

Assessing exposure risks for freshwater tilapia species posed by mercury and methylmercury

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Abstract Waterborne and dietborne exposures of freshwater fish to mercury (Hg) in the forms of inorganic (Hg(II)) and organic (methylmercury or MeHg) affect their growth, development, and reproduction. However, an integrated mechanistic risk model framework to predict the impact of Hg(II)/MeHg on freshwater fish is lacking. Here, we integrated biokinetic, physiological and biogeographic data to calibrate and then establish key risk indices—hazardous quotient and exceedance risk—for freshwater tilapia species across geographic ranges of several major rivers in Taiwan. We found that Hg(II) burden was highest in kidney followed by gill, intestine, liver, blood, and muscle. Our results showed that Hg was less likely to pose mortality risk (mortality rate less than 5 %) for freshwater tilapia species. However, Hg is likely to pose the potential hazard to aquatic environments constrained by safety levels

for aquatic organisms. Sensitivity analysis showed that amount of Hg accumulated in tilapia was most influenced by sediment uptake rate. Our approach opens up new possibilities for predicting future fish population health with the impacts of continued Hg exposure to provide information on which fish are deemed safe for human consumption.

Keywords Mercury · Freshwater tilapia · Modeling · Environmental risk assessment

Introduction

One of the greatest threats to freshwater fish and a major factor demanding an intensive ongoing management is mercury (Hg) contamination—a persistent and pervasive global pollution issue (Amos et al. 2013). When Hg is in the form of methylmercury (CH₃Hg⁺ or MeHg), it is highly toxic to humans and other organisms because of biomagnification through the food web (Kidd and Batchelar 2012; Lavoie et al. 2013). Unlike inorganic forms of Hg (Hg(0) and Hg(II)), which originate from atmospheric deposition and point discharges, MeHg is generated in the environment predominantly by anaerobic bacteria (Krabbenhoff and Sunderland 2013; Parks et al. 2013).

Evidence of elevated Hg exposure in Taiwan major rivers began to emerge in the mid-1970s and Hg contamination may have been a factor for freshwater fish decline in populations in the 1980s (Wu 2006; Chen et al. 2012a, b). As a result, Hg exposures are intensively investigated by Environmental Protection Administration of Taiwan (Taiwan EPA) including surface water, sediment, and fish tissue measurements. Moreover, a growing body of evidence has shown that Hg contamination had moved into the

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adjacent terrestrial food web (Cristol et al. 2008; Tweedy et al. 2013). However, the degree to which Hg contamination impacts fish population health has not been fully understood, in part because these intensive management practices partially compensate for the population-level impacts of Hg, thus obscuring the seriousness of this problem.

Waterborne and dietborne exposures of freshwater fish to highly water-soluble Hg(II) and MeHg affect their growth, development, and reproduction (Kidd and Batchelar 2012). Fish as food is the main source of MeHg exposure. Thus, fish consumptions are the main exposure source of MeHg for most wildlife and humans. MeHg is a potent neurotoxin (Oken et al. 2012). Epidemiological studies on new findings have shown (i) the impacts on long-term neurocognitive deficits in children and impaired cardiovascular health in adults exposed to low-level MeHg (Karagas et al. 2012) and (ii) an adverse relationship between low-level prenatal MeHg exposure and childhood memory loss and learning deficit, particularly visual memory (Orenstein et al. 2014).

In the aquatic environment, methylation of Hg(II) and demethylation of MeHg are key processes in determining the relative abundance of Hg(II) versus MeHg (Kidd and Batchelar 2012). Biokinetics-based mechanistic models have been developed for better understanding the mechanisms underlying the bioaccumulation and biomagnification processes of Hg(II)/MeHg in aquatic organisms (Knights 2008; Knights et al. 2009; Wang et al. 2010; Wang and Wang 2012; Wang 2012; Wang et al. 2013). A probabilistic model was also used to assess the risk trade-offs in Hg-contaminated fish consumption to better understand the balance between fish consumption benefits and Hg exposure (Rheinberger and Hammitt 2012).

In recent years, public attention has become increasingly focused on aquatic environmental contaminants, which may be toxic to fish consumers in sufficient doses. Besides, concerns regarding Hg residues in seafood as well as seafood consumption safety may complicate determinations on what type of seafood are safe to eat (Oken et al. 2012; Karimi et al. 2012; Gerber et al. 2012; Vieira et al. 2015). However, an integrated risk assessment framework composed of mechanistic models is lacking to predict the impact of Hg(II)/MeHg on freshwater fish and further develop fish consumption advisories. Moreover, mercury contamination in freshwater fish illustrates the complexity and consequences of environmental/ecological planning and management when significant environmental hazards are not adequately mitigated.

Recently, Taiwan government has launched the intensive management programme for Hg contamination including the establishment of (i) target values in site-specific sediment clean-up criteria (Taiwan EPA 2012a)

and (ii) the seafood daily dose of MeHg that can be safely consumed over a lifetime (Taiwan FDA 2013). The objectives of this paper are (i) to integrate biokinetic, physiological and biogeographic data to calibrate and establish key risk indices—hazardous quotient and exceedance risk—across geographic ranges of major rivers in Taiwan and (ii) to develop a general mechanistic risk assessment framework that quantifies future fish population health with the impacts of chronic Hg exposure. In this paper, we used freshwater tilapia, an important fish food for the people of Taiwan, as the studied fish species. It is also one of the most abundantly invasive species in local freshwater and estuary ecosystems.

Materials and methods

Study framework and Hg level in specific rivers

Based on a probabilistic risk assessment framework, we combined a Hg-water–sediment dynamic model with a tilapia-Hg physiologically-based toxicokinetic (PBTk) model to investigate ecotoxicological risk for fish exposed to Hg(II) and MeHg in major rivers of Taiwan region. Within the exposure risk scenarios, we explored the differences in each river as well as mortality and hazard burden on Hg(II) and MeHg accumulation in fish. The study framework is schematically illustrated in Supplementary Fig. S1.

Here environmental total Hg (THg) concentrations in sediments were obtained from the published data sets to re-estimate Hg(II) and MeHg concentrations in major rivers (Taiwan EPA 2013a, b; CPDCASS 2012). We chose rivers with THg level in sediments exceeding the criteria recommended by Taiwan EPA (2012b) ranging from 0.23 to 0.87 mg kg⁻¹ dw. Hence, six major rivers were selected, respectively, situating at northern region of Tamsui (NA), Nankan (NB), and Lao-Jie (NC) rivers and southern regions of Luermen creek (SA), Er-Ren (SB) and Love (SC) rivers.

Generally, THg in sediment samples from published studies can be determined following the standard method of Environmental Analysis Laboratory, Taiwan Environmental Protection Administration (NIEA M317.03B) (Taiwan EPA 2012b). In brief, samples were weighed (~0.5 g) and placed in a 250-ml Erlenmeyer flask. Deionized water (5 ml) and aqua regia (5 ml) were added into the flask that was put on a hot plate for 2 min. The digestion process was performed at 95 ± 3 °C for 30 min after adding 50 ml deionized water and 15 ml potassium permanganate, and the solution was put aside until reaching room temperature. The digested solution was then filtered and diluted with deionized water to 100 ml. THg can then

be measured using a cold-vapor atomic absorption spectrometer (CVAAS).

Problem formulation

Here we set a field exposure scenario for downstream aquatic environment composing river water, sediment, and tilapia in that river could receive Hg-containing effluents from factories that may deteriorate environments and pose threat to aquatic organisms. Tilapia tends to inhabit in the bottom layers of water and feeds by digging through sediment in searching food. Consequently, tilapia may have prolonged time to contact sediment, resulting in a high accumulation of Hg in the forms of Hg(II) and MeHg. On the other hand, Hg species could either remain in river water or sediment based on sediment–water partition coefficient depending on various aquatic environments. Consequently, both Hg-contained river water and sediment could be potential exposure sources to freshwater tilapia species (Low et al. 2015; Malczyk and Branfireun 2015).

The fate and transformation of Hg(II) and MeHg in aquatic systems can be described by a first-order four-compartment water–sediment model with methylation rate of Hg(II) in water ($k_{m,w}$) and sediment ($k_{m,s}$), demethylation rate of MeHg in water ($k_{dm,w}$) and sediment ($k_{dm,s}$), as well as photodegradation rate of MeHg ($k_{pd,w}$) due to the importance of maintaining low-level MeHg in water (Morel et al. 1998) (Supplementary Fig. S1A, Table S1). The transfer of THg between river water and sediment as the exposure sources can be described by the sediment–water partition coefficient p_{sw} .

