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Short Communication

Lake Erie fish safe to eat yet afflicted by algal hepatotoxins

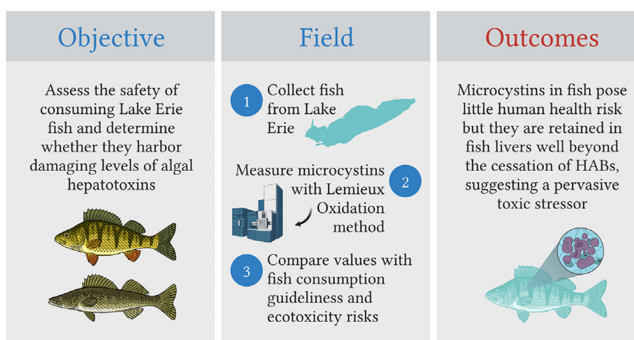
René S. Shahmohamadloo [a,b,*], Satyendra P. Bhavsar [c,d], Xavier Ortiz Almirall [c,e], Stephen A.C. Marklevitz [f], Seth M. Rudman [a], Paul K. Sibley [b]

[a] School of Biological Sciences, Washington State University, 14204 NE Salmon Creek Ave, Vancouver, WA 98686, United States
[b] School of Environmental Sciences, University of Guelph, 50 Stone Rd E, Guelph, ON N1G 2W1, Canada
[c] Environmental Monitoring and Reporting Branch, Ontario Ministry of the Environment, Conservation and Parks, 125 Resources Rd, Toronto, ON M9P 3V6, Canada
[d] Department of Physical & Environmental Sciences, University of Toronto, 1065 Military Trail, Toronto, ON M1C 1A4, Canada
[e] IQS School of Engineering, Universitat Ramon Llull, Via Augusta, 390, 08017 Barcelona, Spain
[f] Lake Erie Management Unit, Ontario Ministry of Natural Resources and Forestry, 320 Milo Road, Wheatley, ON N0P 2P0, Canada

HIGHLIGHTS

- Lake Erie fish were assessed for risks to fish and human consumers from microcystins.
- Toxins were low in fillets but high in livers, well before and after bloom events.
- Pervasive microcystins in livers suggests sublethal effects of algae blooms on fish.

GRAPHICAL ABSTRACT



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ABSTRACT

Toxic harmful algal blooms (HABs) pose serious threats to human health and instances of wildlife death have been documented across taxa. However, the extent of toxicological impacts on wildlife species is largely unresolved, raising uncertainty about the repercussions of increasingly severe HABs on the biodiversity and functioning of aquatic ecosystems. Here, we conducted a field study to assess human health risks from consuming fish caught across all stages of a HAB and to determine the pervasiveness of potentially harmful levels of the cosmopolitan toxin microcystin on fish populations. We collected 190 fish in 2015 and 2017 from Lake Erie, a large freshwater ecosystem that is highly productive for fisheries and is an epicenter of HABs and microcystin toxicity events. Fish muscles and livers were analyzed for total microcystins, which was used to conduct a human health risk assessment for comparison against fish consumption advisory benchmarks available for Lake Erie. We found microcystins pose low risks to human health from fillet consumption (mean 1.80 ng g^{-1} ww) but substantial risks to fish health and recruitment from liver concentrations measured well before and after seasonal bloom events (mean 460.13 ng g^{-1} ww). Our findings indicate HABs are a previously underappreciated but pervasive threat to fish populations.

1. Introduction

It has been over 50 years since the United States and Canada committed to restoring and protecting the waters of the Great Lakes (National Research Council, 1985). Yet, harmful algal blooms (HABs) continue to pose a tremendous risk to freshwater biodiversity conservation (Reid et al., 2019),

* Corresponding author at: School of Biological Sciences, Washington State University, 14204 NE Salmon Creek Ave., Vancouver, WA 98686, United States.
E-mail address: rene.shahmohamadloo@wsu.edu (R.S. Shahmohamadloo).

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precipitating a concerted effort to explore opportunities for intervention to mitigate the emerging threats to populations, communities, and ecosystems (FAO, 2020). The frequency and severity of HABs are increasing due, in part, to global changes in climate and anthropogenic eutrophication (Huisman et al., 2018). The economic losses from HABs are estimated to exceed US$4.2 billion annually in the United States and Canada combined, due to deleterious effects on essential goods and services, including drinking water, recreation and tourism, and fisheries (Ho et al., 2019; Smith et al., 2019). Food recalls linked to tissue accumulation of HAB toxins in fish and poisoning cases in humans and animals are also rising (IPCC, 2022). Among the most widespread and internationally monitored of these toxins are microcystins, a class of hepatotoxins that can be tremendously detrimental to human health (Chorus and Welker, 2021; Huisman et al., 2018).

