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Mercury, microcystins and Omega-3 polyunsaturated fatty acids in farmed fish in eutrophic reservoir: Risk and benefit assessment[☆]

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ABSTRACT

Fish is an important source of nutritional omega-3 (n-3) polyunsaturated fatty acids, but it also readily accumulates toxic mercury (Hg) and microcystins (MC) in eutrophic aquatic systems. In China, farmed fish was widely consumed, and aquaculture has caused pervasive eutrophication of freshwater lakes, resulting in the increasing accumulation of MC in fish tissue. To assess the risk-benefit of consuming farmed fish, 205 fish samples of 10 primary species were collected from the eutrophic Wujiangdu (WJD) Reservoir, SW China. The contents of Hg, microcystin-RR (MC-RR), microcystin-LR (MC-LR), and polyunsaturated fatty acids (PUFA) in fish were analyzed. The results showed that THg and MeHg concentrations in all fish sampls were well below the safety limit (500 ng/g w.w) established by the Standardization Administration of China, with average values of 22.9 ± 22.8 and 6.0 ± 6.6 ng/g wet weight (w.w.), respectively. Average concentrations of MC-RR and MC-LR were 40 ± 80 and 50 ± 80 ng/g w.w., respectively. MC-RR and MC-LR concentrations in fish were significantly higher in silver carp and black carp than in perch and catfish ($p < 0.05$). In nutritional terms, average concentrations of n-3 PUFA and the eicosapentaenoic (EPA) + docosahexaenoic acids (DHA) of fish were 2.0 ± 2.5 and 1.4 ± 0.5 mg/g w.w., respectively. The risk-benefit assessment suggests that the n-3 PUFA benefits from consuming all farmed fish species in the WJD Reservoir outweigh the adverse effects of MeHg. However, except for perch, most fish species still pose a high MC-LR exposure risk that created a requirement for fish consumption advisories and monitoring. Consequently, more attention should be paid on the health risk of combined exposure to pollutants by aquatic product consumption.

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1. Introduction

Fish, an important source of high-quality proteins for humans, is rich in essential n-3 PUFA, especially the two essential fatty acids (EFA), eicosapentaenoic (EPA, 20:5n-3) and docosahexaenoic acids (DHA, 22:6n-3). DHA plays an important role in the retinal and neurological development of humans (Anderson et al., 1990). As the precursor of the n-3 eicosanoids, EPA also shows beneficial effects in the prevention of cardiovascular, arrhythmias, and thrombosis disease (Kinsella et al., 1990). While supplying nutrient n-3 PUFA to the human diet, fish also contain toxic heavy metal Hg. As the most toxic form of Hg, methylmercury (MeHg) biomagnifies during its trophic transfer through aquatic food webs. In some aquatic ecosystems, fish can accumulate MeHg concentrations several orders of magnitude higher than that the surrounding water (Wang et al., 2019). Fish consumption is considered the primary pathway of MeHg exposure for most people in the world (FDA, 2000). As a neurotoxin, MeHg can cause adverse effects on the postnatal neurodevelopment even at low exposure levels, and is a risk factor for cardiovascular disease (Mahaffey, 2004; Mergler et al., 2007).

China produces 62% of the world's commercial fish products (FAOSTAT, 2019). Aquaculture production in China has extensively increased due to the increase in fish consumption and the decrease of wild fishery yields. Aquaculture freshwater fish accounts for ~50% of the total fish consumption in China (China Fisheries Statistical Yearbook, 2018). Aquaculture can accelerate

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eutrophication of water due to excess input of nutrients, which readily lead to cyanobacteria blooms. Cyanobacteria are a group of photosynthetic bacteria that can release large amounts of cyanotoxins into the water, which are hazardous to aquatic organisms and humans (Carmichael, 2010). Most cyanotoxin studies focus on the hepatotoxic microcystins. Microcystin-producing blooms occur in many freshwater systems (Papadimitriou et al., 2012; Wituszynski et al., 2017). More than 279 structural variants of MC have been identified, of which the MC-LR is the most toxic MC variant (Bouaicha et al., 2019). MC can cause acute poisoning in human liver and has a deleterious effect on gastrointestinal tract, kidneys, skin by chronic exposure to low concentration MC (Chen et al., 2009; Žegura et al., 2003). MC in water can be ingested and accumulated by aquatic organisms (Cazenave et al., 2005). MC contamination in fish has reported in many eutrophic freshwater bodies in China, including Taihu, Chaohu, and Dianchi lakes (Jia et al., 2014; Jiang et al., 2017; Peng et al., 2010; Zhang et al., 2007).

Hg, MC, and n-3 PUFA in fish are related to food sources, and the metabolism of Hg, MC, and n-3 PUFA vary among different fish species (Arts et al., 2009; Hall et al., 1997; Tidwell et al., 2007; Wang and Wang, 2018; Žegura et al., 2003). The Hg, MC, and n-3 PUFA concentrations in farmed fish species may be significantly different from that in wild fish, due to their differences in fish feed. Previous studies demonstrated that farmed fish is associated with low MeHg due to the biodilution of MeHg in the water body and the short time of MeHg exposure for farmed fish (Liu et al., 2012; Xu et al., 2018). In addition, compared to wild fish, farmed fish also has much less complex food webs so there is less ability to biomagnifies MeHg across trophic levels. It suggests that farmed fish consumption poses limited human MeHg exposure. However, these studies failed to take n-3 PUFA and MC into consideration (Gao, 2013; Zhang, 2014; Zhang et al., 2015). Fish farming can decrease the n-3 PUFA level but increase the MC level in fish (Peng et al., 2010; Rahman, 2008; Šimat et al., 2015). Most of the existing studies on MC focused only on its exposure risk, without combining with fatty acids to balance the risk-benefit of fish consumption (Jia et al., 2014; Peng et al., 2010; Zhang et al., 2009).

To fill the knowledge gaps mentioned above, the present study investigated the contents of Hg, MC, and n-3 PUFA in farmed fish from the WJD Reservior, SW China. An integrated risk and benefit analysis of different farmed fish species was carried out for the evaluation of the exposure risk of MeHg, MC, and benefits of n-3 PUFA for fish consumers.

2. Material and methods

2.1. Sample collection

WJD Reservoir (106°8′26″E, 26°35′20″N), located in Guizhou Province, SW China, is the oldest reservoir in the Wujiang River. This river is one of the largest tributaries of the Yangtze River and has a 10-year history of net cage culture. Five thousand net cages in WJD produce 152 million kg of farmed fish annually (Guizhou Statistical Yearbook, 2018). WJD Reservoir has a surface area of 27,790 km^2 and a maximum water depth of 150 m. The average concentration of total Hg (THg) and MeHg in water are 1.3 ± 0.6 and 0.12 ± 0.04 ng/L, respectively (Feng et al., 2018). Average concentrations of Chl-a, total nitrogen (TN) and total phosphorus (TP) were 10.0 ± 9.3 μg/L, 4.40 ± 0.1, and 0.06 ± 0.01 mg/L, respectively, indicating the eutrophication of water (Feng et al., 2018).