Exposure model

A PBTK model allows us to quantitatively describe the bioaccumulations in tissues/organs of concern for a specific organism. To implement the PBTK model, several key assumptions were made: (i) there are finite numbers of compartment constituting the PBTK model, (ii) chemicals distribute homogeneously (well-stirred) within each compartment, (iii) all transports between blood and tissues are flow-limited in the circulatory system, (iv) chemicals transferring from/to each tissue/organ is according to the first-order rate constant, and (v) complete equilibrium of chemicals exist between blood and tissue phases (mass–balance relationship).

Based on the experimental study on acute Hg(II) toxicity for blue tilapia (*Oreochromis aureus*) (Allen 1994), a PBTK model consisted of six interested compartments can be constructed based on modifying well-established PBTK models (Peters 2012; Chen and Liao 2014), including blood, gill, liver, kidney, intestine, and muscle (Supplementary Fig. S2, Table S2). The essential physiological and

physicochemical parameters including blood volume (V), tissue/organ weight (W), tissue/organ exchange rate (Q), uptake/elimination/metabolic rate (k), gill sorption factor (α_{wg}), and fraction of Hg(II) dissolved in blood (f_d) can be estimated from published tilapia-related studies (Allen 1994; Liao et al. 2005; Mahmoud and Mazrouh 2008; Nichols et al. 1996; Thomann et al. 1997; Wang et al. 2007). The partition coefficients (p_i), the key PBPK model parameters, were estimated for each tissue or organ based on the experimental data by dividing Hg burden in tissues of that in blood at specific days 0.5, 1, and 7 after 0.1 mg L⁻¹ Hg(II) exposure (Allen 1994).

There were three standard metrics used to assess the performance of PBTK model as well as to validate simulated results with published experimental data: (i) mean absolute percentage error (MAPE) (MAPE < 50 %), (ii) root mean square error (RMSE) in comparison to data standard deviation (SD) (RMSE < data SD), and (iii) coefficient of determination (r^2). The MAPE and RMSE can be formulated accordingly as

$$\text{MAPE} (\%) = \frac{1}{N} \sum_{i=1}^N \frac{|C_{o,i} - C_{s,i}|}{C_{o,i}} \times 100\%, \quad (1)$$

$$\text{RMSE} = \sqrt{\sum_{i=1}^N \frac{(C_{o,i} - C_{s,i})^2}{N}}, \quad (2)$$

where N stands for the number of observations, $C_{o,i}$ and $C_{s,i}$ represent the measured and simulated Hg concentration, respectively.

Effect model

Here the Hg-induced mortality data in tilapia (Sweilum 2006) was adopted to examine the survival effects of Hg exposures. Sweilum (2006) conducted a series of experiments to measure Hg(II) accumulations in specific tissues/organs of liver, gill, and muscle and to estimate survival efficiency for three tilapia species of *O. niloticus*, *S. galilaeus*, and *O. aureus* exposed to waterborne HgCl₂ of 0, 0.078, 0.155, and 0.310 mg L⁻¹ for 180 days.

We reanalyzed the experimental data (Supplementary Table S3) to reconstruct the dose–response profiles describing the relationships between tissue/organ-specific burden of Hg(II) and mortality. Since background as well as maximum mortalities (< 100 %) were observed in the exposure experiment, we thus employed a four-parameter Hill model to describe dose–response relationships as,

$$M(C_{bi}) = M_{\min} + \frac{M_{\max} - M_{\min}}{1 + \left(\frac{MC_{50}}{C_{bi}}\right)^n}, \quad (3)$$

where $M(C_{bi})$ is mortality (%) corresponding to particular Hg(II) burden in specific tissue/organ i (C_{bi} , $\mu\text{g g}^{-1}$ ww),

M_{\min} is the minimum mortality (%), M_{\max} is the maximum mortality (%), MC_{50} is the Hg(II) burden in the specific tissue/organ i giving half-maximum mortality ($\mu\text{g g}^{-1}$ ww), and n is a slope factor referred to as the Hill coefficient determining the overall shape of the dose–response curve.

Risk model

For further characterizing tilapia exposure risk of Hg, this study implemented a probabilistic risk assessment model by linking Hg-PBTK exposure model with Hill-based dose–response model. In particular, the distribution profile of internal Hg exposure concentration in tilapia ($P(C_{bi})$) (i.e., the prior probability) can be estimated based on simulated results of the Hg-PBTK model. On the other hand, a conditional probability taking into account the tilapia mortality risk under certain tissue burden ($P(M|C_{bi})$) (i.e., the likelihood) can be obtained by incorporating the Hill-based dose–response relationships.

Followed by the Bayesian inference, cumulative mortality risks for tilapia under certain internal Hg exposure levels of gill, liver, and muscle ($R(M)$) (i.e., the posterior probability) were the products of prior probabilities and likelihoods, resulting in joint probability functions or exceedance profiles that can be expressed mathematically as,

$$R(M) = P(C_{bi}) \times P(M|C_{bi}). \quad (4)$$

To better assess the adverse effects of chronic Hg exposure on aquatic ecosystem resulting from bioaccumulation in tilapia species, this study employed the hazard quotient (HQ) concept for assessing the potentially environmental risk as,

$$\text{HQ} = \frac{C_{\text{THg},f}}{T_f}, \quad (5)$$

where $C_{\text{THg},f}$ stands for the THg concentration of tilapia whole body obtained by the product of the sum of Hg(II) body burden in each tissue/organ estimated from the PBTK model and the conversion ratio of Hg(II) to THg and T_f is the safety level for fish (Beckvar et al. 2005) or the recommended levels of Hg in fish by WHO (1990) and Japan (Endo et al. 2005). $\text{HQ} > 1$ indicates a potential for toxicological effects to occur. Based on a field survey in Taiwan of Huang et al. (2008), the conversion ratio of Hg(II) to THg was optimally estimated by a lognormal distribution with a geometric mean of 0.33 and a geometric standard deviation of 2.39.

Uncertainty and sensitivity analysis

A Monte Carlo (MC) technique was implemented to generate 2.5- and 97.5-percentiles as 95 % confidence interval

Fig. 1 A Site-specific study data of THg concentrations in sediments and $B-I$ simulated concentration distributions of Hg(II) and MeHg in water and sediments for six selected rivers located in northern region of Tamsui (NA), Nankan (NB), and Lao-Jie (NC) rivers as well as southern regions of Luermen creek (SA), Er-Ren (SB) and Love (SC) rivers