Beyond concerns for human health, HABs can adversely impact wildlife populations with mortality noted across a range of taxa (Breinlinger et al., 2021; Landsberg, 2002). Aquatic species are particularly vulnerable to microcystin toxicity events as they may inhabit waters with recurring HABs that are projected to increase both in duration from climate change (Chapra et al., 2017) and toxicity from nutrient runoff (Hellweger et al., 2022). Controlled laboratory studies have revealed microcystins can enter fish directly by ingestion of water, indirectly by ingestion of zooplankton or lower trophic fish species, or absorption through the gills, altering key aspects of fish life history including stress responses, growth and recruitment (Deblois et al., 2011; Dyble et al., 2011; Le Manach et al., 2016; Malbrouck and Kestemont, 2006; Shahmohamadloo et al., 2022, 2021). However, key questions about how HABs impact fish species are unresolved including the extent to which natural populations of fish are impacted by sublethal concentrations of microcystins. There is also emerging pressure to ensure HABs do not deter the development of aquaculture and fisheries to feed an expanding human population (Brown et al., 2020; IPCC, 2022). Fish species inhabiting Lake Erie, a large and highly productive freshwater ecosystem known for consistent and toxic HABs (Hellweger et al., 2022; Michalak et al., 2013), are particularly at risk. Determining the extent of microcystin accumulation and retention across time and species is therefore a crucial step towards understanding the impacts of HABs on the health of fish and fisheries.

We analyzed 190 Walleye (*Sander vitreus*), White Bass (*Morone chrysops*), White Perch (*Morone americana*), and Yellow Perch (*Perca flavescens*) from Lake Erie in 2015 and 2017 pre-, during, and post-HAB periods occurring in the western, west central, and east central basins. We dissected and analyzed the total microcystin content of: 1) muscles, which is of socioeconomic and cultural significance to Great Lakes fisheries and communities (Smith et al., 2019), and 2) livers, which is the primary target organ of microcystin toxicity and driver of fish mortality (Huisman et al., 2018; Malbrouck and Kestemont, 2006; Shahmohamadloo et al., 2022). The microcystin content of the liver can serve as an overall indicator of fish health to better understand the consequences of HABs exposure. We quantified microcystins in fish tissues using the MMPB Lemieux Oxidation method followed by liquid chromatography coupled to mass spectrometric analysis (Anaraki et al., 2020). This innovative method rectifies issues with prior work that relied heavily on the enzyme linked immunosorbent assay (ELISA), a method that was designed for quantifying microcystins in water samples but is prone to false positives when applied to fish tissues (Flores et al., 2018; Wituszynski et al., 2017). The shortcomings of ELISA combined with an overall lack of field sampling currently limits the characterization of the true risks to both human health from consuming fish and the impacts of HABs on fish populations. Here, we hypothesize that the microcystin concentration of fish muscles will pose low human health risks, but fish will accumulate microcystins in livers commensurate with recent HAB exposure.

2. Materials and methods

Fish capture times and locations were determined following the Lake Erie Harmful Algal Bloom Forecast published biweekly by the National Oceanic and Atmospheric Administration (https://coastalscience.noaa.gov/research/stressor-impacts-mitigation/hab-forecasts/lake-erie/). Water monitoring data was collected by the Ontario Ministry of Natural Resources and Forestry, in conjunction with the National Oceanic and Atmospheric Administration's weekly monitoring program for Lake Erie (https://www.ncei.noaa.gov/access/metadata/landing-page/bin/iso?id=gov.noaa.nodc:GLERL-CIGLR-HAB-LakeErie-water-qual). The total length of fish was measured because it provides a reliable proxy for age and is used in fish consumption advisories (MECP, 2017). Muscles and livers were analyzed for total microcystins (free and bound) using an optimized Lemieux Oxidation method (Anaraki et al., 2020) on individuals and, when many individuals of a given species were captured within a given timeframe, pools of individuals.

Briefly, all microcystins (including free and protein bound forms) were oxidized to a common fragment 2-methyl-3-methoxy-4-phenylbutyric acid (MMPB), which after purification and concentration was analyzed by liquid chromatography coupled to mass spectrometric analysis. The validated method is detailed in Anaraki et al. (2020). A human health risk assessment was performed using microcystin concentrations for fish muscles, and the data generated was compared against fish consumption advisory benchmarks for microcystins in Lake Erie. The margin of exposure and hazard quotient was additionally calculated to estimate the potential for adverse effects to develop in humans from exposure to microcystins. Linear mixed effects (LME) models were used to test for significant concentrations of microcystins and to identify whether species identity, location within Lake Erie, and HAB status influenced concentrations. See *SI Appendix* for further details.

