Journal of Hazardous Materials 186 (2011) 622–628

Contents lists available at ScienceDirect

Journal of Hazardous Materials

journal homepage: www.elsevier.com/locate/jhazmat

Assessing and managing the health risk due to ingestion of inorganic arsenic from fish and shellfish farmed in blackfoot disease areas for general Taiwanese

Ching-Ping Liang[a], Chen-Wuing Liu[b,*], Cheng-Shin Jang[c], Sheng-Wei Wang[d], Jin-Jing Lee[e]

[a] Department of Environmental Engineering and Science, Fooyin University, Kaohsiung 831, Taiwan, ROC
[b] Department of Bioenvironmental Systems Engineering, National Taiwan University, Taipei 106, Taiwan, ROC
[c] Department of Leisure and Recreation Management, Kainan University, Luzhu, Taoyuan 338, Taiwan, ROC
[d] Agricultural Engineering Research Center, Jhongli, Taoyuan 320, Taiwan, ROC
[e] Department of Environmental Sanitation and Toxic Substance Management, Environmental Protection Administration, Executive Yuan 100, Taiwan, ROC

ARTICLE INFO

Article history:
Received 29 June 2010
Received in revised form 8 October 2010
Accepted 10 November 2010
Available online 16 November 2010

Keywords:
Risk
Fish and shellfish
Arsenic
Groundwater
Consumption rate

ABSTRACT

This paper assesses health risks due to the ingestion of inorganic arsenic from fish and shellfish farmed in blackfoot disease areas by general public in Taiwan. The provisional tolerable weekly intake of arsenic set by FAO/WHO and the target cancer risk assessment model proposed by USEPA were integrated to evaluate the acceptable consumption rate. Five aquacultural species, tilapia (*Oreochromis mossambicus*), milkfish (*Chanos chanos*), mullet (*Mugil cephalus*), clam (*Meretrix lusoria*) and oyster (*Crassostrea gigas*) were included. Monte Carlo analysis was used to propagate the parameter uncertainty and to probabilistically assess the health risk associated with the daily intake of inorganic As from farmed fish and shellfish. The integrated risk-based analysis indicates that the associated 50th and 95th percentile health risk are 2.06×10^{-5} and 8.77×10^{-5}, respectively. Moreover, the acceptable intakes of inorganic As are defined and illustrated by a two dimensional graphical model. According to the relationship between C_{inorg} and IR_f derived from this study, two risk-based curves are constructed. An acceptable risk zone is determined (risk ranging from 1×10^{-5} to 6.07×10^{-5}) which is recommended for acceptable consumption rates of fish and shellfish. To manage the health risk due to the ingestion of inorganic As from fish and shellfish in BFD areas, a risk-based management scheme is derived which provide a convenient way for general public to self-determine the acceptable seafood consumption rate.

1. Introduction

The risk of inorganic arsenic (As) contamination in human food sources has recently received a great public attention because of the potential hazard to human health. Inorganic As compounds are carcinogenic to humans, with evidence for an increased cancer risk of the urinary bladder, lung, and skin [1,2]. People can be exposed to As from a variety of sources (food, water, soil and air), but exposure via ingestion of seafood is by far the most significant one. Martí-Cid et al. [3] indicated that fish and shellfish are the main group showing the highest contribution to the dietary intake of inorganic As. The highest dietary As intake (217.7 μg/day) came from the consumption of fish and seafood, as indicated by Falcó et al. [4]. Farmed fish/shrimp bioaccumulates certain amounts of As from aquaculture-used As-contaminated groundwater [5–7]. In recent years, several studies have investigated the amounts of As species contents in seafood to assess the risk of cancer associated with consuming aquatic products obtained from As-contaminated groundwater areas of local inhabitants, such as the coastal regions of southwestern Taiwan [8–17].

It has also been well documented that As is a major risk factor for blackfoot disease (BFD) [18] and indeed, over the past few decades BFD has become prevalent in the southwestern coastal area of Taiwan (Fig. 1) [19]. Extensive epidemiological evidence has proven that drinking groundwater with a high As content is closely associated with the occurrence of BFD [20]. Nowadays, very few inhabitants in this region drink well water directly, but large amounts of groundwater are utilized for fish and shellfish farming [9]. Since As is accumulated in aquatic organisms [21], the high As content in the groundwater ranging 470–897 μg/l used for aquaculture has resulted in an accumulation of As in the cultured fish and shellfish. Tilapia (*Oreochromis mossambicus*), milkfish (*Chanos chanos*), mullet (*Mugil cephalus*), clams (*Meretrix lusoria*) and oysters (*Crassostrea gigas*) are the five major aquaculture species farmed in the BFD areas which are frequently consumed by the general population of Taiwan [22].

The WHO and the Food and Agriculture Organization (FAO) recommended a regular fish consumption of 1–2 servings per week in

* Corresponding author. Tel.: +886 2 2362 6480; fax: +886 2 2363 9557.
E-mail addresses: lcw@gwater.agec.ntu.edu.tw, cwliu@ntu.edu.tw (C.-W. Liu).

0304-3894/$ – see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.jhazmat.2010.11.042