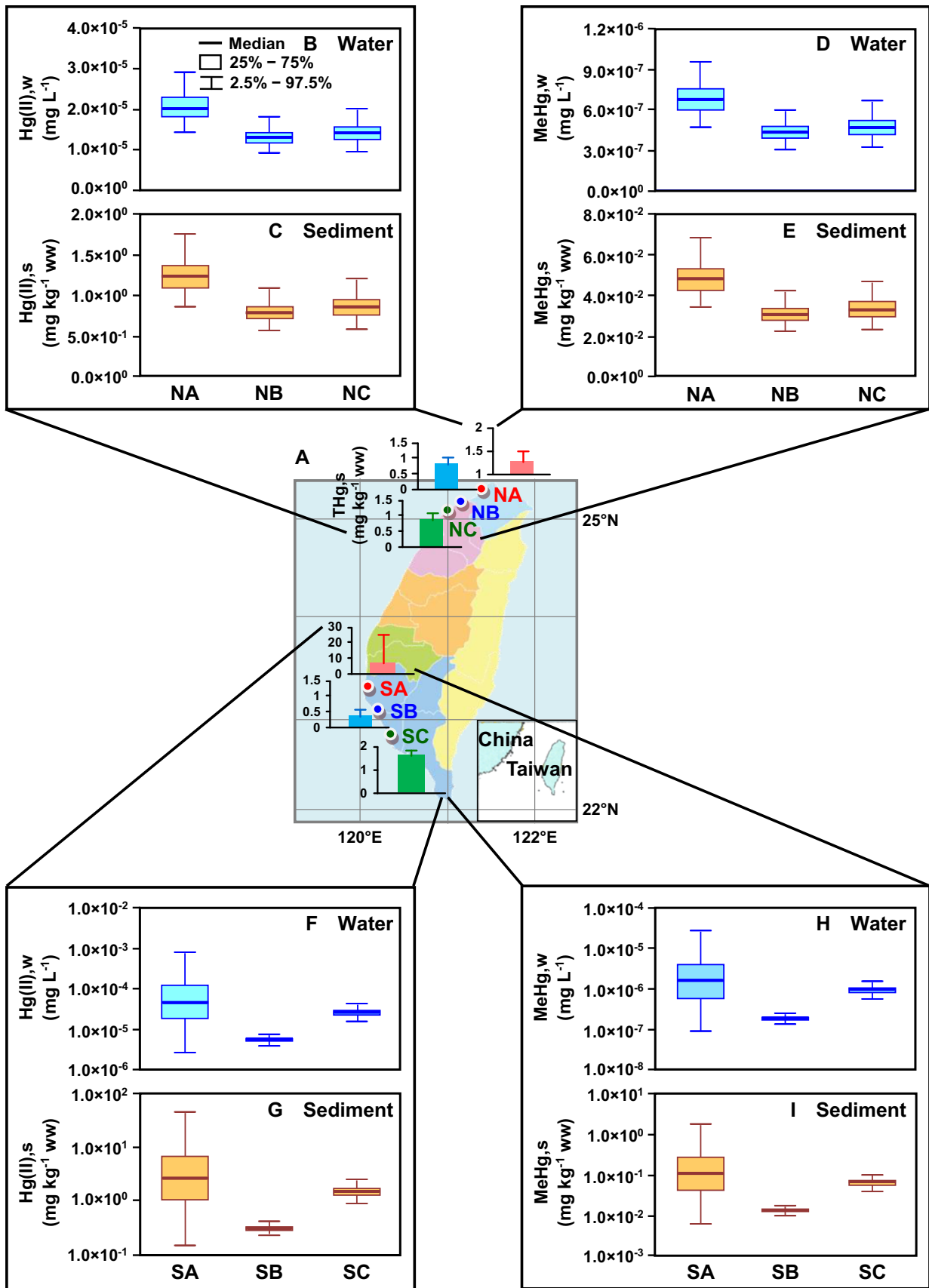
(CI) for quantifying the uncertainty of model parameters, particularly to those of interest involving compound partitioning and exchange in tissues/organs in PBTK model including volume/weight, exchange rate, rate constants and partition coefficients. The Kolmogorov–Smirnov (K–S) goodness-of-fit statistics was used to determine the optimal distributions for parameters. We also applied the MC simulation to quantify the uncertainty and its impact on the estimations of expected risks ($R(C_{bi})$ and HQ). The MC simulation was performed for 10,000 iterations to ensure the stability of results. Crystal Ball software (Version 2000.2, Decisionerrring, Inc., Denver, CO, USA) was employed to implement the MC simulation.

TableCurve 2D (Version 5.01, AISN Software Inc., Mapleton, OR, USA) was used to fit the published experimental data for obtaining the optimal dose–response profiles. The simulations of water–sediment model and PBTK model were performed by Berkeley Madonna 8.0.1 (Berkeley Madonna was developed by Robert Macey and George Oster of the University of California at Berkeley). Moreover, we employed a one-way sensitivity to assess the contribution of each parameter used in the PBTK model to the simulation outcome. Specifically, each parameter is varied individually across the 95 % CI of its uncertainty distribution to calculate the % change in the whole body burden.

Results

Exposure analysis

Here we incorporated the sediment concentration data of THg (Fig. 1a) and the estimates of transport parameters with initial conditions (Supplementary Table S4) into the water–sediment model to estimate the steady-state concentrations of Hg(II) and MeHg in the six study rivers during 180-day simulation (Fig. 1b–i, Supplementary Table S5). Our results showed that large amounts of Hg accumulated in sediments (ranging from 1.55×10^{-1} to 43.56 and 6.06×10^{-3} to 1.70 mg kg^{-1} ww for Hg(II) and MeHg, respectively), compared with those in water with the range of 2.60×10^{-6} to 7.32×10^{-4} and 8.57×10^{-8} to $2.41 \times 10^{-5} \text{ mg L}^{-1}$ for Hg(II) and MeHg, respectively. Figure 1 also indicates that the environmental concentrations of Hg(II) and MeHg were higher in SA than those in other rivers.



To further consider the internal exposure in different tilapia tissues/organs from intake of river water and sediment, a tilapia-Hg PBTK model associated with the related physiological and biokinetic parameters (Supplementary Table S6) was then implemented in six rivers. Based on the estimates, tissue/organ burdens would reach equilibrium before 180 days of exposure in all six rivers. Among all exposed tissues/organs, kidney had the highest internal exposure doses of Hg(II) ranging from 0.0208 to 0.1348 $\mu\text{g g}^{-1}$ ww. In contrast, muscle had the lowest internal exposure doses of 0.0001–0.0003 $\mu\text{g g}^{-1}$ ww Hg(II), indicating that Hg levels in muscle might be well below levels considered at risk for human consumption based on regulation from Taiwan FDA (2013) (Fig. 2). On the other hand, comparing among northern and southern regions of Taiwan, NA and SA had the highest accumulative internal doses of Hg(II) in gill of 0.0050 $\mu\text{g g}^{-1}$ ww (95 % CI 0.0036–0.0070) and 0.0111 (0.0007–0.1907), respectively (Fig. 2a, b).

Dose–response analysis

Figure 3a–c shows that the four-parameter Hill model can well describe the relationships between tissue/organ-

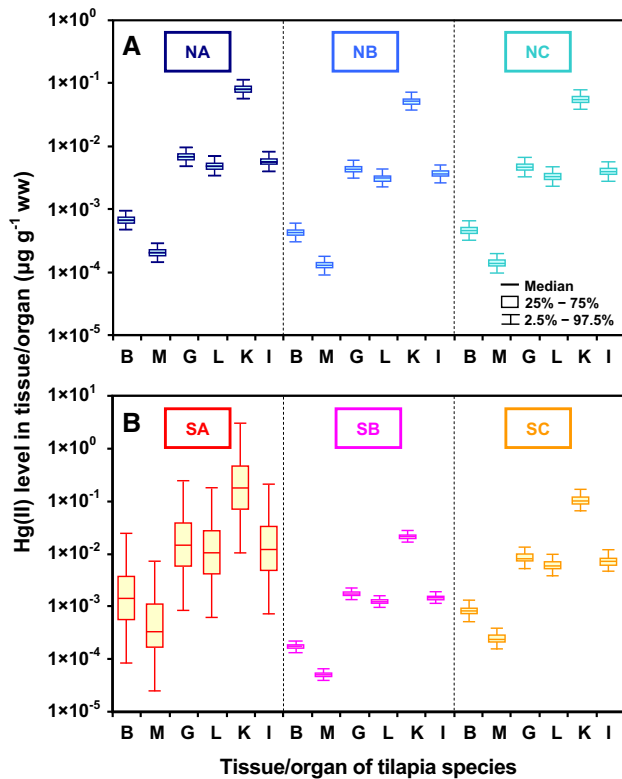


Fig. 2 Hg(II) burden of blood (B), muscle (M), gill (G), liver (L), kidney (K), and intestine (I) in freshwater tilapia species from **a** northern (NA, NB, and NC rivers) and **b** southern (SA, SB, and SC rivers) regions of Taiwan

specific burden of Hg(II) and mortality in tilapia ($r^2 = 0.93\text{--}0.94$; $P < 0.001$) (Supplementary Table S7). Our results showed that the effective Hg(II) burden in tissue/organ at 50 % mortality (MC_{50}) for liver, gill, and muscle were 10.410 ± 1.047 , 6.307 ± 0.756 , and $2.839 \pm 0.575 \mu\text{g g}^{-1}$ ww, respectively. The estimated values of average maximum mortality (M_{\max}) were 80.67, 77.60, and 57.24 %, respectively, for liver, gill, and muscle, whereas there were no significant difference among the estimates of minimum mortality (M_{\min}) with an approximate value of 5 %. The fitted Hill coefficients (n) were