3. Results and discussion

3.1. Muscle concentration and human health risk

Fish muscles contained microcystins ($F_{1,184} = 145.58$, $p < 0.0001$), at a mean concentration of 1.80 ng g^{-1} ww across species and locations (Fig. 1). However, only 2/190 of samples had concentrations exceeding the World Health Organization's (WHO) tolerable daily intake (TDI) value of 0.04 μg kg^{-1} bodyweight per day (Poste et al., 2011), namely two walleye with 13.1 ng g^{-1} ww (TDI, 0.042) and 17.2 ng g^{-1} ww (TDI, 0.056), respectively (Dataset S1). The margin of exposure and the hazard quotient, used in human health risk assessment to estimate the level at which a compound is carcinogenic and can cause adverse effects, both suggest microcystins present a low risk (Dataset S1). Applying these results against the fish consumption advisory benchmarks for Lake Erie, 89 % of muscles were <6 ng g^{-1} ww microcystins, the lowest fish consumption advisory benchmark in Ontario (Table S1). All muscles are in the 'unrestricted' meal category

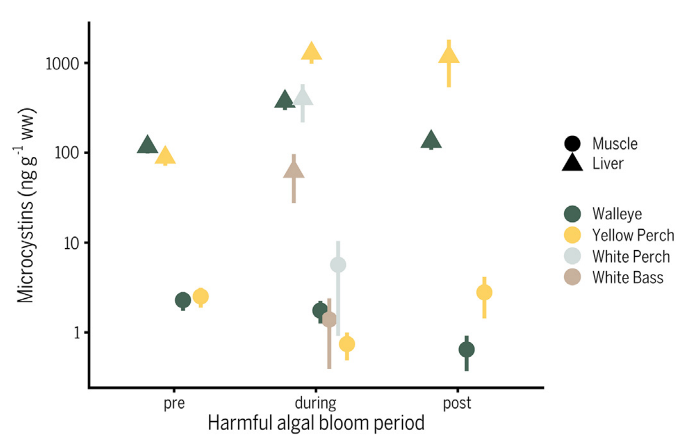

Fig. 1. Total microcystins in muscles and livers from four fish species (Walleye, Yellow Perch, White Perch, White Bass) collected pre-, during, and post-harmful algal bloom in Lake Erie.

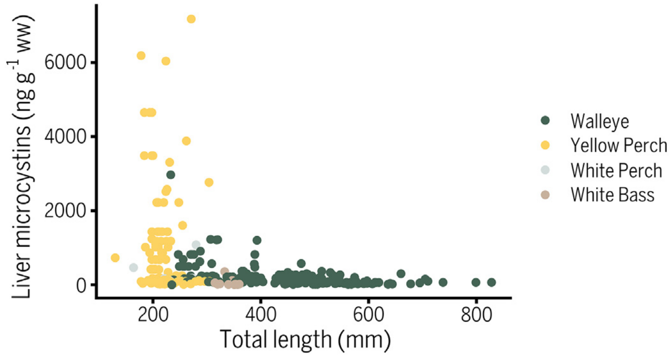

Fig. 2. Relationship between total microcystins in liver and total length of fish.

(<25 ng g^{-1} ww) in Ohio (Table S2). Overall, the contents of microcystins we observed in Lake Erie fish included in our study poses no additional human health risk.

3.2. Liver concentration and fish health impacts

Fish accumulate microcystins in their livers ($F_{1,184}$ = 184.74, p < 0.0001), with a mean of 460.13 ng g^{-1} ww across species and locations (Fig. 1). Liver microcystin concentrations varied across HAB periods ($F_{2,182}$ = 14.43, p < 0.0001), with fish collected during the bloom having >6× the concentration of those collected pre-bloom. However, pre-bloom concentrations were still appreciable, demonstrating that fish retain toxins as a legacy of prior exposure. Fish species also differed in their liver microcystin content ($F_{3,183}$ = 11.51, p < 0.0001), with the highest concentrations in Yellow Perch. The relationship between liver microcystins with length (Fig. 2) and body weight (Fig. 3) further shows higher concentrations in Yellow Perch. Liver concentrations of microcystins varied by location within Lake Erie ($F_{2,182}$ = 39.31, p < 0.0001), with fish caught in the western basin having 44 % higher microcystins than fish from the east central basin.