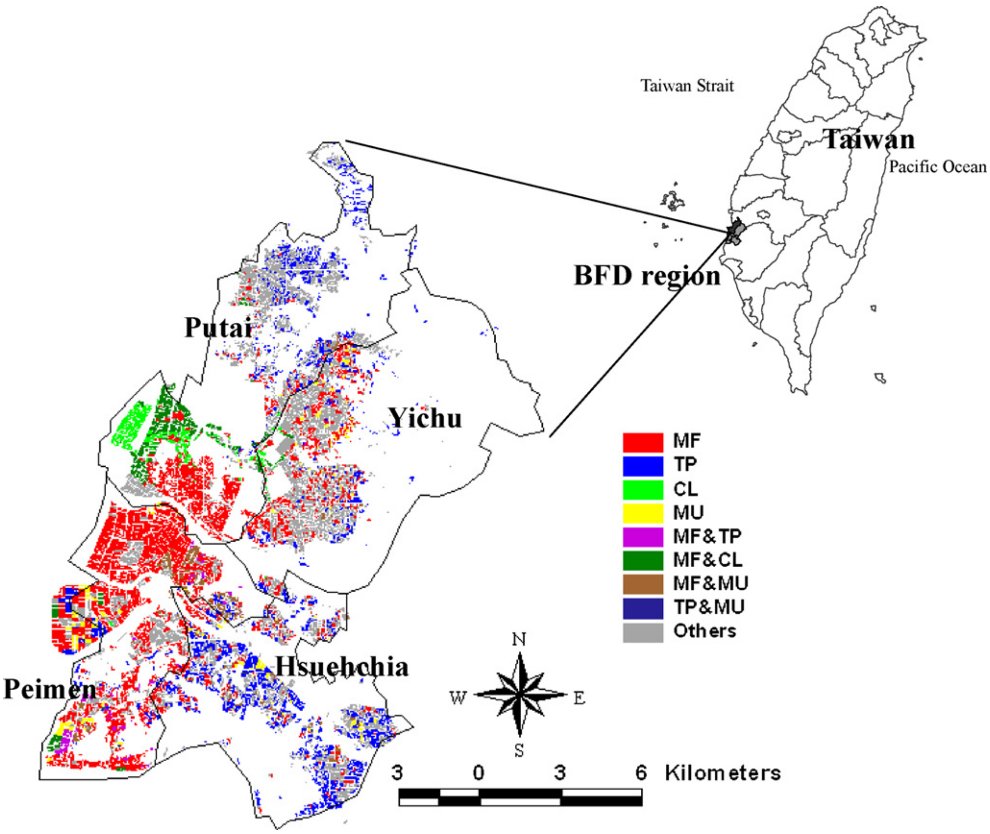

Fig. 1. BFD areas in southwestern Taiwan. The colored areas are the fish ponds where tilapia (TP), milkfish (MF), mullet (MU), and clams (CL) are cultivated. Oysters are farmed in the inner sea of Putai. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

order to provide an equivalent of 200–500 mg of the ω3 polyunsaturated fatty acids (ω3-PUFA) eicosapentaenoic and docosahexaenoic acids [23]. The health benefits of a diet rich in fish have been extensively recognized specially in the last decade. Namely, ω3-PUFA is associated with decreased morbidity and mortality from various diseased. Fish and shellfish are healthy sources of protein, but the risks accrued from consuming contaminated fish and shellfish have become national concerns [24–27]. Most of previous studies

Table 1
Aquatic species, sample size, location, total As concentration in farmed water, inorganic arsenic (As(V), As(III)), total arsenic concentrations and fitted inorganic As concentration distributions of fish and shellfish in the BFD areas.

Species	Sample size	Location	Arsenic species analyzed	Total As concentration in farmed water (μg/l)	As species concentration (mean ± SD (μg/g))			Inorganic As[a] distributions (μg/g)
					As(III)	As(V)	Total As	
Tilapia[b]	68	BFD areas	As(III), As(V), MMA, DMA, AsB, Total As	4.4–302.8 in pond water	0.026 ± 0.043	0.027 ± 0.042	0.85 ± 0.83	LN(0.03, 2.94)[c]
Milkfish[d]	36	BFD areas	Inorganic arsenic, Total As	27 in pond water	0.33 ± 0.45		0.75 ± 0.92	LN(0.21, 2.43)
Mullet[e]	24	Southwestern Taiwan	As(III), As(V), MMA, DMA, AsB, Total As	49 in pond water	0.008 ± 0.005	0.036 ± 0.023	3.28 ± 1.32	LN(0.03, 1.81)
Oyster[f]	252	Southwestern Taiwan	As(III), As(V), MMA, DMA, AsB, Total As	0.15–5 in surface water	0.091 ± 0.104	0.033 ± 0.038	9.90 ± 3.68	LN(0.12, 2.11)
Clam[g]	47	Southwestern Taiwan	As(III), As(V), MMA, DMA, AsB, Total As	40–97 in pond water	0.96 ± 0.65	0.17 ± 0.21	8.48 ± 4.87	LN(0.83, 2.33)

[a] Inorganic As is the summation of As(III) and As(V).
[b] LN(μ_g,σ_g) denotes a log-normal distribution identified by a Kolmogorov–Smirnov (K–S) test with a geometric average of μ_g and a geometric standard deviation of σ_g.
[c] Value was taken from Huang et al. [29].
[d] Value was taken from Lin and Liao [16].
[e] Value was taken from Liu et al. [13–15].
[f] Value was taken from Liu et al. [13–15].
[g] Value was taken from Liu et al. [13–15].

were focused on the health risk assessment of inhabitants in the BFD areas based on the consumption of single As-contaminated fish or shellfish [9,10,12–14,16]. High target cancer risks ($TR \sim 10^{-4}$) were reported [9,16]. However, the health risk associated with the ingestion of these aquatic species produced from BFD areas by the general population of Taiwan is lacking. Moreover, the method used to assess the health effect is limited to the target cancer risk proposed by USEPA, the provisional tolerable weekly intake set by FAO/WHO is not considered [9,12–14,16]. Thus, the study aims to assess the health risk due to ingestion of inorganic As from fish and shellfish farmed in the BFD areas for general Taiwanese. The probabilistic risk assessment method supported by USEPA and the provisional tolerable weekly intake (PTWI) of As set by FAO/WHO are integrated to assess acceptable consumption rates of fish and shellfish farmed in As-contaminated BFD areas. Moreover, Monte Carlo (MC) simulation is adopted to propagate the uncertainty of parameters concerning inorganic As exposure. The results provide a convenient guideline for self-management of acceptable consumption rates while ingesting popular fish and shellfish from As-contaminated BFD areas.

2. Material and methods

2.1. Study region

The study region, the BFD areas, includes the Putai, Yichu, Hsuehchia and Peimen townships located in the plain region of Chiayi and Tainan counties, all of which are As-contaminated groundwater areas in southwestern Taiwan (Fig. 1). Aquaculture is the primary source of revenue for the local inhabitants in these coastal plains. Tilapia, milkfish, mullet, and clams are mainly cultured in inland fishponds, while oysters are farmed in the shallow inner sea of the Putai township. According to the geographical information system (GIS) database obtained from the Taiwan Fishery Agency, approximately 30% of the land in these townships is used for aquaculture ponds [28]. For the inland aquaculture, 37.8%, 18.4%, 2.5% and 7.6% of the fish ponds are farmed milkfish, tilapia, mullet and clams, respectively. The ratio of aquaculture area in the study region to the total aquaculture area in Taiwan (for the aforementioned species) is 22.8% for oysters, 17.9% for milkfish, 14.4% for tilapia, 13.2% for clams and 2.0% for mullet [22]. Moreover, the amount of oysters produced in the Putai township constitutes 35.6% of the total amount produced in Taiwan. Tilapia, milkfish, mullet, clams and oyster are popular farmed species consumed by general population in Taiwan. Large amount of high As content groundwater is withdrawn for aquaculture need. Use of high As contents groundwater for aquaculture has resulted in an accumulation of As in cultured fish and shellfish in BFD areas [15].

