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Perfluorinated Compounds in Human Blood, Water, Edible Freshwater Fish, and Seafood in China: Daily Intake and Regional Differences in Human Exposures

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Supporting Information

ABSTRACT: Despite the growing public interest in perfluorinated compounds (PFCs), very few studies have reported the sources and pathways of human exposure to these compounds in China. In this study, concentrations of 10 PFCs were measured in human blood, water (tap water and surface water), freshwater fish, and seafood samples collected from China. On the basis of the data, we calculated daily intakes of PFCs, regional differences in human exposures, and potential risks associated with ingestion of PFCs from diet, drinking water, and indoor dust for the Chinese population. Perfluorooctane sulfonate (PFOS) was the most predominant PFC found with a mean concentration of 12.5 ng/mL in human blood from Tianjin and 0.92 ng/g wet wt in freshwater fish and seafood; perfluorooctanoic acid (PFOA) was the major PFC found in drinking water at a concentration range of 0.10 to 0.92 ng/L. The estimated daily intake of PFOS and PFOA via fish and seafood consumption ($EDI_{fish\&seafood}$) ranged from 0.10 to 2.51 and 0.13 to 0.38 ng/kg bw/day, respectively, for different age groups (i.e., toddlers, adolescents and children, and adults) from selected locations (i.e., Tianjin, Nanchang, Wuhan, and Shenyang). The $EDI_{fish\&seafood}$ of PFCs decreased ($p < 0.05$) with age. The estimated daily intake of PFOS and PFOA via drinking water consumption ($EDI_{drinking\ water}$) ranged from 0.006 to 0.014 and 0.010 to 0.159 ng/kg bw/day, respectively. Comparison of $EDI_{fish\&seafood}$ and $EDI_{drinking\ water}$ values with those of the modeled total dietary intake (TDI) of PFCs by adults from Tianjin, Nanchang, Wuhan, and Shenyang showed that contributions of fish and seafood to TDI of PFOS varied depending on the location. Fish and seafood accounted for 7%, 24%, 80%, and 84% of PFOS intake in Nanchang, Shenyang, Wuhan, and Tianjin, respectively, suggesting regional differences in human exposure to PFOS. Drinking water was a minor source of PFOS (<1%) exposure in adults from all the study locations.

KEYWORDS: perfluorinated compounds, human blood, tap water, freshwater fish, seafood, regional difference, human exposure

INTRODUCTION

Perfluorinated compounds (PFCs) are a class of man-made chemicals that are widely used in industrial and consumer products including protective coatings for fabrics and carpets, paper coatings, paints, cosmetics, and fire-fighting foams.[1] As a consequence, PFCs are widespread in humans[2−9] and animals.[1,10,11] Potential sources of human exposures include indoor dust,[12−14] diet,[15−18] and drinking water.[19] Human exposure to PFCs is of concern because studies have found that perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA), the two most commonly studied PFCs, elicit hepatotoxicity, developmental toxicity, and immunotoxicity in laboratory animals.[20] On the basis of mounting concern over potential adverse effects of PFCs, the United States Environmental Protection Agency established a provisional reference dose for PFOS and PFOA in drinking water.[21] Moreover, PFOS has been listed as a persistent organic pollutant (POP) under the Stockholm Convention since May 2009.

To date, sources of human exposures to PFCs have not yet been fully characterized, although exposures via dust and diet have been suggested as the primary routes.[12−18] Few studies have suggested that drinking water can be a source of exposure to PFCs for Chinese people;[19,22] the drinking water samples analyzed in those studies[19,22] were collected prior to 2008. Therefore, a timely study on PFCs in tap water is needed due to the rapid development of PFC-related industries in China.

Fish and seafood generally contain measurable levels of PFCs,[15,17,23] and therefore, parallel to other routes of exposure, monitoring of PFCs in fish and seafood is important. Previous studies have shown that fish and seafood accounted for >50% of PFOS exposures in nonoccupationally exposed populations in

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Canada,[3] Spain,[15] and Poland.[10] Further, consumption of fish and seafood has been associated with high levels of PFCs in human blood.[3,10,17] Little is known on PFC levels in fish and seafood from China, and the sampling locations in previous studies were limited;[23,24] furthermore, China is the largest producer and exporter of fishery products in the world. Systematic assessment of human exposure to PFCs via fish and seafood consumption is critical for characterizing exposures and potential health risks to Chinese people.

However, a few studies from Norway[25] and the UK[26] indicated that consumption of fish and seafood is a minor source of PFC exposures (5%−19%). PFC levels in fish and marine products vary by sampling location. PFOS concentrations ranged from 15 to 90 ng/g wet wt in carp and from 25 to 5150 ng/g wet wt in the fillet of fish from the Mississippi River;[27,28] a much lower concentration of PFOS was found in fish fillets from Europe[26,27] and China.[23] Given these regional differences in concentrations of PFOS in fish and seafood, characterization of human exposures to PFOS and other PFCs via fish and seafood consumption should ideally be based on region-specific data. In our earlier study,[14] we assessed human exposure pathways of PFCs for Chinese adults; the results suggested that fish and seafood consumption are a major source of PFOS and that drinking water is a minor source of PFOS and PFOA. However, China is the third largest country in the world. The type of industry, level of development, dietary habit, and population are different depending on the location (for instance, seafood consumption rate can vary greatly depending on coastal and inland regions). This study was aimed at elucidating regional differences in sources of human exposure to PFOS in China.