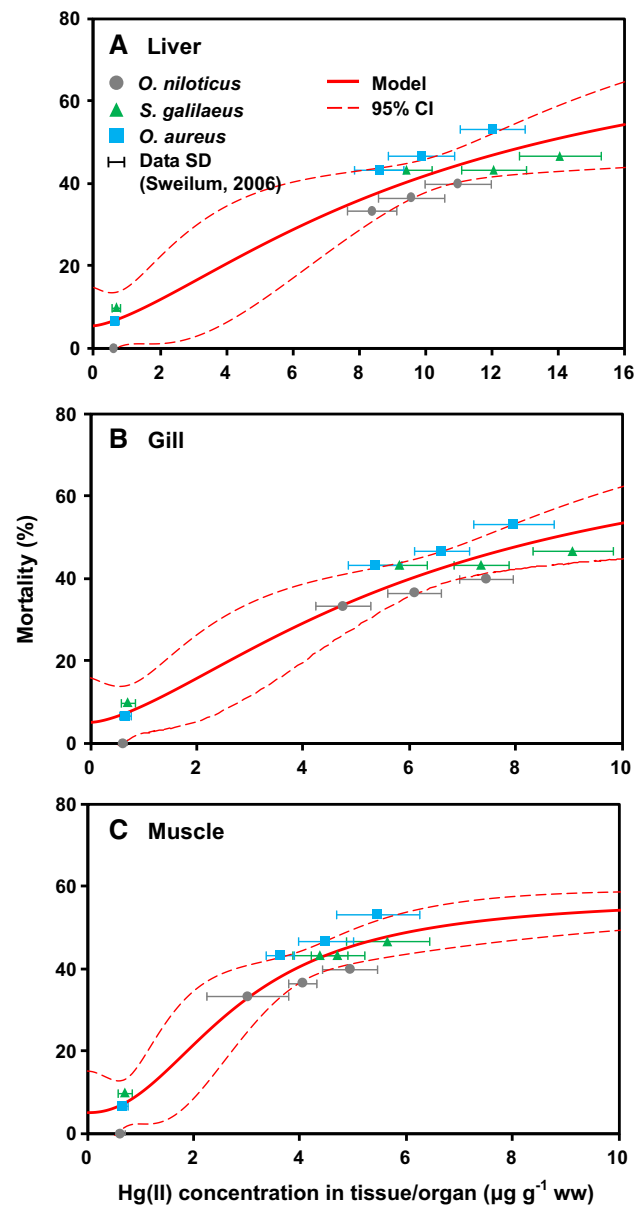


Fig. 3 Reconstructed tissue/organ-specific dose–response profiles by four-parameter Hill models describing the relationships between tilapia mortality and Hg(II) contents in **a** liver, **b** gill, and **c** muscle, respectively

larger than 1 in that muscle had the largest n of 2.186 ± 0.811 .

Risk characterization

This study took account three tissue burden-specific mortality rates to quantify mortality risks of tilapia exposed to Hg(II) and MeHg. Our results indicated that there was 50 % probability for mortality risk of tilapia to exceed 5.0–5.4 % by considering three tissue burden of gill, liver, and muscle (Fig. 4a–i). Noticeably, even if we considered the worst scenario of the highest accumulated internal dose in liver (exceedance risk = 0.2, i.e., the risk probability that might be unlikely to occur), mortality rate of tilapia would not exceed 5.38 %, indicating low mortality risk for tilapia exposed to Hg(II) and MeHg (Fig. 4a–i).

Here we chose three safety levels to examine the potential hazard to the organisms in aquatic environment, i.e., 0.2, 0.4, and $0.5 \mu\text{g g}^{-1}$ ww in tilapia whole body. The results demonstrated that with the stricter safety levels being adopted, the higher hazard would be presenting. In northern region of Taiwan, the median values of HQ in three rivers would be over 1 according to the strictest safety level (Fig. 4j). Nevertheless, the potentially highest environmental hazard was observed under the most seriously polluted situation as in river SA that nearly all percentile estimates of HQ were over 1 taking three different safety levels into consideration (Fig. 4k).

Validation and sensitivity analysis

Figure 5 illustrates the comparison of tissue/organ-specific burden of Hg(II) in tilapia between predictions by the PBTK model and experimental data based on three assessing indicators (MAPE, RMSE, and r^2). Results showed that a reasonable prediction as all MAPEs were ≤ 50 % (Fig. 5a). Compared with the data SD, the RMSE values were less than data SD with r^2 ranging from 0.44 to 0.96, indicating a fair quantitative agreement between model predictions and experimental data (Fig. 5b–g).

Our one-way sensitivity analysis indicated that the amount of Hg accumulated in tilapia whole body was most influenced by sediment uptake rate (k_s), following by partition coefficient of kidney (p_k) and the weight of intestine (W_i) (Fig. 6). Compared with the baseline levels of Hg(II) in specific tissues/organs (Fig. 2), the k_s , p_k , and W_i would increase whole body concentration by 104, 31 and 17 %, respectively. The k_s and W_i were associated with the Hg accumulation through sediments, demonstrating that sediment was the major source of Hg exposure in tilapia, whereas p_k corresponded to the highest burden of Hg accumulate in kidney (Fig. 2).

Discussion

Hg(II)/MeHg in aquatic environments

course concentrations of different Hg species in water and sediment where the THg concentration in sediment is known a water–sediment dynamic model was developed and used. Our model did not consider the elemental mercury (Hg^0) because Hg(II) and MeHg are the two major forms of Hg in aquatic environments. Additionally, the direct waste discharges and atmospheric deposition were assumed to be negligible in the model based on previous study (Tong et al. 2014). They demonstrated that Hg levels in inflow of water from wastewater and air were less than 1 %.

Our results showed that Hg(II) was the predominant species in both water and sediment, accounting for nearly 96 % of THg, which was similar to the results from field investigations of 86.6–98.5 % (Watras et al. 1998) and model predictions of 80–97 % (Knightes 2008; Tong et al. 2014). We also found that the concentration of Hg accumulated dramatically in sediment, which was consistent with the results from field investigations (Watras et al. 1998; Bloom et al. 2004; Wu 2006). These results support that sediment is the major reservoir for Hg in aquatic environments. Even though there is no direct discharge into water from Hg-contaminated wastes, Hg in sediment can be transported into water through sediment resuspension and diffusion processes (Bloom et al. 2004; Ethier et al. 2012; Tong et al. 2014).

Our water–sediment model is simple yet robust enough to be used to address the complex transformation and distribution of different Hg species in water and sediment. However, the speciation and content of Hg can be affected by environmental factors such as dissolved organic carbon (DOC), inorganic ligands (e.g., sulfate, chloride), redox potential, pH, and temperature (Celo et al. 2006; Kidd and Batchelar 2012). We thus anticipate that some of these factors can be incorporated into our model to improve the predictability in a specific aquatic environment.

Hg(II)/MeHg accumulation in fish

This study constructed a PBTK model to predict the chronic accumulation patterns of Hg(II) in tissues/organs of tilapia. PBTK model performance that relies heavily on the experimental data of time-series tissue/organ burdens is not easy to achieve due to limited data sources with uncertainties resulting from different experimental species and protocols. Although the experimental data (Allen 1994) we used was obtained from short-term experiments, it provides us a rare opportunity to examine the predictability of PBTK