2.2. Inorganic arsenic contents in fish and shellfish

Huang et al. [29], Lin and Liao [16], and Liu et al. [13–15] have sampled farmed tilapia, milkfish, mullet, oysters and clams and reported the measurements for inorganic As contents, respectively (Table 1). Table 1 presents the aquatic species, sample size, location, As concentration of farmed water, measured inorganic As (As(V), As(III)) and total As concentrations of fish and shellfish in As-contaminated groundwater areas. Detailed description of analysis of As species in fish and shellfish can be found in previously published literatures [13–16,29]. The inorganic As contents of five fish and shellfish were fitted by various probability density functions and followed log-normal distributions as determined by the χ^2 and Kolomogorov–Smirnov (K–S) statistics which optimized the goodness of fit of distribution.

Table 2
Used parameters for cancer risk estimation for ingestion of fish and shellfish farmed in the BFD areas.

Species	Parameters					
	IR_w [a] (g/day)	α [b]	β [c]	ω [d]	C_{inorg} (μg/g)	
					50‰	95‰
Tilapia [e]	12.7	0.32	0.073	0.773	0.03	0.17
Milkfish [f]	10.9	0.32	0.441	0.773	0.21	0.92
Mullet [g]	0.6	0.32	0.016	0.76	0.04	0.10
Oyster [h]	12.4	0.2	0.015	0.85	0.12	0.44
Clam [i]	6.1	0.2	0.135	0.83	0.83	3.44

[a] Council of Agriculture, Taiwan (2007).
[b] α is the ratio of edible weight to total weight of fish and shellfish.
[c] β is the ratio of inorganic As content to total As content in fish and shellfish.
[d] ω is the water content in fish and shellfish.
[e] Value was taken from Huang et al. [29].
[f] Value was taken from Lin and Liao [16].
[g] Value was taken from Liu et al. [13–15].
[h] Value was taken from Liu et al. [13–15].
[i] Value was taken from Liu et al. [13–15].

2.3. Dietary exposure via the ingestion of fish and shellfish

We assessed the human health risk of intake of inorganic As via the ingestion of the fish and shellfish farmed in As-contaminated BFD areas. The potential carcinogenic risk due to the uptake of inorganic As from various seafood species was assessed using the method suggested by the US EPA [30,31]. Table 2 shows used parameters for cancer risk estimation. The 50th and 95th percentiles were also tabulated for the analyses of the daily consumer intake of inorganic As from seafood. This work probabilistically treats inorganic As contents in various fish and shellfish species. Data on daily consumption of aquaculture species by the general population of Taiwan were obtained from the Taiwanese Food Supply and Demand Annual Report of 2008 [22]. The daily intake of inorganic As from each type of fish and shellfish was calculated by multiplying the individual As concentration in each species with the average amount of fish and shellfish consumed by the public. The total intake of inorganic As was obtained by summing the products for all five aquaculture species. Thus, the total daily intake of inorganic As (DI) can be calculated as follows:

$$DI = \sum_{i=1}^{5} IR_i \cdot C_{inorg,i} = \sum_{i=1}^{5} (IR_{w,i} \cdot \alpha_i)[C_{f_i} \cdot \beta_i(1 - w_i)] \quad (1)$$

where DI is the total daily intake of inorganic As (μg/day); IR_i is the estimated individual ingestion rate of fish and shellfish (g/day); the subscript i = 1–5 corresponding to tilapia, milkfish, mullet, oysters and clams, respectively; $C_{inorg,i}$ is the concentration of inorganic As in i fish or shellfish (μg/g wet wt). $IR_{w,i}$ is the estimated individual ingestion amount of i fish or shellfish (g/day); α_i is the ratio of the edible weight to total weight of i fish or shellfish; C_{f_i} is the As concentration in the i fish or shellfish (μg/g wet wt); β_i is the ratio of the inorganic As content to the total As content in the i fish or shellfish; and ω_i is the water content in the i fish and shellfish. The average water content in the fish or shellfish sample is utilized to convert the dry weight. The total consumption amount of fish and shellfish was obtained from the Taiwanese Food Supply and Demand Annual Report of 2008 [22]. The Taiwanese population over the age of four years old was 21.55 million in 2008 [32]. IR_w was obtained by dividing the total amount consumed by the total Taiwanese population.

The distributions of $C_{inorg,i}$ follow log-normal distributions as identified by a Kolmogorov–Smirnov (K–S) test. Owing to sparsely measured data in the organism experiments of the aquatic species, the MC technique was then employed to characterize uncertainty based on the log-normal distribution of inorganic As content in fish and shellfish. Probabilistic analyses of the daily consumer intake corresponding to the 50th and 95th percentiles were conducted. The Risk (version 4.5, Professional Edition, Palisade Corp.) software was used to analyze statistically the measured data and to carry out MC simulation.

2.4. Provisional tolerable daily intake (PTDI) of fish and shellfish

The FAO/WHO Joint Expert Committee on Food Additives (JECFA) set the provisional tolerable weekly intake (PTWI) for inorganic As at 15 μg/kg of body weight per week [33]. The PTWI can be translated to the value of 127.3 μg/day for an average 59.4 kg Taiwanese adult.