Sampling was conducted from WJD Reservoir in December 2016, and March and August 2017. One integrated water sample, which composes of 0.5 L of surface water (0.5 m below the surface) and 0.5 L of bottom water (0.5 m above the bottom) was collected at next to the cages from the center of the WJD Reservoir. The water sample was filtered through a 0.45 μm Durapore® PVDF membrane filters (Millipore, USA). The filtered water samples were transferred in a cooler to the laboratory and stored at 4 °C for the analysis of MCs.

A total of 205 fish samples covering 10 dominant species of farmed fish were purchased from aquaculture farmers, including 13 grass carps (*Ctenopharynodon idellus*), 24 bluntnose black breams (*Parabramis pekinensis*), 16 silver carps (*Hypophthalmichthys molitrix*), 20 bighead carps (*Aristichthys nobilis*), 27 common carps (*Cyprinus carpio*), 14 crucian carps (*Carassius auratus*), 23 tench (*Tinca tinca*), 12 black carps (*Mylopharyngodon piceus*), 5 perch (*Lateolabrax japonicas*), and 51 catfish (*Parasilurus asotus)*. Among them, 85 fish samples covering all species were collected in August 2017 in summer, 48 and 72 fish samples covering 8 species were collected in December 2016 and March 2017 in winter, respectively. The basic information of fish is summarized in Supplementary Table S1. These fish can be grouped into four feeding habits, i.e., grass carp is herbivorous, silver carp and bighead carp are planktivorous, bluntnose black bream, common carp, crucian carp, and tench are omnivorous, and black carp, perch, and catfish are carnivorous. Most fish species are fed on artificial fish feed, except for planktivorous fish. Planktivorous silver carps and bighead carps are mainly fed on natural phytoplankton and zooplankton, respectively (Cremer and Smitherman, 1980). The artificial fish feeds used for farmed fish was composed of corn, soybean, fish powder and vitamins, and the brand of artificial fish feeds was Tongwei which produced in Shangdong Province. Samples were stored alive in barrels with water and air purge until transported to the laboratory for analysis.

All fish samples were about 1–2 years old, and their body weights and lengths were recorded individually. The sizes of the same fish species were similar, while the length and weight of different fish species varied significantly ($p < 0.05$). About 10–20 g dorsal muscle of each fish was removed and kept at −80 °C until lyophilization, and then homogenized with ballmill grinder and stored at −80 °C until analysis. Samples were weighed before and after free-drying to get the water content.

2.2. Hg analysis

All samples were analyzed for THg, by digesting the muscle tissue in HNO_3:H_2SO_4 ratio of 7:3 (v/v) at 95 °C for 3 h before measuring by CVAFS (Pfeil and Stalvey, 2004; Yan et al., 2005). The samples were analyzed for MeHg, by digesting the muscle tissue in 5 mL KOH solution at 75 °C for 3 h before measuring by GC-CVAFS (Yan et al., 2005). . The detection limits for THg and MeHg were 0.013 ng/g (3σ) and 0.002 ng/g (3σ), respectively. Blank spikes (5%) and duplicates (>10% of samples) were taken regularly throughout the sample preparation. Tort-3 from the National Research Council of Canada was used as the certified reference material (CRM). Recoveries of THg and MeHg in TORT-3 were 93–114% and 101–106%, respectively. THg and MeHg concentrations (ng/g) in dry weight were converted to wet weight (w.w.) using the water content.

2.3. Microcystins analysis

Analysis of MCs in water samples followed a previous method (Chen, 2016). Briefly, the filtrate (1 L) was concentrated on solid-phase extraction cartridge (Agilent Bond Elut C18, USA), which was previously activated with 15 mL of methanol (100%) followed by 15 mL distilled water. The cartridges were then washed with 25 ml distilled water and 25 ml methanol (30%) followed MCs were eluted from the cartridges with 25 mL elution (methanol: Trifluoroacetate (TFA): distilled water; 80:0.02:19.8) and then evaporated to dryness. The residues were dissolved in 1 mL 50% methanol and used for final detection and identification of MCs by high-performance liquid chromatography (HPLC), which consisted of a Shimadzu LC-10 A system with two LC-10 A pumps and a UV detector. Qualitative and quantitative analysis of MCs were performed according to the reference method (Chen, 2016).

Analysis of MC in fish muscle was performed using the solid phase extraction – high-performance liquid chromatography (SPE-HPLC) method (Wu et al., 2011). Briefly, 2.0 g of sample was weighed into an acrylic centrifuge tube and extracted twice in 5 ml 80% methanol. After vortex mixing for 2 min, ultrasonic digesting at 100 W for 10 min, and centrifuging at 3000 r/min for 15 min, the supernatant was transferred and rotary evaporated to dryness. The residue was dissolved in 5 ml 80% Methanol, and the solution was transferred into the solid-phase extraction cartridge (Agilent Bond Elut C18, USA) which had been preconditioned by 6 ml Methanol and 6 ml Milli-Q water. The cartridge was washed with 100 ml water-Methano (25%) and 5 ml Methano- TFA (0.1%). The elution was evaporated to dryness and dissolved in 1 ml 50% Methano, and the solution was subjected to HPLC (Waters-e2695/PDA, USA). The sample was separated by cartridge (Agilent ZORBAX SB-C18, USA) (5 μm, 4.6 × 250 mm) with a mobile phase consisting of solvent A (Acetonitrile) and solvent B (Water-Methano (0.05% TFA)). The linear gradient elution program was described as follow: 0–1 min 70% B, 1–15 min 30% B, 15–20 min 30% B, 20–23 min 70% B, and 23–25 min 70% B. The flow rate was held at 1 ml/min. The detection spectrum was 238 nm. The column temperature was maintained at 40 °C and the injection volume was 10 μl. Quantification of MC was calculated on the basis of known amounts of standard dilutions (0.1, 0.2, 0.5, 1.0, 2.0, 5.0 and 10 μg/ml). MC concentrations (ng/g) in dry weight were converted to wet weight using the water content.

2.4. Fatty acid analysis

Lipid and fatty acid analysis followed the method established by Chinese national food safety standards (GB 5009.168-2016, 2016). The lipid was extracted in the hydrolysis-ether solution. Fatty acids (FA) were trans-esterified to fatty acid methyl esters (FAME) under alkaline conditions. FAME was analyzed by a gas-chromatograph (Agilent 7890, USA). The detailed analysis procedure is presented in Supplementary Section S1.

2.5. Calculation of bioaccumulation factor of MeHg and MC-LR

The Bioaccumulation Factor (BAF) refers to the ratio of the concentration of a toxin in tissue to its concentration in the ambient water, in situations where both the organism and its food are exposed and the ratio does not change substantially. In the present study, we focused on the bioaccumulation of the most toxic variant of Hg and MC. Because the lipid content of aquatic organisms has been shown to affect the bioaccumulation of nonionic organic chemicals. The BAF of MeHg or MC-LR in fish based on lipid normalization is expressed in liters per gram of lipid. Lipid normalization is the process of dividing the total concentration of a chemical in tissue by the fraction of the tissue that is lipid (USEPA, 2000).

$$\mathrm{BAF(x)} = \frac{C_{(x)} \times 100}{C_{(x\ in\ water)} \times C_{total\ lipid}} \tag{1}$$

where x refers to MeHg or MC-LR; $\mathrm{BAF}_{(x)}$ refers to BAF (L/g of lipid) of MeHg or MC-LR; $C_{(x)}$ is the MeHg or MC-LR concentration in fish muscle tissue (ng/g w.w.); $C_{(x\ in\ water)}$ is the MeHg or MC-LR concentration in water (ng/L); and $C_{total\ lipid}$ is the total lipid concentration in fish muscle tissue (mg/g).