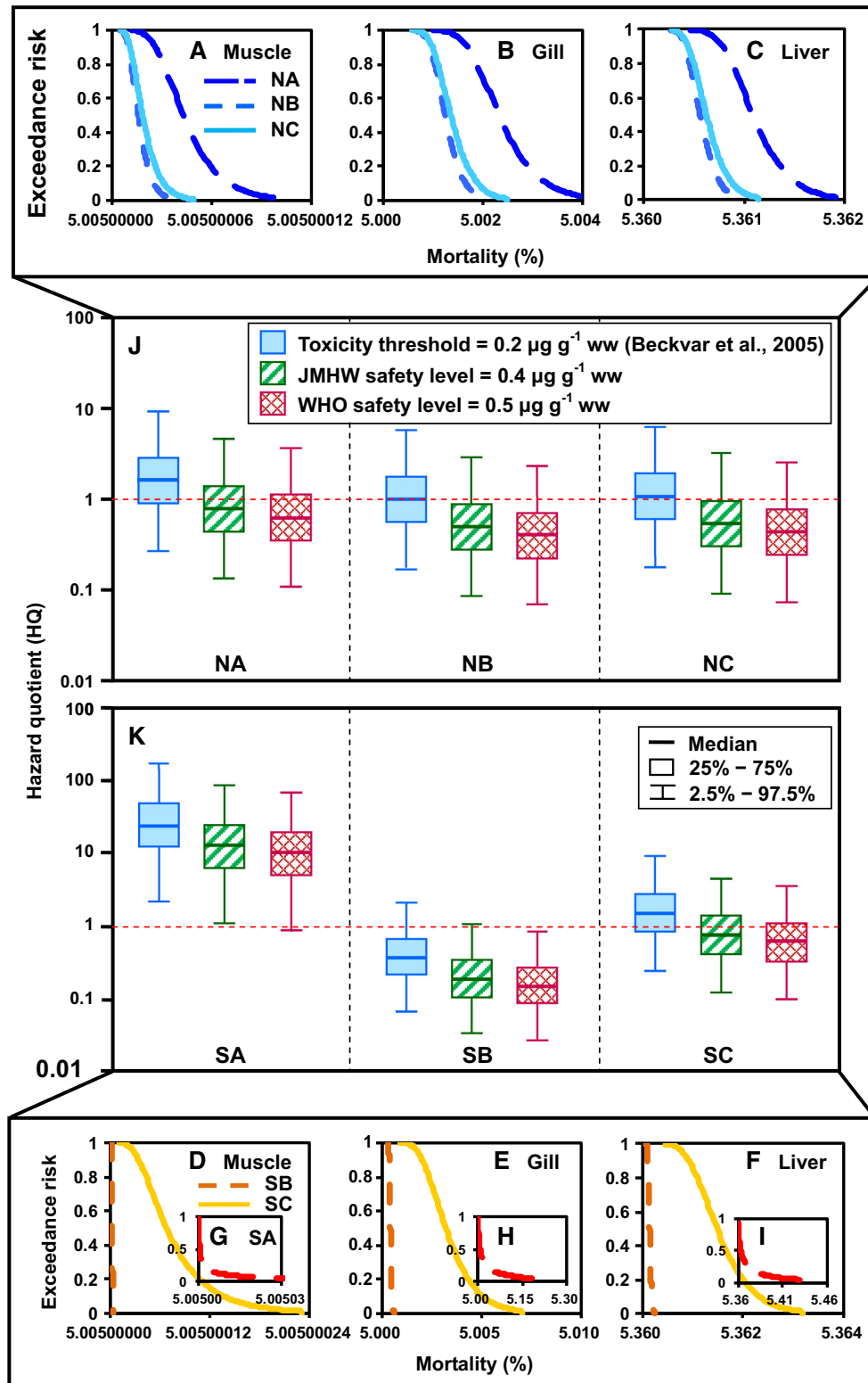
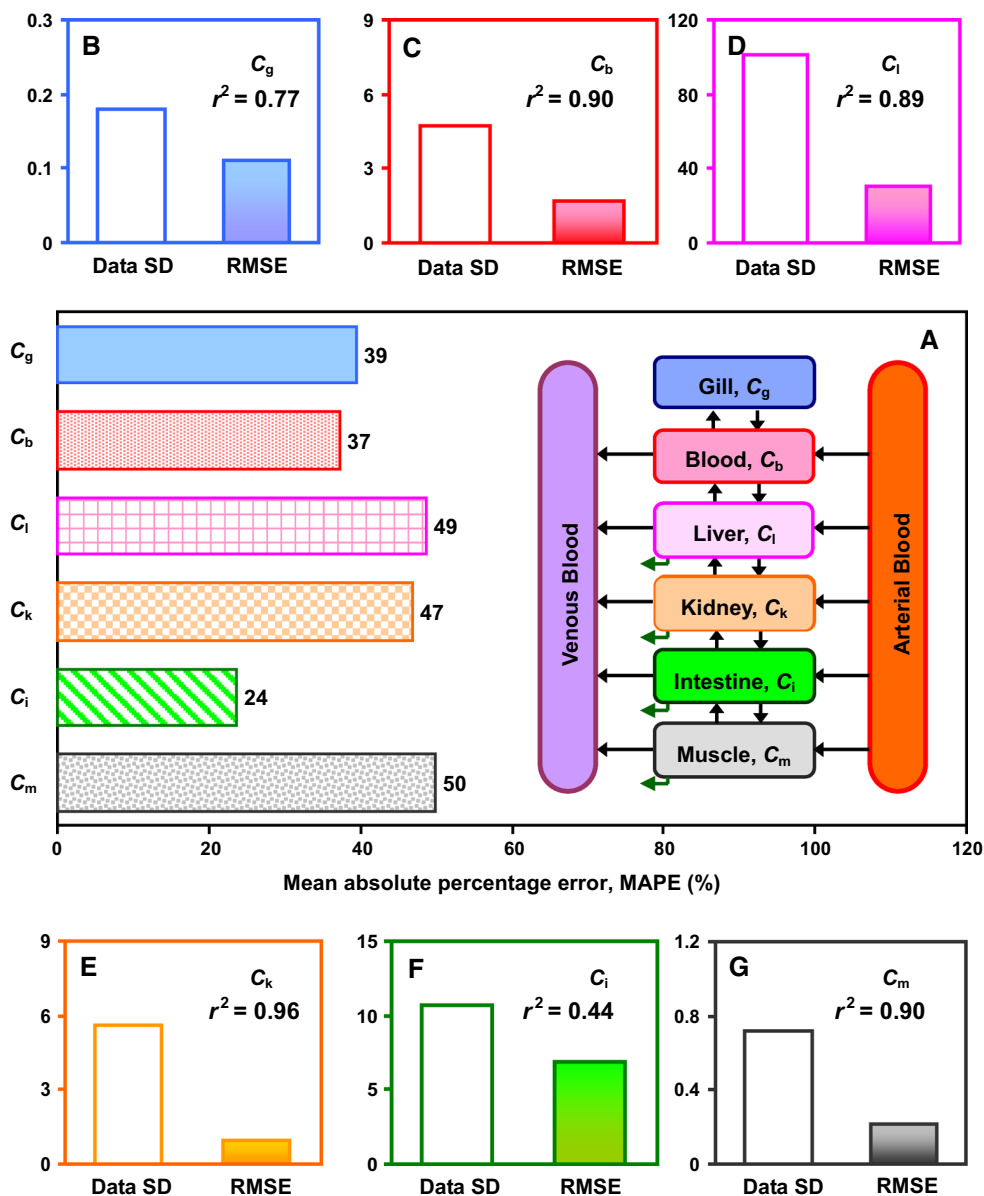


Fig. 4 Tissue or organ burden-based mortality exceedance risk profiles of muscle (a, d, and g), gill (b, e, and h), and liver (c, f, and i) in northern and southern regions of Taiwan. j and k show the

hazard quotient (HQ) in northern and southern Taiwan, respectively, estimated based on three safety levels for fish determined by Beckvar et al. (2005), Japan (Endo et al. 2005), and WHO (1990)

Fig. 5 Model performance by comparing predicted tissue/organ-specific burden of Hg(II) in tilapia by the PBTk model with experimental data (Allen 1994) based on **a** mean absolute percentage error (MAPE) as well as **b–g** root mean square error (RMSE) and coefficient of determination (r^2)



model. We also acknowledged that quantitative simulation should be drawn by incorporating biologically meaningful parameters from realistic and conditioned exposure bioassays. Yet, our proposed mechanistic risk assessment approach incorporating water–sediment Hg fates and transports, Hg-PBTk model for tilapia, as well as dose–response relationship of Hg induced mortality may provide insights in designing more realistic toxicokinetic and toxicodynamic experimental protocols and more precise model validation in the near future.

Our simulated PBTk results demonstrated that the estimated Hg(II) burden was highest in kidney followed by gill, intestine, liver, blood, and muscle, which was consistent with the previous results (Allen 1994). While considering only very short exposure period (e.g. 0.25–1 day)

would the accumulated Hg(II) burden of kidney and gill be similar (Allen, 1994). We found that the ratio of Hg(II) burden in kidney to gill at 0.5 day was 1.50 lower than the ratio of 2.43 estimated from Allen (1994), which is due in part to the different exposure routes being considered including water and sediment intakes. However, given long exposure period taken into account (e.g., 180 days), the estimated ratio of Hg(II) burden could reach 12 as high.