WHO reported that food is generally the principal contributor to the daily intake of total As in non-occupationally exposed individuals and fish is the main source of As in the diet [34]. Schoof et al. [35,36] and Ysart et al. [37] also pointed out that the intake of As from fish and shellfish contributes over 90% of the total dietary As intake. Background information about community public health was provided by the Nutrition and Health Surveys in Taiwan (NAHSIT) conducted by the Bureau of Food Hygiene, Department of Health (DOH) from 1993 to 1996. The five aquatic species are in the list of 100 types of seafood surveys by the NAHSIT [38]. For general Taiwanese, the consumption behavior is diversified and the five fish and shellfish comprise a small portion of seafood sources. Therefore, we used a weight ratio of 1/20 (the five fish and shellfish to the 100 surveyed seafood) to estimate the daily intake of inorganic As from the five fish and shellfish produced in the BFD areas. Multiplying the weight ratio of 1/20 with the provisional tolerable daily intake of inorganic As (127.3 μg/day) set by the FAO/WHO [33] yields approximately 6.37 μg/day. The value of 6.37 μg/day was adopted as the provisional tolerable daily intake (*PTDI*) of five fish and shellfish produced from the BFD areas for general public in Taiwan. The *PTDI* is expressed as follows.

$$PTDI = \sum_{i=1}^{5} PTIR_i \times C_{inorg,i} = 6.37, \tag{2}$$

where $PTIR_i$ is the provisional tolerable ingestion rate of i fish or shellfish (g/day) and 6.37 μg/day denotes provisional tolerable daily intake of inorganic As from fish and shellfish (*PTDI*) for general public in Taiwan.

2.5. Potential health risks

The US EPA Region III Risk-Based Concentration Table [31] supports a method for estimating the target cancer risk (TR). The risk of the carcinogenic effects of inorganic As is expressed as exceeding the probability of contracting the cancer over a lifetime of 70 years. A model for estimating the target cancer risks (lifetime cancer risks) is,

$$TR = \frac{EFr \times EDtot \times IR \times C_{inorg} \times CPSo}{BWa \times ATc} \times 10^{-3} \tag{3}$$

where *TR* represents the target cancer risk or the risk of cancer over a lifetime; *EFr* is the exposure frequency (350 days/year) [31]; *EDtot* is the exposure duration (30 years) [31]; *IR* is the estimated individual ingestion rate of fish and shellfish (g/day wet wt); C_{inorg} is the concentration of inorganic As in fish and shellfish (μg/g wet wt); *CPSo* is the oral carcinogenic potency slope of inorganic As (risk per mg/kg/day) (1.5(mg/kg/day)$^{-1}$) [31]; *BWa* is the body weight of a Taiwanese adult (59.4 kg) [32]. An averaging time of 365 days/year for 76 years (ATc = 76 × 365 days) is used to characterize the lifetime exposure of a Taiwanese in calculation of the cancer risk [39].

2.6. Evaluation of the risk-based ingestion rate (RBIR)

Risk assessment is the process that evaluates the potential health effects from doses to humans of one contaminant received through one or more exposure pathways. The dose of one contaminant is estimated by assuming daily ingestion rates. We evaluate the risk-based ingestion rate (*RBIR*, g/day) of inorganic As contained fish and shellfish, based on the inorganic As level in fish and shellfish and the acceptable values for TR, using Eq. (4),

$$RBIR = \frac{TR \times BWa \times ATc}{EFr \times EDtot \times C_{inorg} \times CPSo} \times 10^{3} \tag{4}$$

where *RBIR* represents the risk-based ingestion rate in fish and shellfish (g/day). Values of *TR*, *BWa*, *ATc*, *EFr*, *EDtot*, C_{inorg} and *CPSo* in Eq. (4) are the same as those used in Eq. (3).

The acceptable consumption rate of fish and shellfish was evaluated from the BFD areas on the basis of acceptable lifetime risk and the estimation of the actual dietary intake of inorganic As which compared with their corresponding toxicological reference intakes, such as PTWI. The goal of most health actions is to ensure excess lifetime cancer risks do not exceed levels deemed "acceptable," typically 10^{-5} to 10^{-6} (although in some contexts, risks from individual sources as high as 1×10^{-4} may be permitted by regulatory agencies) [40]. By substituting all the parametric values as denoted in Section 2.5 of *BWa*, *ATc*, *EFr*, *EDtot*, C_{inorg} and *CPSo*, Eq. (4) was further simplified to

$$RBIR = \frac{TR}{C_{inorg}} \times 1.05 \times 10^{5} \tag{5}$$

For a given TR, Eq. (5) provides a quantitative relationship between RBIR and C_{inorg}. If the inorganic As in the fish and shellfish (C_{inorg}) is high, the ingestion rate (RBIR) should decrease accordingly to comply with the acceptable health risk (*TR*) and vice versa. By applying Eq. (5) we can manage the health risk associated with ingestion of seafood from BFD areas.

3. Results and discussion

3.1. As contents in fish and shellfish

The inorganic As contents for the five aquaculture species follow a log-normal distribution as determined by performing a K–S test. Geometric averages and geometric standard deviations of inorganic As in tilapia, milkfish, mullet, oysters and clams are obtained from the log-normal distributions (Table 1). Based on the observed data, ten thousand sets of inorganic As concentration were generated by MC simulation to quantify the uncertainty of the evaluated parameters. The simulation results show that the inorganic As contents in five aquaculture species are generally predicted to fall within the range from the 5th to 95th percentiles. The distribution of inorganic As concentration in clams is more skewed with a long tail at higher concentrations. In the 50th percentile, the highest and lowest inorganic As contents are in clam (0.83 μg/g wet wt) and in tilapia (0.03 μg/g wet wt), while in the 95th percentile, the highest and lowest inorganic As contents are in clam (3.44 μg/g wet wt) and in mullet (0.1 μg/g wet wt), respectively (Table 1).