2.6. Assessments of risks and benefits

We estimated the potential health risks and benefits of consuming farmed fish in WJD Reservor with the following methods. In method 1, the Estimated Daily intakes (EDI) of MeHg and MC-LR were calculated to evaluate the daily exposure Hg and MC, respectively. EDI of EPA + DHA is daily essential fatty acids for an average person. EDI is calculated as:

$$EDI = \frac{C_{(x)} \times \mathrm{A}}{60kg} \tag{2}$$

where x refers to MeHg, MC-LR or EPA + DHA, and $C_{(x)}$ refers to MeHg, MC-LR or EPA + DHA concentrations in fish; A refers to daily consumption of fish, 300 g/day is selected as a reference standard for the amount fish consumed by an adult, and 60 kg per capita as the default weight for an adult (Magalhães et al., 2001; Peng et al., 2010; Rezaitabar et al., 2017; Zhang et al., 2009).

We also present an integrated risk-benefit estimate for adult cardiovascular and in *uetro* neurodevelopment endpoints on a species-specific basis. In method 2, the net risk/benefit for adult coronary heart disease (CHD) and infant visual recognition memory (VRM) are calculated using the following equations (Ginsberg and Toal 2000, 2009, 2015):

$$\begin{aligned} &Net\ risk/benefit\ for\ adult\ CHD = [(n-3PUFA\ mg/meal) \times (no.\ meals/week) \times (1\ week/7\ days) \times (14.6\%\ lower\ risk/100mg\ n-3\ PUFA)] \\ &-\{[hair\ Hg\ change/fish\ meal) \times (no.\ meals/week)] - 0.51ppm\ hair\ Hg\} \times (23\%\ higher\ risk/1ppm\ hair\ Hg) \end{aligned} \tag{3}$$

$$\begin{aligned} Net\ risk/benefit\ for\ \mathrm{inf}ant\ VRM = {} & [(n-3PUFA\ mg/meal) \times (no.\ meals/week) \times \\ & (1week/7days) \times (3.04VRM\ points) - [(hair\ Hg\ change\ per\ fish\ meal) \times \\ & (no.\ meals/week) \times (3.5VRM\ points/1ppm\ hair\ Hg)] \end{aligned} \tag{4}$$

Species yield positive results from equations (4) have a net benefit, whereas a negative result signifies an increased risk. The detailed description of this method can be seen in Supplementary Section 1. We estimated net risk/benefit from specific species consumption by four possible consumption patterns. According to (CPC, 2019), the mean value of fish intake (including marine fish and freshwater fish) in China is 24.8 g/day, while the urban Chinese has a higher consumption of fish, the average consumption of fish for urban residents in China is 64.5 g/day; The joint FDA/USEPA recommends 8 oz (227 g)/day (USEPA, 2019); Besides, we also choose 300 g/day as a possible maximum consumption of fish.

2.7. Fish consumption advisories

The advised maximum daily consumption of fish according to the RfD_{MeHg} or $TDI_{MC\text{-}LR}$ is calculated using the following formulations (5–6):

$$\mathrm{Max}_{\mathrm{MeHg}} = \frac{RfD_{MeHg} \times \mathrm{AW}}{C_{MeHg}} \tag{5}$$

$$\mathrm{Max}_{\mathrm{MC-LR}} = \frac{TDI_{MC-LR} \times \mathrm{AW}}{C_{MC-LR}} \tag{6}$$

where Max_{MeHg} and $\mathrm{Max}_{MC\text{-}LR}$ (g/day) are the advised maximum quantities of daily consumption of fish based on RfD_{MeHg} and $TDI_{MC\text{-}LR}$, respectively.

2.8. Statistical analysis

Concentrations and BAF values of Hg and MC in fish are expressed as "mean ± standard deviation (SD)". Statistical analysis is performed with SPSS V.21. Comparisons of THg, MeHg, MC-RR, MC-LR, and PUFA concentrations by fish species and feeding habits are conducted using ANOVA (analysis of variance) after testing these variables for normal distribution. In all cases, p-value of <0.05 is considered significant.

3. Results and discussion

3.1. THg and MeHg in fish

As shown in Fig. 1a, the ranges of THg and MeHg concentrations in all fishes from WJD Reservoir were 3.0–185.1 and 0.2–49.9 ng/g w.w., with average values of 22.9 ± 22.8 and 6.0 ± 6.6 ng/g w.w., respectively (n = 205). THg and MeHg concentrations of farmed fish in WJD Reservoir were much lower than the limit of Hg content (500 ng/g w.w.) established by the national limit recommended by the Standardization Administration of China (GB 2762-2017, 2017), and agreed well with previous studies that demonstrated low Hg contents in farmed fish from China (Liu et al., 2012; Yan et al., 2019).

Hg concentrations in fish varied significantly among fish species with the highest values in bighead carp ($p < 0.05$) (53.6 ± 14.8 ng/g w.w. for THg and 13.0 ± 3.8 ng/g w.w. for MeHg, respectively; n = 20) and the lowest values in tench (10.0 ± 4.8 ng/g w.w. for THg and 1.8 ± 1.2 ng/g w.w. for MeHg, respectively; n = 23) ($p < 0.05$) (Fig. 1a). Hg concentrations were highest in planktivorous fish