Numerous studies had pointed out that gill, muscle, brain, and viscera including liver, kidney, and intestine may be the target tissues/organs for Hg accumulation depending on different ingestion patterns (Allen 1994; Pereira et al. 2015; Squadrone et al. 2013; Wang et al. 2013). This study identified similar target organ/tissue including kidney, gill, intestine, and liver except muscle

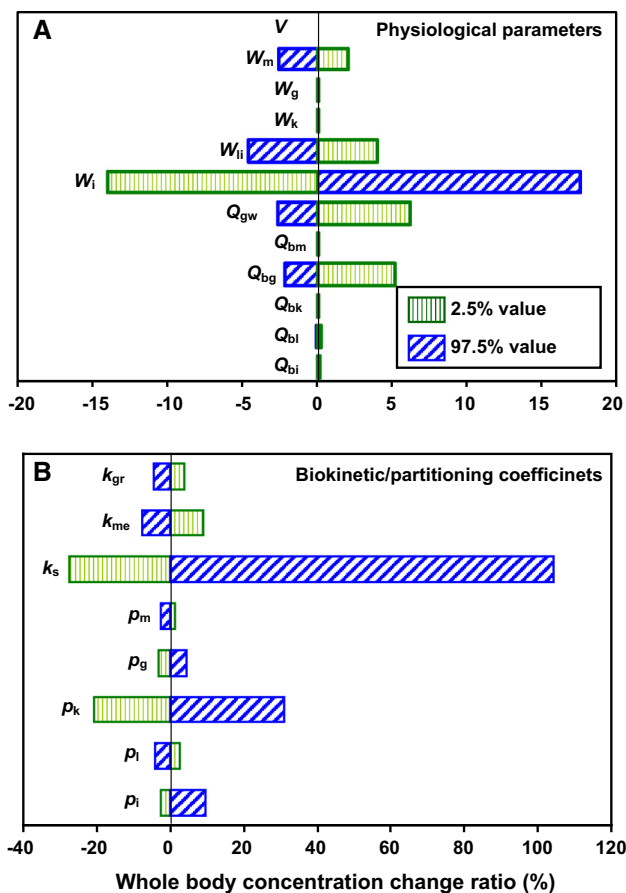


Fig. 6 One-way sensitivity analysis for the contributions of **a** physiological parameters and **b** biokinetic/partitioning coefficients to THg concentration in tilapia whole body

which we found it might be relatively safe for consumptions compared to regulation of Taiwan FDA (2013a, b). This study considered simultaneously water and sediment Hg exposure, yet it turned out that Hg(II) burdens found in gill and intestine are similar. Wang et al. (2013) supports our idea that Hg(II) might be the major speciation in freshwater tilapia due to low-potential *in vivo* mercury methylation. On the other hand, our sensitivity analysis demonstrated that sediment uptake rate (k_s) was the most important factor in determining the Hg accumulation, indicating sediment exposure is a potential risk factor to aquatic organisms.

Wang and Wang (2012) conducted a dietary Hg exposure to investigate accumulation patterns of Hg(II) and MeHg as well the somatic growth dilution (SGD) effects in tilapia (*O. niloticus*). Not quite different from other studies, they found that MeHg was the major retained form of Hg in fish post dietary exposure. They also indicated that the overall accumulation of Hg(II) depended mainly on assimilation efficiency and elimination rate and that of MeHg was critically related to growth rate instead,

implying that SGD was more likely to take place given MeHg exposure (Wang and Wang 2012).

Other aquatic conditions such as pH, DOC, and salinity were known factors impacting mercury uptake in freshwater fish (Jardine et al. 2013; Klinck et al. 2005; Wang et al. 2010). Generally, increments in both DOC and pH have inhibitory effects on mercury uptake. Moreover, previous study demonstrated that salinity together with water pH would have potentially complex effects on Hg bioaccumulation by altering the metal speciation (Laporte et al. 2002). On the other hand, MeHg largely affects Hg concentration and biomagnification in food web in aquatic ecosystems. Mason et al. (1995) further indicated that biomagnification of MeHg through food web was up to 4 times more efficient than Hg(II). Moreover, Clayden et al. (2013) pointed out MeHg biomagnification was higher in systems with lower aqueous nutrient/MeHg/chloride scores.

Taken together, these factors could lead to profound impacts on Hg accumulation in fish as well as environmental hazard to the aquatic ecosystem that worth further exploration. Future study would incorporate aquatic environmental conditions (e.g., pH, DOC, and salinity), various exposure routes (e.g., waterborne, dietborne, and sedimentborne), as well as effects of bioconcentration, biomagnifications, and growth inhibition into the well-established PBTK/TD model to assess the hazards for aquatic ecosystem and human health.

Implications for human exposure: sustaining seafood for public health

As early as in the 1950s, Hg contamination incidents occurred frequently in Minamata, Japan, have evidenced strongly that MeHg compared to Hg(II) is much more likely to pose a great health risk to humans who consumed Hg-contaminated fish. A recent statistical report has pointed out that the per capital fish consumption worldwide is increasing continuously from 10 kg in the 1960s to more than 19 kg in 2012 (FAO 2014). Taiwan is an island with high fish consumption of 47.38 ± 153.24 g day⁻¹ (MOHW 2008). Once ingested, nearly 90–100 % of MeHg in fish is likely to be absorbed rapidly through the human gastrointestinal tract, where it easily enters the blood stream and distributes throughout the body including the blood–brain barrier and placenta (Counter and Buchanan 2004; Zillioux 2015). This resulted in not only extreme fetal abnormalities but also neurotoxicity in adults and fetuses of mothers exposed during pregnancy (i.e., microcephaly, blindness, severe mental and physical developmental retardation) (Harada 1995).

However, the main concern today is of more subtle health effects arising from prenatal exposure, such as

delayed development and cognitive changes in children (Clarkson 1997; Zillioux 2015). The high level of prenatal exposure to MeHg was found to have significant correlation with neurological disabilities for children, especially in language, attention, memory, visuospatial, and motor functions (Grandjean et al. 1997; Jedrychowski et al. 2006). Axelrad et al. (2007) integrated epidemiological data to provide a robust dose–response relationship between maternal hair Hg levels during pregnancy and child IQ, showing a decrement of 0.18 points (95 % CI –0.378 to –0.009) for each ppm increase of maternal hair Hg. In Taiwan, Hsu et al. (2007) found that 89 % pregnant woman had blood Hg concentrations exceeding the US National Research Council recommended limit of $5.8 \mu\text{g L}^{-1}$ that is correlated significantly with Hg-contaminated fish consumption. Moreover, Jiang et al. (2010) found that Hg concentration in meconium of Taiwanese fetuses ($79.2 \pm 7.3 \text{ ng g}^{-1}$) was higher than other sites in Manila of 1.9 ± 2.3 (Ostrea et al. 1997) and Tagum of 48.6 ± 43.5 (Ramirez et al. 2003). They also highlighted that various daily Hg exposure concentrations for Taiwanese mothers were mainly attributable to varied Hg concentration in fish as well as fish ingestion rate.

Although current global Hg exposure is at level much lower than the previous case in Minamata, a growing number of studies have raised concern about the potential impact of low-level MeHg exposure on a variety of adverse health outcomes in both adults and children (Karagas et al. 2012; Driscoll et al. 2013). Based on a review of epidemiological researches targeting at low-dose MeHg exposure, Driscoll et al. (2013) found the possibility of adverse effects on fetal growth and infant growth, whereas prenatal exposure may cause early childhood neurological effects. They also concluded that no conclusive evidence on the MeHg-associated cardiovascular disease and immune function at low-dose exposure. However, on the basis of a case–control study, a significant dose–response relationship between toenail Hg level and the risk of myocardial infarction was constructed (Guallar et al. 2002). Recently, Furieri et al. (2011) suggested that chronic exposure to Hg could be a risk factor affecting heart function based on a series of in vivo animal experiments.

Our risk assessment results showed that Hg was less likely to pose mortality risk for freshwater tilapia species, even with such high concentration in Luermen creek (SA), implicating that tilapia species have high environmental stress tolerance and tend to accumulate high Hg concentration. In light of this finding, we suggest that tilapia species can be biocontrol agents in the polycultural systems for benefiting other fishes such as milkfish by reducing concentrations of toxic elements in the water (Ju et al. 2014). While Asian may be at risk and suffer from adverse effects as a result of consuming tilapia with high

concentration of Hg(II)/MeHg since Asia is the largest emitter of Hg and the emissions are continually increasing (Pirrone et al. 2010; Driscoll et al. 2013). Consequently, it is of interest to conduct the risk assessment for human health in the scenario of chronic consumption of tilapia in the near future.

Conclusions

This study presents a mechanistic risk assessment framework by integrating water–sediment, PBTK, and probabilistic risk assessment models to predict the impact of Hg(II)/MeHg on freshwater tilapia species, one of the major edible fish. Our results showed that Hg was less likely to pose mortality risk (mortality rate less than 5 %) for freshwater tilapia. Yet, a dramatically high HQ was found in our risk assessment, implying that the chronic sublethal risk (e.g., growth, reproduction, development, and behavior) posed by Hg was alarming. Hence, we suggest more dose–response data of sublethal and chronic effects for aquatic organisms are required to improve risk assessment approach in a more realistic and practical way. We also found that sediment borne Hg exposure was the most influential factor on accumulation of tilapia that is bottom-feeding fish. In a broader way, our mechanistic framework can be applied to predict environmental risks associated with continuously chronic exposure to certain hazards for fish that are deemed safe for human consumption.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Informed consent Informed consent was obtained from all individual participants included in the study.