The mean ratios for inorganic As content to total As content in tilapia, milkfish, mullet, oysters and clams range from 1.51% to 44.1%, with As content in milkfish being especially high (44.1%) (Table 2). It has been assumed in several previous studies that inorganic As comprises about 5–10% of the total As in seafood [41–45]. Other studies suggest that the proportion of inorganic As in fish and marine animals is generally low, less than 1–4% of the total As [41,46]. Munoz et al. reported the ratio ranging from 0.02% to 11% [47]. The widely varied ratios of inorganic As content to total As content in seafood reported in this study exceed data reported

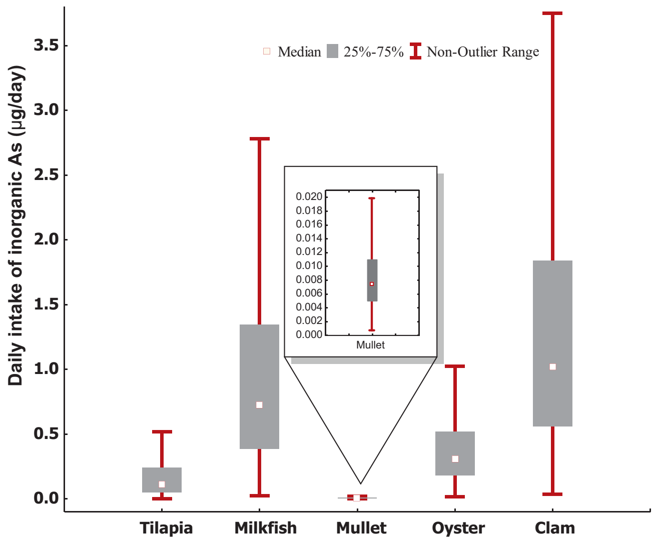

Fig. 2. Distributions of daily intake of inorganic As of fish and shellfish by a box and whiskers plot in the BFD areas.

in previous studies. Arbitrarily assume some ratio of inorganic As to total As may lead to significant error and further invalidate the health risk assessment.

3.2. Daily inorganic As intakes via fish and shellfish

On the basis of the fish and seafood consumption, the total daily intake (*DI*) associated with inorganic As is expressed using Eq. (1) as probability distribution to account the uncertainty. Fig. 2 illustrates the distributions of daily intake of inorganic As from the five major aquaculture species by a box-and-whiskers plot. In the 95th and 50th percentiles of daily intake, clams contribute the highest percentages to the total intake of inorganic As: 46% and 47%, respectively. The second highest contribution is from milkfish (33–35%) and the lowest one is from mullet (<1%). The total daily intakes of inorganic As from the five aquaculture species are 2.17 and 9.22 μg/day for the 50th and 95th percentiles, respectively. Notably, the distributions of daily inorganic As intake varied widely in both clams and milkfish (Fig. 2). These total daily intakes of inorganic As (*DI*) of the five aquaculture species were used to compare with the value of 6.37 μg/day, the provisional tolerable daily intake for fish and shellfish (*PTDI*). The 50th percentile (2.17 μg/day) of the total *DI* is lower than the *PTDI*. Nevertheless, the 95th percentile (9.22 μg/day) of the total *DI* is higher than the *PTDI*, and is also higher than the 95th percentile of 6.2 μg/day reported by Yost et al. [48]. Related to the importance of the contribution of fish and shellfish to inorganic As intake, our results show large variation in the inorganic As content among the five investigated aquaculture species. A single value used for all seafood may lead to significant errors in estimating potential health risks. The NAHSIT recently investigated the contribution of various food groups, including fish and shellfish to the total food in the Taiwanese diet, but it did not consider the inorganic As uptake. This study estimated the *PTDI* to illustrate the potential impact of the variation of intake level of inorganic As on human health.

According to the 1997 UK Total Diet Study, the greatest portion of As due to dietary exposure (94% of the total As) comes from the fish group. The fish group also had the highest mean As concentration (4.4 mg/kg) [37]. Delgado-Andrade et al. reported total As mean concentrations in fish and seafood of 2.72, 1.06, and 61.0 μg/g per fresh weight of fish, mollusks, and cephalopods, respectively [49]. Falcó et al. reported mean As concentrations ranging from 1.12 μg/g to 16.6 μg/g of fresh weight for 14 species of fish and shellfish, giving an intake of As in the range of 0.12–65 μg/day [4]. The probabilistic risk approach of this study for the estimation of dietary intake of inorganic As provides a wider range corresponding to various dietary intake of inorganic As, which is more robust.

Table 3
Statistical results of different percentiles *TR* for ingestion of fish and shellfish farmed in the BFD areas.

Species	Percentiles of risks ($\times 10^{-6}$)				
	95th	75th	50th	25th	5th
Tilapia	6.55	2.28	1.08	0.50	0.18
Milkfish	30.57	12.79	6.87	3.68	1.56
Mullet	0.19	0.10	0.07	0.05	0.03
Oyster	10.3	4.94	2.93	1.75	0.85
Clam	40.09	17.49	9.67	5.35	2.35
Cumulative risks	87.70	37.60	20.62	11.33	4.97

3.3. Carcinogenic risks assessment

The TRs for various levels of percentile are estimated for the different aquaculture species to facilitate the assessment of the potential health risks due to the above intake (Table 3). The TRs for clams and milkfish all exceed 10^{-6}. The TR values are significantly higher for calms than for the other aquaculture species in all percentiles. Milkfish has the second highest TRs for all percentiles while mullet has the lowest TR in all percentiles (all less than one millionth). The cumulative risks from five aquaculture species show cancer risks in the range of 10^{-6} to 10^{-4}. Toxicologically, this indicates that ingesting some aquaculture species every day for a lifetime at higher ingestion rates might be harmful to human health.

3.4. Risk-based management of scheme

The 50th percentile RBIR calculated by Eq. (4) based on $TR = 10^{-5}$ of tilapia, milkfish, mullet, oyster and clam are 37.5, 5.1, 27.7, 8.5 and 1.3 g/day, respectively. The *RBIR* of tilapia and mullet are higher than the average Taiwanese ingestion rates, while the *RBIR* of milkfish and clam are far lower than the average Taiwanese ingestion rates (see Table 2). The *RBIR* of oyster is close to the average Taiwanese ingestion rate. Based on the current Taiwanese seafood consumption behavior, the ingestion of tilapia and mullet pose less threat to human health than the ingestion of milkfish and clam. We herein adopt the revised value of 6.37 μg/day for provisional tolerable daily intake (*PTDI*) of inorganic As from five aquaculture species and incorporate with the target cancer risk method to determine the acceptable consumption rate of fish and shellfish for general public in Taiwan. We used Eq. (3) to evaluate the maximum acceptable risk of 6.07×10^{-5}. We then calculated the cumulative risk based on the estimated daily ingestion rate. The 5th, 25th, 50th, 75th and 95th percentiles of risks are 4.97×10^{-6}, 1.13×10^{-5}, 2.06×10^{-5}, 3.76×10^{-5} and 8.77×10^{-5}, respectively. The 5th to 75th percentile risks of daily ingestion rate of fish and shellfish are within the risk of *PTDI*. However, the 95th percentile risk of 8.77×10^{-5} is higher than the maximum acceptable risk of 6.07×10^{-5}. The risk level is closely related to the inorganic As content in fish and shellfish and the *IR*. We can construct a risk diagram using C_{inorg} as the abscissa and *IR* as the ordinate (Fig. 3). The risk diagram graphically illustrates the relationship of C_{inorg} versus *IR*. The two curves of $PTIR \times C_{inorg} = 6.37$ μg/day and $PTIR \times C_{inorg} = 1.05$ μg/day, corresponding to risks of 6.07×10^{-5} and 1×10^{-5}, respectively, were plotted in Fig. 3. A range of 10^{-4} to 10^{-6} is typically considered as an acceptable risk to consumers via seafood ingestion [50,51]. Because this study combines five different seafood species, the cancer risk of 1×10^{-4} to 1×10^{-5}