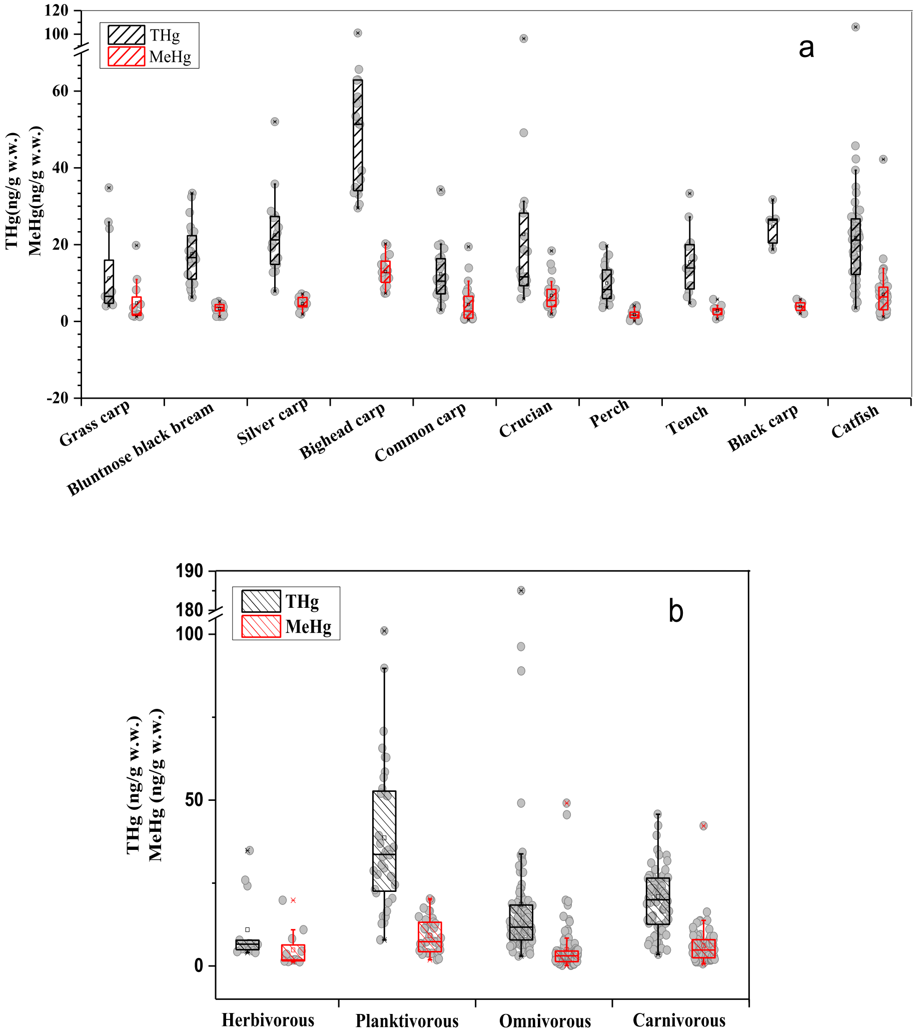

Fig. 1. THg and MeHg concentrations of fish species and feeding habits in the Wujiangdu (WJD) Reservoir.

(38.6 ± 21.9 and 9.3 ± 5.2 ng/g w.w. for THg and MeHg, respectively; n = 36), which were 2–3 times of those in herbivorous fish (11.8 ± 10.9 and 5.3 ± 6.1 ng/g w.w. for THg and MeHg, respectively; n = 13). THg and MeHg concentrations were similar between carnivorous (18.6 ± 25.6 and 5.4 ± 8.1 ng/g w.w. for THg and MeHg, respectively; n = 68) and omnivorous fish (21.0 ± 14.0 ng/g w.w. and 6.8 ± 6.1 ng/g w.w. for THg and MeHg, respectively; n = 64) (Fig. 1b). The various Hg concentration levels in fish species were related to their diets. It seems that the higher THg and MeHg contents in planktivorous fish were because they were mainly feed on plankton instead of pelleted artificial fish food.

Calculating MeHg BAF by the ratio of concentration in tissue to water can not accurately identify the bioaccumulation of different fish species (Barbara et al., 2015; Feng et al., 2018), but the result would be affected by fish age and species. Normalization of BAF values to lipid content can reduce variability when comparing measured BAF values for different fish species at different life stages (USEPA, 2000). BAF that is expressed using the lipid-normalization concentration is considered to be the most reliable way for understanding the bioaccumulation of a toxin in aquatic organisms. It has been used to compare BAF of MC in fish (Rezaitabar et al., 2017), but no studies have calculated the BAF of MeHg based on lipid-normalization. In the present study, BAF_{MeHg} values, calculated based on lipid normalization, range from 17.2 to 8.0 × 10^2 L/g of lipid, with an average of 9.6 ± 12.2 × 10^2 L/g of lipid. Similar to MeHg concentration in fish, BAF_{MeHg} value was highest in bighead carp (32 ± 16 × 10^2 L/g of lipid, n = 20) and lowest in tench (2.1 ± 1.5 × 10^2 L/g of lipid, n = 23) (Fig. 2a). Categorized by feeding habits, average BAF_{MeHg} value of planktivorous fish (21 ± 17 × 10^2 L/g of lipid) was the highest, followed by herbivorous fish (15 ± 21 × 10^2 L/g of lipid). Average BAF_{MeHg} values of omnivorous (6.4 ± 7.6 × 10^2 L/g of lipid) and carnivorous fish (6.1 ± 5.9 × 10^2 L/g of lipid) were lower and approached ($p > 0.05$) (Fig. 2b). This may be explained by the fact that most of the farmed fish was merely feed on the artificial fish feed and grew in a similar living environment (net cages), resulting in a similar level of lipid contents ($p > 0.05$) (Table S1 SI).

3.2. MC-RR and MC-LR in fish

Among all fish samples, only 53.6% and 51.7% samples were associated with detectable MC-RR (1.7–678 ng/g w.w., n = 110) and MC-LR concentrations (1.0–450 ng/g w.w, n = 106), respectively. As shown in Fig. 3a, MC-RR and MC-LR concentrations were highest in silver carp (180 ± 230 ng/g w.w.; n = 11 and 150 ± 160 ng/g w.w., n = 8, respectively) and lowest in catfish (33 ± 22 ng/g w.w., n = 13 and 20 ± 14 ng/g w.w., n = 15, respectively). MC contents of the farmed fish collected from WJD were in the range of those fish from eutrophic lakes in China (Chen et al., 2009; Jia et al., 2014; Peng et al., 2010; Xie et al., 2010; Zhang et al., 2009).

Planktivorous fish showed the highest MC concentrations, whereas herbivorous, omnivorous, and carnivorous fish showed similar lower MC concentrations. For instance, the average MC-RR concentrations of planktivorous, herbivorous, omnivorous, and carnivorous fish were 101 ± 100 ng/g w.w. (n = 26), 49 ± 41 ng/g w.w. (n = 10), 63 ± 101 ng/g w.w. (n = 42) and 13 ± 39 ng/g w.w. (n = 32), respectively; Their average MC-LR concentrations were 58 ± 87 ng/g w.w. (n = 23), 41 ± 65 ng/g w.w. (n = 8), 41 ± 80 ng/g w.w. (n = 42) and 41 ± 91 ng/g w.w. (n = 33), respectively (Fig. 3b). The possible reason for the higher MC concentrations in planktivorous fish were that they feed on algae. As the main producer of MC, algae contained higher MC content than the artificial fish feed which composed of corn, soybean, fish powder and vitamin (Bischoff, 2001).

To evaluate the MC BAF of different fish species, we determined the aqueous MC concentrations in WJD Reservoir. MC-LR concentration of water in WJD Reservoir was 0.07 ± 0.05 μg/L and MC-RR concentration of water was lower than the detection limit (0.04 μg/L), both were far below 1.0 μg/L by WHO guidelines for drinking-water quality (WHO, 2017) and also Chinese standard for drinking water quality (GB 5749-2006, 2006). $BAF_{MC\text{-}LR}$ of fish ranged from 0.1 to 114 L/g of lipid, with an average value of 12 ± 15 L/g of lipid (Fig. 4a). $BAF_{MC\text{-}LR}$ was highest in planktivorous fish (21 ± 27 L/g of lipid, n = 23), followed by omnivorous (12 ± 15 L/g of lipid, n = 42), herbivorous (8.4 ± 5.1 L/g of lipid, n = 8) and carnivorous fish (7.6 ± 13 L/g of lipid, n = 33) (Fig. 4b). Specifically, $BAF_{MC\text{-}LR}$ was highest in silver carp (22 ± 27 L/g of lipid), which was almost 10 times that of catfish (2.2 ± 1.5 L/g of lipid) (Fig. 4a). $BAF_{MC\text{-}LR}$ of silver carp and carnivorous fish from WJD Reservoir was higher than that of the wild ones with the same feeding habits (1.0 ± 0.2 L/g of lipid for silver carp and 1.3 ± 0.2 L/g of lipid for carnivorous, respectively) from Anzali wetland in Iran (Rezaitabar et al., 2017). The higher $BAF_{MC\text{-}LR}$ of fish in WJD probably resulted from the higher MC-LR concentrations of fish muscle but lower MC-LR concentrations of water in WJD.

