate microcystins removal and water treatment resiliency using mechanistic risk modelling. *Water Research*, 116763. https://doi.org/10.1016/j.watres.2020.116763
Weirich, C. A., & Miller, T. R. (2014). Freshwater harmful algal blooms: Toxins and children's health. *Current Problems in Pediatric and Adolescent Health Care, 44*, 2–24. https://doi.org/10.1016/j.cppeds.2013.10.007
WHO. (2017). Guidelines for drinking water quality: Fourth edition incorporating the first addendum. *World Health Organization.*
WHO. (2015). *Management of cyanobacteria in drinking water supplies: Information for regulators and water suppliers*. Switz.
WHO. (2009). *Water safety plan manual*. World Health Organization.
WHO. (2003). Cyanobacterial toxins: Microcystin-LR in drinking-water, In *Background document for development of WHO guidelines for drinking-water quality*, (p. 18). World Health Organization Geneva, Switzerland.
Yeager, N., & Carpenter, A. (2019). State approaches to addressing cyanotoxins in drinking water. *AWWA Water Science, 1,* e1121.
Yi, X., Xu, S., Huang, F., Wen, C., Zheng, S., Feng, H., Guo, J., Chen, J., Feng, X., & Yang, F. (2019). Effects of chronic exposure to microcystin-LR on kidney in mice. *International Journal of Environmental Research and Public Health, 16*, 5030. https://doi.org/10.3390/ijerph16245030
Zamyadi, A., Fan, Y., Daly, R. I., & Prévost, M. (2013). Chlorination of Microcystis aeruginosa: Toxin release and oxidation, cellular chlorine demand and disinfection by-products formation. *Water Research, 47*, 1080–1090. https://doi.org/10.1016/j.watres.2012.11.031
Zamyadi, A., MacLeod, S. L., Fan, Y., McQuaid, N., Dorner, S., Sauvé, S., & Prévost, M. (2012). Toxic cyanobacterial breakthrough and accumulation in a drinking water plant: A monitoring and treatment challenge. *Water Research, 46*, 1511–1523. https://doi.org/10.1016/j.watres.2011.11.012
Zhang, D., Xie, P., & Chen, J. (2010). Effects of temperature on the stability of microcystins in muscle of fish and its consequences for food safety. *Bulletin of Environment Contamination and Toxicology, 84*, 202–207. https://doi.org/10.1007/s00128-009-9910-6
Zhang, H., Zhu, G., Jia, X., Ding, Y., Zhang, M., Gao, Q., Hu, C., & Xu, S. (2011). Removal of microcystin-LR from drinking water using a bamboo-based charcoal adsorbent modified with chitosan. *Journal of Environmental Sciences, 23*, 1983–1988. https://doi.org/10.1016/S1001-0742(10)60676-6

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.