Research involving human participants and animal rights The article does not contain any studies with human participants or animals performed by any of the authors.

References

- Allen P (1994) Distribution of mercury in the soft tissues of the blue tilapia *Oreochromis aureus* (Steindachner) after acute exposure to mercury (II) chloride. *Bull Environ Contam Toxicol* 53:675–683
- Amos HM, Jacob DJ, Streets DG, Sunderland EM (2013) Legacy impacts of all-time anthropogenic emissions on the global mercury cycle. *Glob Biogeochem Cycle* 27:410–421
- Axelrad DA, Bellinger DC, Ryan LM, Woodruff TJ (2007) Dose–response relationship of prenatal mercury exposure and IQ: an integrative analysis of epidemiologic data. *Environ Health Perspect* 115:609–615

- Beckvar N, Dillon TM, Read LB (2005) Approaches for linking whole-body fish tissue residues of mercury or DDT to biological effects thresholds. *Environ Toxicol Chem* 24:2094–2105
- Bloom NS, Moretto LM, Scopece P, Ugo P (2004) Seasonal cycling of mercury and monomethyl mercury in the Venice Lagoon (Italy). *Mar Chem* 91:85–99
- Celo V, Lean DR, Scott SL (2006) Abiotic methylation of mercury in the aquatic environment. *Sci Total Environ* 368:126–137
- Chen WY, Liao CM (2014) Interpreting copper bioaccumulation dynamics in tilapia using systems-level explorations of pulsed acute/chronic exposures. *Ecotoxicology* 23:1124–1136
- Chen CW, Chen CF, Dong CD (2012a) Contamination and potential ecological risk of mercury in sediments of Kaohsiung River Mouth, Taiwan. *Int J Environ Sci Dev* 3:66–71
- Chen CW, Chen CF, Dong CD (2012b) Enrichment and potential toxicity of mercury in the sediments of Jen-Gen River Mouth, Taiwan. *Adv Biomed Eng* 7:166–170
- China Petrochemical Development Corporation An-Shun Site (CPDCASS) (2012) China Petrochemical Development Corporation's Remediation Plan for the An-shun Site and the East Bush Side of the Section 2-9 Road (in Chinese). <http://epb3.tainan.gov.tw/cpdc/ch/upload/Case120120521133200.pdf>
- Clarkson TW (1997) The toxicology of mercury. *Crit Rev Clin Lab Sci* 34:369–403
- Clayden MG, Kidd KA, Wyn B, Kirk JL, Muir DC, O'Driscoll NJ (2013) Mercury biomagnification through food webs is affected by physical and chemical characteristics of lakes. *Environ Sci Technol* 47:12047–12053
- Counter SA, Buchanan LH (2004) Mercury exposure in children: a review. *Toxicol Appl Pharmacol* 198:209–230
- Cristol DA, Brasso RL, Condon AM, Fovargue RE, Friedman SL, Hallinger KK, Monroe AP, White AE (2008) The movement of aquatic mercury through terrestrial food webs. *Science* 320:335
- Driscoll CT, Mason RP, Chan HM, Jacob DJ, Pirrone N (2013) Mercury as a global pollutant: sources, pathways, and effects. *Environ Sci Technol* 47:4967–4983
- Endo T, Haraguchi K, Hotta Y, Hisamichi Y, Lavery S, Dalebout ML, Baker CS (2005) Total mercury, methyl mercury, and selenium levels in the red meat of small cetaceans sold for human consumption in Japan. *Environ Sci Technol* 39:5703–5708
- Ethier AL, Atkinson JF, Depinto JV, Lean DR (2012) Estimating mercury concentrations and fluxes in the water column and sediment of Lake Ontario with HERMES model. *Environ Pollut* 161:335–342
- Food and Agriculture Organization of the United Nations (FAO) (2014) The State of World Fisheries and Aquaculture (2014) Report Highlights. <http://www.fao.org/3/a-i3807e.pdf>
- Furieri LB, Fioresi M, Junior RF, Bartolomé MV, Fernandes AA, Cachofeiro V, Lahera V, Salices M, Stefanon I, Vassallo DV (2011) Exposure to low mercury concentration in vivo impairs myocardial contractile function. *Toxicol Appl Pharmacol* 255:193–199
- Gerber LR, Karimi R, Fitzgerald TP (2012) Sustaining seafood for public health. *Front Ecol Environ* 10:487–493
- Grandjean P, Weihe P, White RF, Debes F, Araki S, Yokoyama K, Murata K, Sørensen N, Dahl R, Jørgensen PJ (1997) Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. *Neurotoxicol Teratol* 19:417–428
- Guallar E, Sanz-Gallardo MI, van't Veer P, Bode P, Aro A, Gómez-Aracena J, Kark JD, Riemersma RA, Martín-Moreno JM, Kok FJ (2002) Mercury, fish oils, and the risk of myocardial infarction. *N Engl J Med* 347:1747–1754
- Harada M (1995) Minamata disease: methylmercury poisoning in Japan caused by environmental pollution. *Crit Rev Toxicol* 25:1–24
- Hsu CS, Liu PL, Chien LC, Chou SY, Han BC (2007) Mercury concentration and fish consumption in Taiwanese pregnant women. *BJOG* 114:81–85
- Huang S, Chen C, Chen M (2008) Total and organic Hg in fish from the reservoir of a chlor-alkali plant in Tainan, Taiwan. *J Food Drug Anal* 16:75–80
- Jardine TD, Kidd KA, O'Driscoll N (2013) Food web analysis reveals effects of pH on mercury bioaccumulation at multiple trophic levels in streams. *Aquat Toxicol* 132–133:46–52
- Jedrychowski W, Jankowski J, Flak E, Skarupa A, Mroz E, Sochacka-Tatara E, Lisowska-Miszczuk I, Szpanowska-Wohn A, Rauh V, Skolicki Z, Kaim I, Perera F (2006) Effects of prenatal exposure to mercury on cognitive and psychomotor function in one-year-old infants: epidemiologic cohort study in Poland. *Ann Epidemiol* 16:439–447
- Jiang CB, Yeh CY, Lee HC, Chen MJ, Hung FY, Fang SS, Chien LC (2010) Mercury concentration in meconium and risk assessment of fish consumption among pregnant women in Taiwan. *Sci Total Environ* 408:518–523
- Ju YR, Chen WY, Liao CM (2014) Model-based risk assessment for milkfish and tilapia exposed to arsenic in a traditional polyculture system with seasonal variations. *Aquac Eng* 62:1–8
- Karagas MR, Choi AL, Oken E, Horvat M, Schoeny R, Kamai E, Cowell W, Grandjean P, Korrick S (2012) Evidence on the human health effects of low-level methylmercury exposure. *Environ Health Perspect* 120:799–806
- Karimi R, Fitzgerald TP, Fisher NS (2012) A quantitative synthesis of mercury in commercial seafood and implications for exposure in the United States. *Environ Health Perspect* 120:1512–1519
- Kidd K, Batchelar K (2012) Mercury. In: Wood CM, Farrell AP, Brauner CJ (eds) Homeostasis and toxicology of non-essential metals. Academic Press, Amsterdam, pp 237–295
- Klinck J, Dunbar M, Brown S, Nichols J, Winter A, Hughes C, Playle RC (2005) Influence of water chemistry and natural organic matter on active and passive uptake of inorganic mercury by gills of rainbow trout (*Oncorhynchus mykiss*). *Aquat Toxicol* 72:161–175
- Knightes CD (2008) Development and test application of a screening-level mercury fate model and tool for evaluating wildlife exposure risk for surface waters with mercury-contaminated sediments (SERAFM). *Environ Model Softw* 23:495–510
- Knightes CD, Sunderland EM, Craig Barber M, Johnston JM, Ambrose RB (2009) Application of ecosystem-scale fate and bioaccumulation models to predict fish mercury response times to changes in atmospheric deposition. *Environ Toxicol Chem* 28:881–893
- Krabbenhoff DP, Sunderland EM (2013) Global change and mercury. *Science* 341:1457–1458
- Laporte JM, Andres S, Mason RP (2002) Effect of ligands and other metals on the uptake of mercury and methylmercury across the gills and the intestine of the blue crab (*Callinectes sapidus*). *Comp Biochem Physiol C* 131:185–196
- Lavoie RA, Jardine TD, Chumchal MM, Kidd KA, Campbell LM (2013) Biomagnification of mercury in aquatic food webs: a worldwide meta-analysis. *Environ Sci Technol* 47:13385–13394
- Liao CM, Liang HM, Chen BC, Singh S, Tsai JW, Chou YH (2005) Dynamical coupling of PBPK/PD and AUC-based toxicity models for arsenic in tilapia *Oreochromis mossambicus* from blackfoot disease area in Taiwan. *Environ Pollut* 135:221–233
- Low KH, Zain SM, Abas ME, Salleh KM, Teo YY (2015) Distribution and health risk assessment of trace metals in freshwater tilapia from three different aquaculture sites in Jelebu Region (Malaysia). *Food Chem* 177:390–396
- Mahmoud HH, Mazrouh MM (2008) Biology and fisheries management of tilapia species in Rosetta branch of the Nile River, Egypt. *J Aquat Res* 34:272–284