The consistently high microcystin concentrations in fish livers indicate a potential biological issue not currently considered by management agencies. Acute exposure to microcystins has long been postulated to be among several stress factors involved in fish kills during HAB events (Ibelings et al., 2005). It is well-documented that microcystins are potent inhibitors of protein phosphatases in hepatocytes (Chorus and Welker, 2021; Huisman et al., 2018), causing tumor-promotion, liver damage, and protein dysregulation in juvenile and adult fish even at sublethal levels (Malbrouck and Kestemont, 2006; Shahmohamadloo et al., 2021). Microcystin levels observed here are comparable with concentrations previously shown to have toxic effects during the development of embryos and larvae across a range of fish species in the laboratory (Malbrouck and Kestemont, 2006). These sublethal effects suggest the concentrations we observed in wild fish may translate to negative impacts on population dynamics. Fish livers contained comparatively high values of microcystins even prior to the yearly bloom period, demonstrating microcystins are accumulated and retained. Sustained microcystin levels, with peaks corresponding with seasonal HABs, reinforces the supposition that sublethal impacts on fish could have considerable effects on fish growth and recruitment. These effects could be an undocumented cause of reduced Yellow Perch recruitment (Marcek et al., 2021), a major economic and management issue in Lake Erie. Planned phosphorus load reduction is predicted to increase algal toxins in Lake Erie (Hellweger et al., 2022) which may exacerbate any fish recruitment issues.

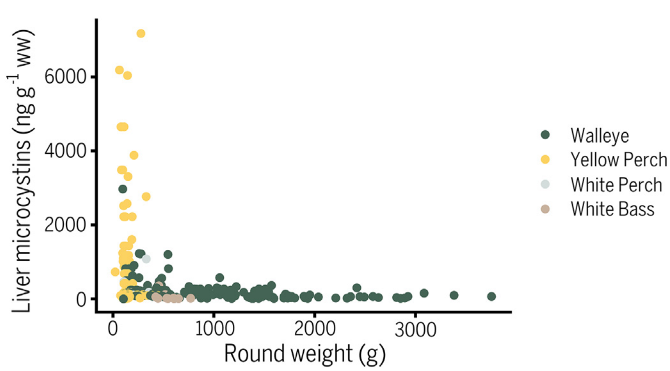

Fig. 3. Relationship between total microcystins in liver and round weight of fish.

Concerns about toxicant exposure via human consumption are centered on muscle concentrations based on the convention of consuming fillets. Whole fish consumption is practiced in various communities due, in part, to added nutritional benefits (Beveridge et al., 2013). Microcystins are stable during cooking and boiling (Harada et al., 1996) and can potentially leach out of organs and spread onto fillets. These data suggest that general and sensitive populations should avoid eating whole fish from Lake Erie and other waterbodies with recurring seasonal blooms, restricting consumption to fillets.

4. Conclusions

This study demonstrates microcystins are retained in fish livers well after a HAB event and may be a persistent contaminant in aquatic ecosystems. Many fish species are highly mobile and some go on large-scale seasonal migrations within the Great Lakes, owing to factors such as foraging opportunities, behavioral thermoregulation to avoid warm waters, competitive pressure, selective fishing pressure, genetic predisposition, and reduced habitat quality due to HABs (Matley et al., 2020). Thus, the possibility exists that fish tissue concentrations may not necessarily correlate with capture location and associated water toxins (Qian et al., 2021), raising the profile of HABs as a wildlife and resource management issue for the entirety of Lake Erie. Our study shows that eating fish fillets from Lake Erie poses little human health risk. However, recurring and increasingly severe toxic HABs likely have major effects on freshwater fish and fisheries and deserve future study to protect the health of these ecologically and economically important species.

CRediT authorship contribution statement

René S. Shahmohamadloo: Methodology, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization. **Satyendra P. Bhavsar:** Conceptualization, Methodology, Resources, Writing – review & editing, Supervision, Project administration, Funding acquisition. **Xavier Ortiz Almirall:** Methodology, Validation, Resources, Writing – review & editing. **Stephen A.C. Marklevitz:** Investigation, Resources, Writing – review & editing. **Seth M. Rudman:** Software, Formal analysis, Writing – original draft, Writing – review & editing. **Paul K. Sibley:** Conceptualization, Methodology, Resources, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Data availability

I have shared the link to my data at the Attach File step.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2022.160474.

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