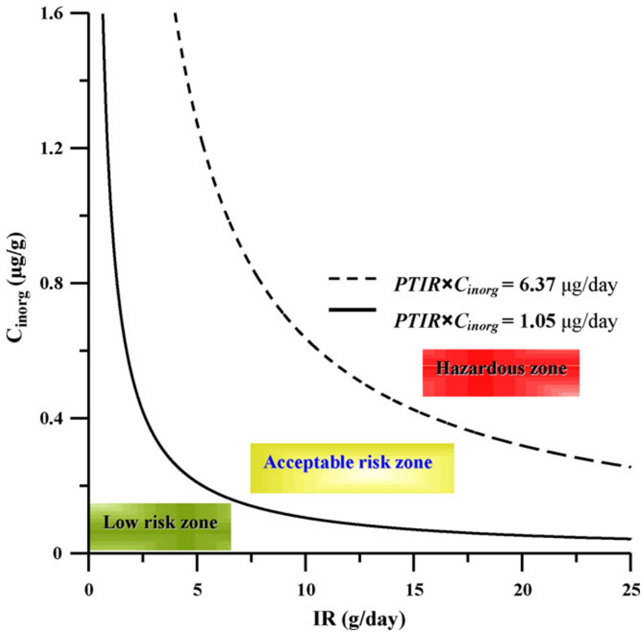

Fig. 3. Two dimensional risk diagram for the determination of acceptable consumption rates. The two curves of $PTIR \times C_{inorg} = 6.37$ μg/day and $PTIR \times C_{inorg} = 1.05$ μg/day, corresponding to risks of 6.07×10^{-5} and 1×10^{-5}, respectively. Low risk, acceptable risk, hazardous zones are delineated by two curves where the dotted line denotes $TR = 6.07 \times 10^{-5}$ and the solid line denotes $TR = 1 \times 10^{-5}$, respectively.

is adopted to determine the acceptable consumption rate of fish and shellfish. The plotted two curves were used to delineate three zones – the low risk zone, the acceptable risk zone and the hazardous zone. The low risk zone (i.e. risk below 1×10^{-5}) denotes that the intake of inorganic As is less than 1.05 μg/day, indicating no threat to human health. Moreover, nutritional and inorganic As intakes should be balanced when evaluate the acceptable consumption rate of fish and shellfish. If the low risk zone is used to define the acceptable consumption rate of fish and shellfish, the corresponding recommended daily ingestion rate of fish and shellfish is too strict to consumers. To rationally manage the nutrition benefits and health risk of seafood consumption, this study suggests that the consumption rate of fish and shellfish can be loosely moved to the acceptable risk zone. The acceptable risk zone, bounded by two curves, $PTIR \times C_{inorg} = 6.37$ μg/day and $PTIR \times C_{inorg} = 1.05$ μg/day, denotes a risk range from 1×10^{-5} to 6.07×10^{-5}, and the intake of inorganic As from fish and shellfish honors the *PTDI* (6.37 μg/day). The total *DI* (2.17 μg/day) in the 50th percentile is within the acceptable risk zone, while the total *DI* (9.22 μg/day) of the 95th percentile falls to the hazardous zone. The hazardous zone implies that the health risk exceeds 6.07×10^{-5} corresponding to an intake of inorganic As higher than the *PTDI* (6.37 μg/day). To protect general public health, seafood consumption rates fall to the hazardous zone should be avoided.

The acceptable risk zone (with risk ranging from 1×10^{-5} to 6.07×10^{-5}) is recommended as the seafood ingestion rate for protecting general public health in Taiwan. Moreover, the two dimensional consumption risk diagram offers a convenient way to determine rational levels of consumption rate of seafood produced from As-contaminated BFD areas.

4. Conclusions

Ingesting fish and shellfish produced in As-contaminated farm regions is a major source of background exposure to inorganic As. To balance the health benefits of fish consumption and the risk of over-ingesting fish and shellfish produced from As-contaminated BFD areas, we use a probabilistic-risk method supported by USEPA and the provision tolerable weekly intake of arsenic set by FAO/WHO to define acceptable consumption rates of fish and shellfish based upon the published data for general public. The intakes of inorganic As were defined and illustrated by a two dimensional graphical model. According to the relationship between C_{inorg} and *IR* derived from this study, two risk-based curves were constructed. An acceptable risk zone is determined (risk ranging from 1×10^{-5} to 6.07×10^{-5}) which is recommended as the acceptable consumption rates of fish and shellfish for general public. Translate to lay language, the general Taiwanese is advised to eat more tilapia and mullet, eat less milkfish and clam, and maintain the current ingestion habit for oyster. From a human health perspective, this study integrates dietary information related to the ingestion of five fish and shellfish produced from As-contaminated BFD areas and determines the acceptable seafood consumption for the alleviation of general public concerns.

Acknowledgements

The authors would like to thank the National Science Council of Taiwan ROC for financially supporting this work under Contract nos. NSC-95-2313-B-002-050-MY3 and NSC-96-2313-B-242-001.

References

[1] I.A.R.C., Monographs on the Evaluation of Carcinogenic Risks to Humans: Some Drinking-water Disinfectants and Contaminants, Including Arsenic, vol. 84, International Agency for Research on Cancer, Lyon, France, 2002, http://monographs.iarc.fr/htdocs/announcements/.