3.3. Polyunsaturated fatty acids in fish

As shown in Fig. 5, there were substantial differences of polyunsaturated fatty acids profiles among fish species in WJD Reservoir. The varied ranges of n-6 PUFA, n-3 PUFA and EPA + DHA concentrations in different fishes were 0.2–20.1 mg/g w.w., 0.1–25.0 mg/g w.w. and 0.1–22.7 mg/g w.w., with average values of 3.9 ± 3.8, 2.0 ± 2.5 and 1.4 ± 0.5 mg/g w.w., respectively. Except for

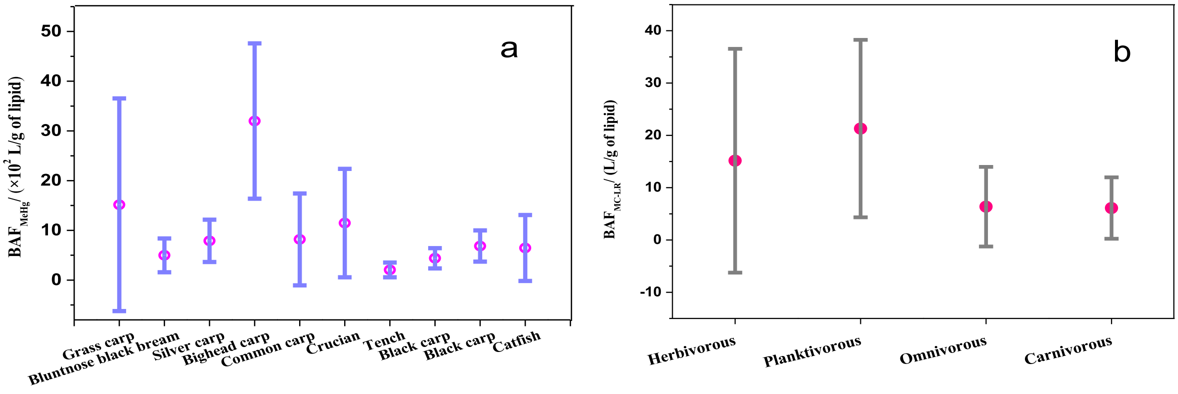

Fig. 2. Bioaccumulation factor (BAF) of MeHg based on lipid normalization of fish species and feeding habits in the Wujiangdu (WJD) Reservoir.

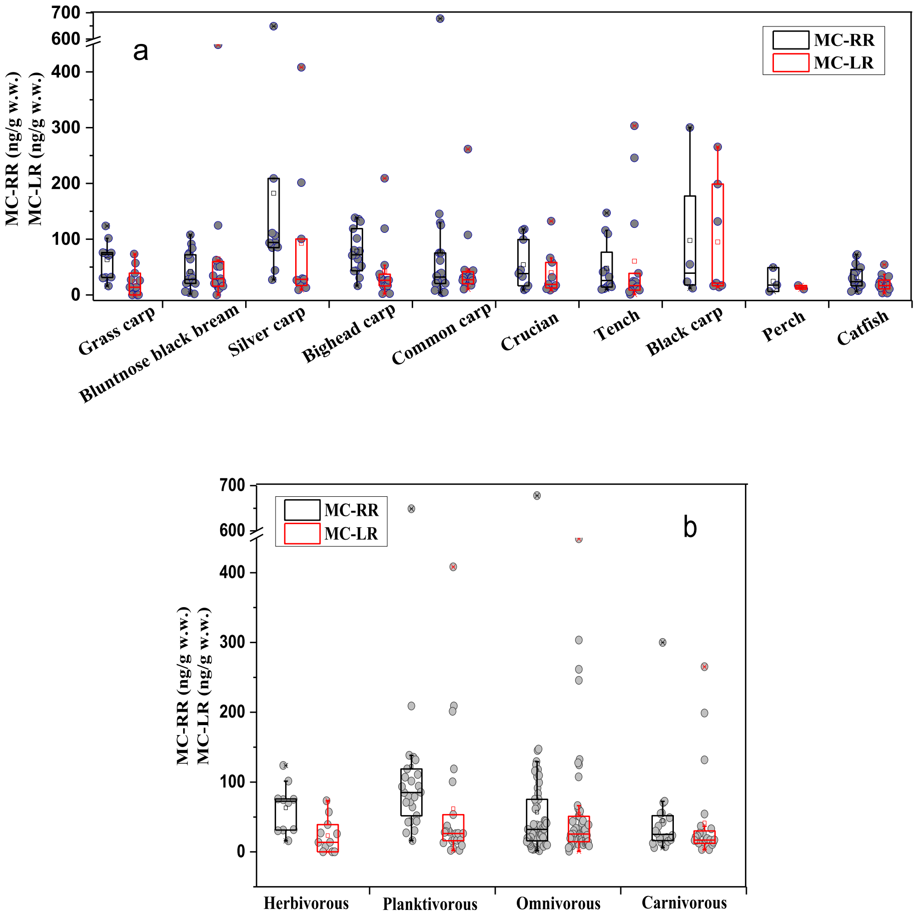

Fig. 3. Microcystin (MC)-RR and microcystin (MC)-LR concentrations of fish species and feeding habits in the Wujiangdu (WJD) Reservoir.

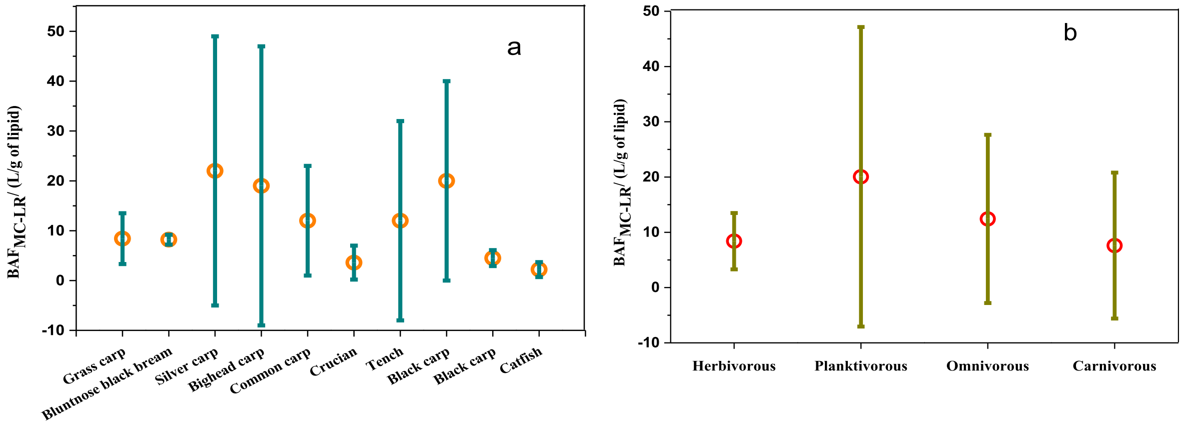

Fig. 4. Bioaccumulation factor (BAF) of MC-LR based on lipid normalization of fish species and feeding habits in Wujiangdu (WJD) Reservoir.

silver carp, most farmed fish contained a higher n-6 PUFA than n-3 PUFA EPA + DHA concentration varied consistently with the n-3 PUFA concentration in different fish species. Both n-3 PUFA and EPA + DHA concentrations were highest in silver carp (2.7 ± 1.4 and 2.4 ± 1.0 mg/g w.w., respectively) and lowest in grass carp (0.8 ± 0.2 and 0.6 ± 0.2 mg/g w.w., respectively), while n-6 PUFA concentration was highest in catfish (7.2 ± 4.6 mg/g w.w.) and lowest in bighead carp (0.8 ± 0.7 mg/g w.w.).