- Malczyk EA, Branfiren BA (2015) Mercury in sediment, water, and fish in a managed tropical wetland-lake ecosystem. *Sci Total Environ* 524–525:260–268
- Mason RP, Reinfelder JR, Morel FMM (1995) Bioaccumulation of mercury and methylmercury. *Water Air Soil Pollut* 80:915–921
- Ministry of Health and Welfare (MOHW, R.O.C., Taiwan) (2008) Compilation of exposure factors. Report NO. DOH96-HP-1801. (in Chinese)
- Morel FMM, Kraepiel AML, Amyot M (1998) The chemical cycle and bioaccumulation of mercury. *Annu Rev Ecol Syst* 29:543–566
- Nichols JW, McKim JM, Lien GJ, Hoffman AD, Bertelsen SL, Elonen CM (1996) A physiologically based toxicokinetic model for dermal absorption of organic chemicals by fish. *Fundam Appl Toxicol* 31:229–242
- Oken E, Choi AL, Karagas MR, Mariën K, Rheinberger CM, Schoeny R, Sunderland E, Korrick S (2012) Which fish should I eat? Perspectives influencing fish consumption choices. *Environ Health Perspect* 120:790–798
- Orenstein ST, Thurston SW, Bellinger DC, Schwartz JD, Amarasingwardena CJ, Altshul LM, Korrick SA (2014) Prenatal organochlorine and methylmercury exposure and memory and learning in school-age children in communities near the New Bedford Harbor Superfund site, Massachusetts. *Environ Health Perspect* 122:1253–1259
- Ostrea EM Jr, Preccilla R, Moroles V, Go J, Tan E, Hernandez E, Baens-Ramirez G, Manlapaz M (1997) Significant fetal exposure to heavy metals as detected by meconium analysis. *Pediatr Res* 41:168A
- Parks JM, Johs A, Podar M, Bridou R, Hurt RA Jr, Smith SD, Tomanicek SJ, Qian Y, Brown SD, Brandt CC, Palumbo AV, Smith JC, Wall JD, Elias DA, Liang L (2013) The genetic basis for bacterial mercury methylation. *Science* 339:1332–1335
- Pereira P, Raimundo J, Barata M, Araújo O, Pousão-Ferreira P, Canário J, Almeida A, Pacheco M (2015) A new page on the road book of inorganic mercury in fish body—tissue distribution and elimination following waterborne exposure and post-exposure periods. *Metallomics* 7:525–535
- Peters SA (2012) Physiologically-based pharmacokinetic (PBPK) modeling and simulations. Wiley, New Jersey
- Pirrone N, Cinnirella S, Feng X, Finkelman RB, Friedli HR, Leaner J, Mason R, Mukherjee AB, Stracher GB, Streets DG, Telmer K (2010) Global mercury emissions to the atmosphere from anthropogenic and natural sources. *Atmos Chem Phys* 10:5951–5964
- Ramirez GB, Pagulayan O, Akagi H, Francisco Rivera A, Lee LV, Berroya A, Vince Cruz MC, Casintahan D (2003) Tagum study II: follow-up study at two years of age after prenatal exposure to mercury. *Pediatrics* 111:e289–e295
- Rheinberger CM, Hammitt JK (2012) Risk trade-offs in fish consumption: a public health perspective. *Environ Sci Technol* 46:12337–12346
- Squadrone S, Prearo M, Brizio P, Gavinelli S, Pellegrino M, Scanzio T, Guarise S, Benedetto A, Abete MC (2013) Heavy metals distribution in muscle, liver, kidney and gill of European catfish (*Silurus glanis*) from Italian Rivers. *Chemosphere* 90:358–365
- Sweilum MA (2006) Effect of chronic exposure to sublethal levels of mercury on total production, physiological functions and economical efficiency of tilapia fish, with regard to properties of ponds water. *Egypt Aquat Biol Fish* 10:165–183
- Taiwan EPA (Environmental Protection Administration, Executive Yuan, R.O.C., (Taiwan)) (2012a) Category management and usage restrictions for sediment quality indicators (in Chinese). <http://epb3.tainan.gov.tw/cpdc/ch/upload/Case120120521104142.pdf>
- Taiwan EPA (Environmental Protection Administration, Executive Yuan, R.O.C., (Taiwan)) (2013a) Survey on the environmental distribution of toxic chemicals, (2013) (in Chinese). <http://www.epa.gov.tw/ct.asp?xItem=13891&ctNode=32227>
- Taiwan EPA (Environmental Protection Administration, Executive Yuan, R.O.C., (Taiwan)) (2013b) Investigation for contamination source in sediment and its transport modeling—take internal major river for example (in Chinese). <http://epr.epa.gov.tw/upload/openFull/100/1007131085/epa-G1-1007131085-06-05.pdf>
- Taiwan EPA (Taiwan Environmental Protection Administration, Executive Yuan, R.O.C., (Taiwan)) (2012b) The determination of total mercury in soils, sediments, and wastes by cold vapor atomic absorption spectroscopy (NIEA M317.03B) (in Chinese). <http://www.niea.gov.tw/niea/pdf/REFSOIL/M31703B.pdf>
- Taiwan FDA (Food and Drug Administration, Ministry of Health and Welfare, R.O.C. Taiwan) (2013) Sanitation Standard for Aquatic Animal. <https://www.consumer.fda.gov.tw/Law/Detail.aspx?no=deID=518&lang=1&lawid=100>
- Thomann RV, Shkreli F, Harrison S (1997) A pharmacokinetic model of cadmium in rainbow trout. *Environ Toxicol Chem* 16:2268–2274
- Tong Y, Zhang W, Chen C, Chen L, Wang W, Hu X, Wang H, Hu D, Ou L, Wang X, Wang Q (2014) Fate modeling of mercury species and fluxes estimation in an urban river. *Environ Pollut* 187:54–61
- Tweedy BN, Drenner RW, Chumchal MM, Kennedy JH (2013) Effects of fish on emergent insect-mediated flux of methyl mercury across a gradient of contamination. *Environ Sci Technol* 47:1614–1619
- Vieira HC, Morgado F, Soares AM, Abreu SN (2015) Fish consumption recommendations to conform to current advice in regard to mercury intake. *Environ Sci Pollut Res* 22:9595–9602
- Wang WX (2012) Biodynamic understanding of mercury accumulation in marine and freshwater fish. *Adv Environ Res* 1:15–35
- Wang R, Wang WX (2012) Contrasting mercury accumulation patterns in tilapia (*Oreochromis niloticus*) and implications on somatic growth dilution. *Aquat Toxicol* 114–115:23–30
- Wang SW, Lin KH, Hsueh YM, Liu CW (2007) Arsenic distribution in a tilapia (*Oreochromis mossambicus*) water-sediment aquacultural ecosystem in blackfoot disease hyperendemic areas. *Bull Environ Contam Toxicol* 78:147–151
- Wang R, Wong MH, Wang WX (2010) Mercury exposure in the freshwater tilapia *Oreochromis niloticus*. *Environ Pollut* 158:2694–2701
- Wang R, Feng XB, Wang WX (2013) In vivo mercury methylation and demethylation in freshwater tilapia quantified by mercury stable isotopes. *Environ Sci Technol* 47:7949–7957
- Watras CJ, Back RC, Halvorsen S, Hudson RJ, Morrison KA, Wentz SP (1998) Bioaccumulation of mercury in pelagic freshwater food webs. *Sci Total Environ* 219:183–208
- WHO (World Health Organization) (1990) Environmental Health Criteria 101: Methylmercury. WHO, Geneva
- Wu TN (2006) Distribution of methylmercury in a mercury-contaminated ecosystem. *Pract Period Hazard Toxic Radioact Waste Manag* 10:192–197
- Zillioux EJ (2015) Mercury in fish: history, sources, pathways, effects, and indicator usage. In: Armon RH, Hänninen O (eds) *Environmental indicators*. Springer, Dordrecht, pp 743–766