[2] W.H. Yu, C.M. Harvey, C.F. Harvey, Arsenic in groundwater in Bangladesh: a geostatistical and epidemiological framework for evaluating health effects and potential remedies, Water Resour. Res. 39 (2003) 1146, doi:10.1029/2002WR001327.

[3] R. Martí-Cid, A. Bocio, J.M. Llobet, J.L. Domingo, Intake of chemical contaminants through fish and seafood consumption by children of Catalonia, Spain: health risks, Food Chem. Toxicol. 45 (2007) 1968–1974.

[4] G. Falcó, J.M. Llobet, A. Bocio, J.L. Domingo, Daily intake of arsenic, cadmium, mercury, and lead by consumption of edible marine species, J. Agric. Food Chem. 54 (2006) 6106–6112.

[5] C.M. Liao, B.C. Chen, S. Singh, M.C. Lin, B.C. Han, Acute toxicity and bioaccumulation of arsenic in tilapia *Oreochromis mossambicus* from blackfoot disease area in Taiwan, Environ. Toxicol. 18 (2003) 252–259.

[6] J.K. Lin, H.C. Chiang, Arsenic Concentration in Drinking Well Water in Lanyang Area and Its Preliminary Health Risk Assessment, National Science Council, ROC, Taipei, Taiwan, 2002 (NSC-90-2218-E-238-003).

[7] C.P. Liang, C.S. Jang, C.W. Liu, K.H. Lin, M.C. Lin, An integrated GIS-based approach in assessing carcinogenic risks via food-chain exposure in arsenic-affected groundwater areas, Environ. Toxicol. 25 (2010) 113–123, doi:10.1002/tox.20481.

[8] B.C. Chen, W.C. Chou, W.Y. Chen, C.M. Liao, Assessing the cancer risks associated with arsenic-contaminated seafood, J. Hazard. Mater. 181 (2010) 161–169, doi:10.1016/jjhadmat.2010.0.4.112.

[9] C.M. Liao, M.P. Ling, Assessment of human health risks for arsenic bioaccumulation in tilapia (*Oreochromis mossambicus*) and large-scale mullet (*Liza macrolepis*) from blackfoot disease area in Taiwan, Arch. Environ. Contam. Toxicol. 45 (2003) 264–272.

[10] C.S. Jang, C.W. Liu, K.H. Lin, F.M. Huang, S.W. Wang, Spatial analysis of potential carcinogenic risks associated with ingesting arsenic in aquacultural tilapia (*Oreochromis Mossambicus*) in blackfoot disease hyperendemic areas, Environ. Sci. Technol. 40 (2006) 1707–1713.

[11] C.S. Jang, K.H. Lin, C.W. Liu, M.C. Lin, Risk-based assessment of arsenic-affected aquacultural water in blackfoot disease hyperendemic areas, Stoch, Environ. Res. Risk Assess. 23 (2009) 603–612, doi:10.1007/s00477-008-0245-3.

[12] C.W. Liu, F.M. Huang, Y.M. Hsueh, Revised cancer risk assessment of inorganic arsenic upon consumption of tilapia (*Oreochromis mossambicus*) from blackfoot disease hyperendemic areas, Bull. Environ. Contam. Toxicol. 74 (2005) 1037–1044.

[13] C.W. Liu, C.P. Liang, F.M. Huang, Y.M. Hsueh, Assessing the human health risks from exposure of inorganic arsenic through oyster (*Crassostrea gigas*) consumption in Taiwan, Sci. Total Environ. 361 (2006) 57–66.

[14] C.W. Liu, C.P. Liang, K.H. Lin, C.S. Jang, S.W. Wang, Y.K. Huang, Y.M. Hsueh, Bioaccumulation of arsenic compounds in aquacultural clams (*Meretrix lusoria*) and assessment of potential carcinogenic risks to human health by ingestion, Chemosphere 69 (2007) 128–134.