The n-3:n-6 PUFA ratio of dietary is an important nutritional quality index for human consumption because increasing intake of n-6 PUFA and n-3 PUFA deficiency might pose risks for coronary heart disease mortality (CHD), cancers, and cerebrovascular diseases (Rhee et al., 2016). The recommended dietary ratio of n-3/n-6 PUFA for health benefits is 1:2–1:1 (Simopoulos, 2016). The n-3: n-6 PUFA ratio was variable among different fish species in WJD. The n-3: n-6 PUFA ratio was highest in silver carp (3.9 ± 2.1), followed by bighead carp (2.3 ± 1.8), while obviously lower in grass carp (0.4 ± 0.1), common carp (0.4 ± 0.4), tench (0.5 ± 0.1) and catfish (0.3 ± 0.2). The n-3: n-6 PUFA ratio of bluntnose black bream (0.9 ± 0.8), crucian (0.9 ± 0.6), and perch (0.8 ± 0.5) were

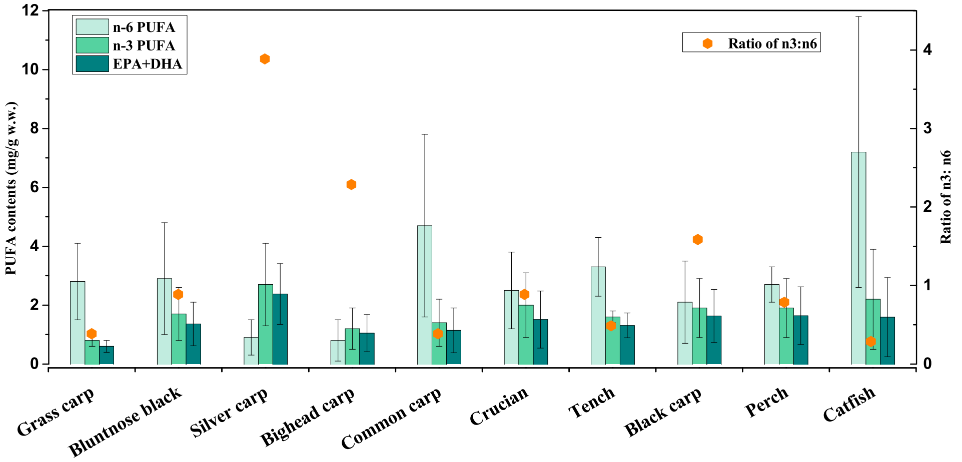

Fig. 5. Concentrations of omega-3 (n-3) polyunsaturated fatty acids (PUFA), omega-6 (n-6) PUFA, eicosapentaenoic (EPA) + docosahexaenoic acids (DHA) (mg/g w.w.) and n-3: n-6 PUFA ratio of different fish species in Wujiangdu (WJD) Reservoir.

considered benefit to human health.

Fatty acids profiles of fish varied with diet sources (Tidwell et al., 2007). In our study, both n-3 PUFA and EPA + DHA concentrations showed a following decreasing pattern: carnivorous fish (2.1 ± 1.5 and 1.7 ± 1.2 mg/g w.w., respectively), planktivorous fish (1.9 ± 0.3 and 1.6 ± 1.1 mg/g w.w., respectively), omnivorous (1.6 ± 0.9 and 1.3 ± 0.7 mg/g w.w., respectively) and herbivorous fish (0.8 ± 0.2 and 0.6 ± 0.2 mg/g w.w., respectively) (Fig. 6). In general, the EPA + DHA contents in farmed fish in the eutrophic WJD Reservoir were higher than that of the wild planktivorous fish in eutrophic Taihu (1.1 ± 0.4 mg/g w.w.) and lower than that of wild planktivorous fish from oligotrophic lakes in Canada (13.6 ± 4.8 mg/g d.w.) and Italian (12.2 mg/g d.w.) (Kainz et al., 2004; Vasconi et al., 2015). This might be explained by the fact that eutrophication could decrease the essential EPA and DHA contents accumulated in fish due to the increasing biomasses of chlorophyta and cyanobacteria (Razavi et al., 2014; Taipale et al., 2016).

3.4. *Assessments of risks and benefits of fish*

The EDI values of MeHg, MC-LR, and EPA + DHA varied among different fish species from WJD (Fig. 7). Except for grass carp, consumption of 300 g fish per day can reach the recommended intake of EPA + DHA (>4.2 mg/kg bw/day) for most fish species. EDI values of MeHg via all fish species were lower than the MeHg limitation (0.1 μg/kg bw/day). However, the EDI values of MC-LR from all fish species exceeded the TDI value. Both the highest EDI of EPA + DHA and MC-LR were from silver carp (11.9 mg/kg bw/day and 0.07 μg/kg bw/day, respectively), while the highest of MeHg was from bighead carp (0.065 μg/kg bw/day). The lowest EDI values of EPA + DHA, MC-LR and MeHg were from grass carp (3.0 mg/kg bw/day), perch (0.05 μg/kg bw/day) and tench (0.01 μg/kg bw/day), respectively.

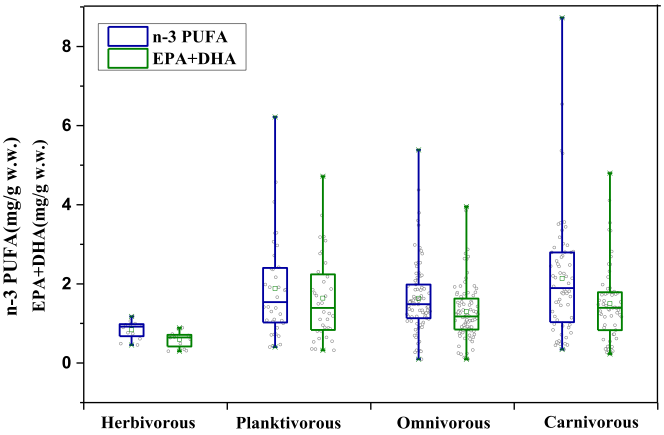

Fig. 6. Concentrations of omega-3 (n-3) polyunsaturated fatty acids (PUFA), omega-6 (n-6) PUFA, eicosapentaenoic (EPA) + docosahexaenoic acids of fishes with different feeding habits in Wujiangdu (WJD) Reservoir.

The present analysis provided an integrated risk-benefit estimate for fish consumption in adult cardiovascular (CHD mortality) and neurodevelopmental of 6-month-old infant (infant VRM) endpoints on a species-specific basis. The evaluation method assumed a long-term fish consumption, enough time to reach steady-state blood and hair concentrations of MeHg, and EPA and DHA benefits also required consistent exposure over time (Ginsberg et al., 2009). The dose response for MeHg effects on CHD mortality risk has a hair Hg threshold of 0.51 ppm before any adverse effect is evident (Guallar et al., 2002). While the threshold is a source of uncertainty that may be related to measurement error and variability in the baseline population that obscures a Hg effect below that level (Ginsberg et al., 2009). The MeHg one-compartment biokinetic model (Ginsberg et al., 2000) was used to predict changes in hair concentrations for a given single-meal exposure to MeHg.

As shown in Table 1, all the fish species in WJD showed a positive effect on neurodevelopmental and cardiac outcomes. Silver carp had the maximum while grass carp had a minimal net beneficial effect on the two endpoints. Different meal sizes didn't alter the species-specific risk-benefit patterns, and the positive effects increased with fish consumption. The average hair Hg concentration predicted from the largest fish meal size (300 g/day) was 3.7 ± 2.2 ppb. Though the uncertainty of the hair Hg threshold, hair Hg concentrations calculated in this study were two orders of magnitude lower than the 0.51 ppm. We thus believe that the consumption of fish in WJD presented a slight MeHg health risk on CHD mortality and neurodevelopment, and the net risk-benefit by species was determined by the n-3 PUFA benefits.

3.5. *Fish consumption advisories*

Either the estimate acute MeHg exposure for general adult from a single fish meal per day, or the integral risk/benefit analysis for

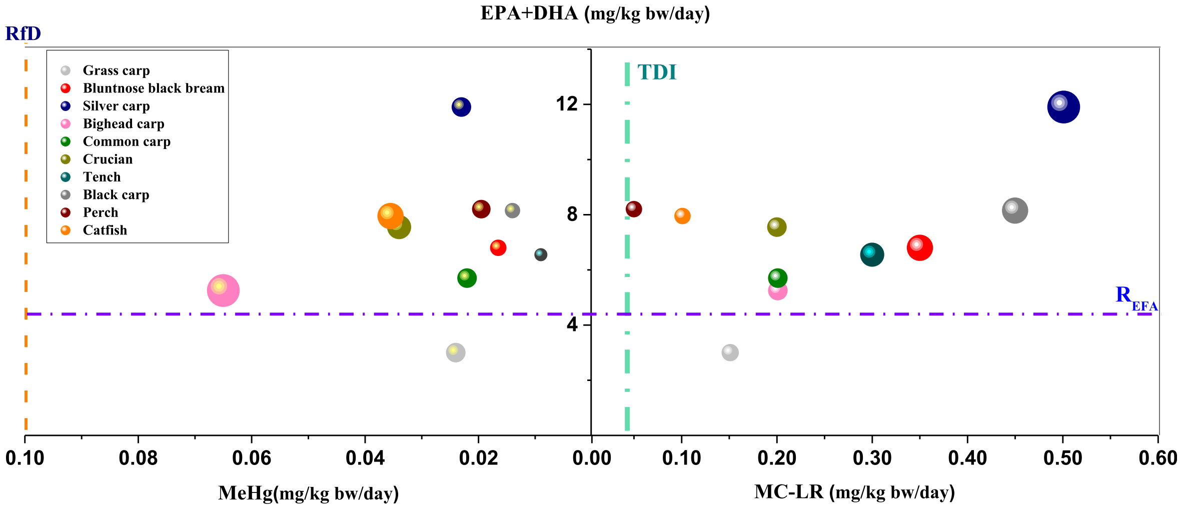

Fig. 7. Estimated daily intake (EDI) of eicosapentaenoic (EPA) + docosahexaenoic acids (DHA), methylmercury (MeHg) and microcystins (MC)-LR from different farmed fish species in WJD Reservoir. RfD of MeHg: reference dose for MeHg (0.1 μg/kg bw/day); TDI of MC-LR: tolerable daily intake of MC-LR (0.04 μg/kg bw/day); R_{EFA}: recommended intake of EPA + DHA (4.2 mg/kg bw/day).

Table 1
Effect of net effect of MeHg and n-3 PUFA on cardiovascular risk and neurodevelopment at 6 months of age under different fish consumption scenarios (g/day). A positive result indicates a decreased risk of CHD mortality and promotion of neurodevelopment.

	CHD Risk				VRM Score			
Fish species	24.8 g/day	64.5 g/day	227 g/day	300 g/day	24.8 g/day	64.5 g/day	227 g/day	300 g/day
Grass carp	2.2	5.7	19.9	26.3	0.4	1.2	4.1	5.5
Bluntnose black bream	4.9	12.8	45.1	59.6	1.0	2.7	9.4	12.4
Sliver carp	8.6	22.4	78.9	104.2	1.8	4.7	16.4	21.7
Bighead carp	3.8	9.9	34.8	46	0.8	2	7.2	9.5
Common carp	4.1	10.7	37.8	49.9	0.8	2.2	7.9	10.4
Crucian	5.5	14.2	50.0	66.1	1.1	2.9	10.4	13.8
Tench	4.7	12.3	43.4	57.4	1.0	2.6	9.0	11.9
Black carp	5.9	15.3	54	71.4	1.2	3.2	11.2	14.9
Perch	5.9	15.4	54.4	71.8	1.2	3.2	11.3	14.9
Catfish	5.8	15.0	52.7	69.6	1.2	3.1	11.0	14.5

those in the neurodevelopmental and the cardiovascular risk groups from chronic fish ingestion indicated that ingestion of fish in WJD posed low MeHg risk and provided n-3 PUFA benefits. Therefore, increasing the consumption of fish was taken into consideration to enhance the intake of EPA and DHA. However, our results showed that farmed fish in the WJD Reservoir would pose a health risk due to the high MC-LR exposure, which determines the consumption advisory limits of fish in WJD.

Based on the TDI for MC-LR, we estimated the maximum consumption of each fish species from WJD as a general advisory for ordinary adults (bodyweight set as 60 kg). As shown in Fig. 8, the recommended maximum consumption of farmed fish in WJD ranged from 24.0 g/day for silver carp to 240 g/day for perch. The average fish consumption level of Chinese resident (24.8 g/day) is close to the advised maximum quantity of silver cap and black carp (26.7 g/day) (CPC, 2019), yet lower than that of the other 8 fish species, indicating that most species were suitable for general population consumption, but silver carp and black carp could pose MC-LR exposure risk. Compared to the village residents, urban residents could consume more fish. The average consumption of fish for urban residents in China is 64.5 g/day (CPC, 2019), exceeding the advised maximum quantity of most fish species in WJD, and only grass carp, perch, and catfish were identified as the optimum choices for fish consumption. Except for perch, the advised maximum consumptions of most farmed fish species in WJD were far lower than the USEPA-suggested value of 8 oz (227 g) of cooked fish fillet for the general adult population (USEPA, 2019). To reduce the probability of exceeding TDI of MC-LR, we suggested that consumption of silver carp and black carp should be avoided, and consumption of bluntnose black bream, bighead carp, common