[15] C.W. Liu, Y.K. Huang, Y.M. Hsueh, K.H. Lin, C.S. Jang, L.P. Huang, Spatiotemporal distribution of arsenic species of oysters (*Crassostrea gigas*) in the coastal area of southwestern Taiwan, Environ. Monit. Assess. 138 (2008) 181–190.
[16] M.C. Lin, C.M. Liao, Assessing the risks on human health associated with inorganic arsenic intake from groundwater-cultured milkfish in southwestern Taiwan, Food Chem. Toxicol. 46 (2008) 701–709.
[17] C.W. Liu, K.H. Lin, C.S. Jang, Tissue accumulation of arsenic compounds in aquacultural and wild mullet (*Mugil Cephalus*), Bull. Environ. Contam. Toxicol. 77 (2006) 36–42.
[18] S.L. Chen, S.R. Dzeng, M.H. Yang, K.H. Chiu, G.M. Shieh, C.M. Wai, Arsenic species in groundwater of the blackfoot disease area, Taiwan, Environ. Sci. Technol. 28 (1994) 877–881.
[19] W.P. Tseng, Effects and dose–response relationships of skin cancer and blackfoot disease with arsenic, Environ. Health Perspect. 19 (1977) 109–119.
[20] I.C. Ch'i, R.Q. Blackwell, A controlled retrospective study of blackfoot disease, an endemic peripheral gangrene disease in Taiwan, Am. J. Epidemiol. 88 (1968) 7–24.
[21] D.J.H. Phillips, Arsenic in aquatic organisms: a review, emphasizing chemical speciation, Aquat. Toxicol. 16 (1990) 151–186.
[22] C.O.A., Taiwan Fisheries Yearbook, Council of Agriculture, Executive Yuan: Taiwan, 2008, http://www.fa.gov.tw/eng/index.php.
[23] F.A.O./W.H.O., Diet, nutrition and the prevention of chronic diseases. Report of a joint WHO/FAO expert consultation, Geneva, 2003.
[24] C. Cardoso, I. Farias, V. Costa, M. Nunes, L. Gordo, Estimation of risk assessment of some heavy metals intake through black scabbardfish (*Aphanopus carbo*) consumption in Portugal, Risk Anal. 30 (2010) 952–961, doi:10.1111/j.1539-6924.2010.01374.x.
[25] H.R. Guo, Cancer risk assessment for arsenic exposure through oyster consumption, Environ. Health Perspect. 110 (2002) 123–124.
[26] J. Burger, Fishing, fish consumption, and awareness about warnings in a university community in central New Jersey in 2007, and comparisons with 2004, Environ. Res. 108 (2008) 107–116.
[27] F. Gagnon, T. Tremblay, J. Rouette, J.F. Cartier, Chemical risks associated with consumption of shellfish harvested on the north shore of the St. Lawrence River's lower estuary, Environ. Health Perspect. 112 (2004) 883–888.
[28] T.F.A., Annual Report of Fishery Agency in 2003 – Establishment of Geographical Information Systems in Aquacultural Fish, Taiwan Fishery Agency, Taipei, 2003, 47 pp.
[29] Y.K. Huang, K.H. Lin, H.W. Chen, C.C. Chang, C.W. Liu, M.H. Yang, Y.M. Hsueh, Arsenic species contents at aquacultural farm and in farmed mouthbreeder (*Oreochromis mossambicus*) in blackfoot disease hyperendemic areas, Food Chem. Toxicol. 41 (2003) 1491–1500.
[30] U.S.E.P.A., Special Report on Ingested Inorganic Arsenic: Skin Cancer; Nutritional Essentiality, EPA/625/3-87/013, U.S. Environmental Protection Agency, Risk Assessment Forum, Washington, DC, 1988.
[31] U.S.E.P.A., USEPA region III risk-based concentration table: technical background information, 2006, http://www.epa.gov/reg3hwmd/risk/human/rbc/rbc1006.pdf.
[32] D.O.H., Health and National Health Insurance Annual Statistics Information Service, Department of Health, Executive Yuan, Taiwan, 2008, http://www.doh.gov.tw/statistic/index.htm.
[33] F.A.O./W.H.O., Evaluation of certain Food Additives and Contaminants; Technical Report Series 837, World Health Organization, Geneva, Switzerland, 1993.
[34] W.H.O., Arsenic and arsenic compounds. Environmental Health Criteria 224, International Programme on Chemical Safety, World Health Organization, Geneva, 2001.
[35] R.A. Schoof, J. Eickhoff, L.J. Yost, D.W. Cragin, D.M. Meacher, D.B. Menzel, Dietary exposure to inorganic arsenic, in: W.R. Chappell, C.O. Abernathy, R.L. Calderon (Eds.), Arsenic Exposure and Health Effects, Elsevier, Amsterdam, 1999, pp. 81–88.
[36] R.A. Schoof, L.J. Yost, J. Eickhoff, E.A. Crecelius, D.W. Cragin, D.M. Meacher, D.B. Menzel, A market basket survey of inorganic arsenic food, Food Chem. Toxicol. 37 (1999) 839–846.
[37] G. Ysart, P. Miller, M. Croasdale, H. Crews, P. Robb, M. Baxter, C. L'Argy, N. Harrison, 1997 UK total diet study-dietary exposures to aluminum, arsenic, cadmium, chromium, copper, lead, mercury, nickel, selenium, tin and zinc, Food Addit. Contam. 17 (2000) 775–786.
[38] D.O.H., Nutrition and Health Survey in Taiwan, NAHSIT 1993–1996, Department of Health, Executive Yuan, Taiwan, 1999.
[39] D.O.S., MOI Statistical Information Service, Department of Statistical, Ministry of the Interior, Taiwan, 2008, http://www.moi.gov.tw/stat.
[40] B.L. Harper, S.G. Harris, A possible approach for setting a mercury risk-based action level based on tribal fish ingestion rates, Environ. Res. 107 (2008) 60–68.
[41] J.S. Edmonds, K.A. Francesconi, Arsenic in seafoods: human health aspects and regulations, Mar. Pollut. Bull. 26 (1993) 665–674.
[42] D.L. Macintosh, J.D. Spenglet, H. Ozkaynak, L.H. Tsai, P.B. Ryan, Dietary exposure to selected metals and pesticides, Environ. Health Perspect. 104 (1996) 202–209.
[43] B.C. Han, W.L. Jeng, R.Y. Chen, G.T. Fang, T.C. Hung, R.J. Tseng, Estimation of target hazard quotients and potential health risks for metals by consumption of seafood in Taiwan, Arch. Environ. Contam. Toxicol. 35 (1998) 711–720.
[44] M.C. Lin, H.Y. Lin, H.H. Cheng, Y.C. Chen, C.M. Liao, K.T. Shao, Risk assessment of arsenic exposure from consumption of cultured milkfish, *Chanos chanos* (Forsskål), from the arsenic-contaminated area in southwestern Taiwan, Bull. Environ. Contam. Toxicol. 75 (2005) 637–644.
[45] H.T. Lin, S.W. Chen, C.J. Shen, C. Chu, Arsenic speciation in fish on the market, J. Food Drug Anal. 16 (2008) 70–75.
[46] N.R.C., Arsenic in Drinking Water, National Academy Press, National Research Council, Washington, DC, 1999.
[47] O. Munoz, V. Devesa, M.A. Suner, D. Velez, R. Montoro, I. Urieta, M.L. Macho, M. Jalon, Total and inorganic arsenic in fresh and processed fish products, J. Agric. Food Chem. 48 (2000) 4369–4376.
[48] L.J. Yost, S.H. Tao, S.K. Egan, L.M. Barraj, K.M. Smith, J.S. Tsuji, Y.W. Lowney, R.A. Schoof, N.J. Rachamn, Estimation of dietary intake of inorganic arsenic in U.S. children, Human Ecol. Risk Assess. 10 (2004) 473–483.
[49] C. Delgado-Andrade, M. Navarro, H. López, M.C. López, Determination of total arsenic levels by hydride generation atomic absorption spectrometry in foods from south-east Spain: estimation of daily dietary intake, Food Addit. Contam. 20 (2003) 923–932.
[50] T.C. Benner, Brief survey of EPA standard-setting and health assessment, Environ. Sci. Technol. 38 (2004) 3457–3464.
[51] N.K. Karouna-Renier, R.A. Snyder, J.G. Allison, M.G. Wagner, K.R. Rao, Accumulation of organic and inorganic contaminants in shellfish collected in estuarine waters near Pensacola, Florida: contamination profiles and risks to human consumers, Environ. Pollut. 145 (2007) 474–488.