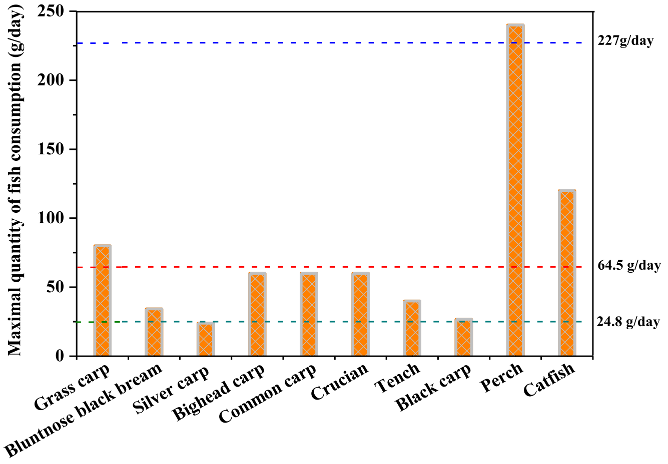

Fig. 8. The maximum daily quantity of fish consumption according to the TDI for MC-LR (0.04 μg/kg/day).

carp, crucian, and tench should be reduced. Perch was recommended as the most appropriate consumption choice for being able to provide higher health benefits of EPA and DHA while minimizing the exposure risk of MC-LR. Grass carp and catfish were identified as the second recommended options because they are safe under the Chinese fish consumption level. At the same time, management strategies should be formulated to control the eutrophication in water to reduce the MC accumulated in fish.

3.6. Worldwide comparison of MeHg, MC and n-3PUFA in fish

To understand the risk and benefit of fish in WJD Reservoir, risk-benefit analysis based on EPA + DHA and MeHg contents together with MC-LR exposure risk of fish in this study were compared with previously published reports from other parts of the world. To reconciling MeHg risks and n-3 PUFA benefits of fish consumption, several net risk-benefit analysis of fish consumption on CHD mortality and infant neurodevelopmental endpoints have been carried out in specific areas using various models/formulas. Wang et al. (2019, 2020) have assessed the benefit and risk of commonly consumed marine fish species from Bohai Sea and South Sea in China, respectively, suggesting the positive effects of eating marine fish outweigh the negative effects. Nevertheless, Gao et al. (2014) found some marine fish species from Zhoushan Archipelago, China harmed fetus neurodevelopment via maternal consumption. Dellinger et al. (2018) indicated the health tradeoff of consuming wild-caught and store-bought freshwater fish in the Great Lakes region, except for walleye, all fish tested impart benefits to reduce cardiovascular risk and promote neurodevelopment. Compared to farmed freshwater fish in WJD, marine fish in China and freshwater fish from Great Lakes mostly showed more net benefits on reducing the cardiovascular risk and infant neurodevelopment contributed by their higher n-3 PUFA contents. Moreover, there are some risk-benefit assessment of fish consumption using other quantitative approaches. Strandberg et al. (2016) estimated the potential health risks vs. benefits of consuming European perch with hazard quotient (HQ) method, suggesting the perch pose greater MeHg risks yet provided fewer benefits. Laird et al. (2018) use the *de minimus* ratios as a preliminary quantitative approach for the risk-benefit analysis of freshwater fish consumption in the Dehcho Region, Northwest Territories, and concluded that n-3 benefits of regularly consuming these species outweigh the MeHg risks. However, compared to the risk-benefit analysis reported in this work, the limitation of these assessments is that they did not reflect the relative potency of MeHg and n-3 PUFA on underlying endpoints of interest.

Although we have assessed the balance between the benefits and risks of co-ingesting n-3 PUFA and MeHg, there were no nutrients reported that can offset the adverse effects of MC-LR in fish on human liver. As shown in Figure S2, EDI values of MC-LR through freshwater fishes from different eutrophic freshwater systems in the world exceeded the TDI of MC-LR, manifesting that fishes from eutrophic reservoirs and lakes presented a global high risk of MC-LR. The average EDI values of MC-LR via fishes from WJD Reservoir (0.25 ± 0.15 mg/kg bw/day) and wild fishes from eutrophic lakes (0.27 ± 0.34 mg/kg bw/day) in China were identical, but the MC-LR accumulations in farmed and wild fishes were different. Unlike the accumulation pattern of MC-LR in WJD Reservoir, in Chaohu and Taihu Lakes, the MC-LR contents in some omnivorous and carnivorous fish were higher than planktivorous fish. Besides, the MC-LR content of farmed fish in WJD was significantly higher than the same wild species in Taihu Lake. While the MC-LR contents of bighead carp and crucian carp in WJD were significantly lower than the same wild species in Chaohu Lake (Table S2). The lower MC-LR content in fish from Taihu likely resulted from the lower MC-LR concentrations in water (range: 0.0007–0.003 μg/L, average: 0.002 μg/L) (Zhang et al., 2009), and the higher MC-LR content of fish in Chaohu Lake was due to its higher MC-LR concentration in water (0.115 μg/L) (Zhu et al., 2018; Peng et al., 2010), which might be associated with its eutrophic-hypereutrophic state.

In general, EDI values of MC-LR of freshwater fish from China were significantly higher than that of fish from Europe (0.10 ± 0.01 mg/kg bw/day) (Larson et al., 2014), North America (0.07 ± 0.09 mg/kg bw/day) (Poste et al., 2011; Wituszynski et al., 2017b; Zamora-Barrios et al., 2019), and Africa (0.08 ± 0.07 mg/kg bw/day) (Poste et al., 2011). We inferred that the higher MC-LR contents of fish in China were due to the more serious cyanobacterial blooms caused by the increasing anthropogenic nutrient loading in water (Michalak et al., 2013). Similarly, in North America and Africa, MC-LR contents of fish in eutrophic-hypereutrophic lakes (North America: 17.9 ± 23.3 mg/kg bw/day; Africa: 28.7 ± 71.9 mg/kg bw/day (Poste et al., 2011; Zamora-Barrios et al., 2019)) were higher than that in meso-eutrophic lakes (North America: 5.9 ± 7.5 mg/kg bw/day; Africa: 19.3 ± 19.5 mg/kg bw/day (Poste et al., 2011)), suggesting that eutrophication can increase the MC-LR contents in fishes.

4. Conclusions

In this study, we simultaneously examined contaminants Hg and MC and nutrient PUFA of economically important farmed fish species from a typical aquaculture Reservoir in China, and for the first time provided an integrated benefit and risk assessment based on MeHg, MC-LR, and EPA + DHA concentrations of species-specific farmed fish. All farmed fish species provided more n-3 PUFA benefits and posed less MeHg risk. However, except for perch, most farmed fish species posed high MC-LR exposure risk, which overbalanced the EPA + DHA benefit of fish consumption. The consumption advisories of different fish species were given in this study to minimize MC exposure to the general population. We concluded that the consumption of fish in China did not present MeHg-related health risks, yet MC-LR risk should be a special concern for fish in eutrophic freshwater bodies. Although our study was based on a region survey, it undoubtedly provided a new approach to evaluate the risk and benefit of fish consumption for the general population worldwide.

Author contributions

Conceived and designed the research: HY.Y.; managed the research project: HY.Y.; performed the experiments: D.L., M.J., J.L; supervised the experiments:HY.Y; analyzed the data: HY.Y., M.J.; wrote the paper: HY.Y., M.J., XB.F,QH.L. All authors have given approval to the final version of the manuscript.

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.envpol.2020.116047.

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