In this study, we determined concentrations of 10 PFCs in human blood, tap water, surface water, freshwater fish, and seafood collected from 13 cities in 11 provinces and municipalities of China. We estimated the daily intake of PFCs and potential health risks associated with drinking water, fish, and seafood consumption. Further, we analyzed the sources of PFCs in human blood, surface water, and freshwater fish, based on the composition profiles of PFCs found in these matrixes. Finally, we explored regional differences in human exposures to PFOS for Chinese adults by using PFC levels measured in human blood, tap water, fish, and seafood. To our knowledge, this is the first study to document regional differences in human exposure to PFCs.

MATERIALS AND METHODS

Human blood, fish, and seafood samples were extracted by the ion-pair extraction method as described earlier;[9,14] water samples were extracted using an Oasis WAX extraction cartridge.[28] Concentrations of 10 PFCs were determined with a Waters Alliance 2695 high performance liquid chromatograph (HPLC) equipped with a Quattro Micro atmospheric pressure ionization (API) triple quadrupole mass spectrometer (MS/MS). Details regarding reagents and chemicals, sample extraction, instrumental analysis, blanks, and matrix spikes are given in the Supporting Information.

Sample Collection and Preparation. *Human Blood.* A total of 50 whole blood samples were collected from February to April, 2009 from Tianjin, China. These blood samples were collected (2 mL) as part of a routine clinical test or for heavy metal (e.g., lead) analysis. The residual sample was left after the clinical test was used for PFC analysis. All the samples were obtained from residents aged from 18 to 70 yrs. The overall age distribution was 20% for each age group (i.e., 18−30, 30−40, 40−50, 50−60, and 60−70 yrs), and 50% of the participants were female. The detailed demographic information including sample size, age, and gender are shown in Table S1 (Supporting Information). All human blood samples were stored at −20 °C in polypropylene (PP) tubes before analysis. The sampling locations are shown in Figure S1a (Supporting Information). The blood collection was approved by the Institutional Review Board (IRB) of Nankai University, China.

Freshwater Fish and Seafood. Thirteen freshwater fish and marine species were selected based on the fish-consumption patterns in China; these include six freshwater fish, i.e., crucian carp (*Carassius auratus*), common carp (*Cyprinus carpio*), grass carp (*Ctenopharyngodon idellus*), silver carp (*Hypophthalmichthys molitrix*), northern snakehead fish (*Channa argus*), and catfish (*Siluriformes*); and seven marine species, i.e., yellow croaker (*Pseudosciaena polyactis*), hairtail (*Trichiurus lepturus Linnaeus*), greasyback shrimp (*Metapenaeus ensis*), swimming crab (*Portunus Trituberctus*), oyster (*ostrea*), squid (*Teuthida*), and mentis shrimp (*Oratosquilla oratoria*). During February to April of 2010, 72 fish and seafood composite or individual samples were randomly purchased from local markets and large supermarkets from 13 cities in 11 provinces and municipalities in China. The sampling locations represent northeastern, northern, southwestern, central, and eastern regions of China and include two major PFC-related industrial cities (Wuhan and Shenyang) and an important coastal city (Tianjin located along Bohai Bay). The sampling locations are shown in Figure S1b (Supporting Information). To ensure the representativeness of samples, 5−10 individuals of each species collected from different markets were composited into a single sample for Tianjin (12 species), Shenyang (9 species), and Nanchang (10 species); 5 composite samples (one species per sample) and 6 individuals of crucian carp collected in Wuhan were analyzed. The samples (n = 30) collected in other cities were individual samples. All analyzed samples represent 232 fish and seafood specimens. Detailed information on the samples is presented in Table S2 (Supporting Information). Only edible portions of fish and seafood were chosen for analysis. Composite samples were prepared by mixing 10 g of filleted muscle from each individual; the samples were freeze-dried, homogenized, and ground into a fine powder. The moisture content of the samples was recorded to enable reporting of PFC concentration on a wet weight basis (ng/g wet wt). All dried fish and seafood samples were stored at −20 °C in PP tubes before analysis.

Water. Tap water samples were collected from Tianjin, Shenyang, and Nanchang in May 2011; each sample was pooled from 5 individual samples obtained from a different administrative district of each city. One pooled surface water sample was collected from the major water body of Nanchang (The Gan River); this sample was pooled from 3 individual samples collected from the same monitoring station at 8:00 a.m., 1:00 p.m., and 7:00 p.m. in one day. The concentrations of PFCs in surface water from Tianjin and Shenyang were reported in our earlier studies;[28,29] the PFC levels in tap water and surface water from Wuhan have been previously studied.[19,30] All water samples were stored at −20 °C in PP container before analysis.

Daily Intake Calculations and Dietary Survey. The daily intake of PFCs via fish and seafood consumption ($EDI_{fish\&seafood}$) was calculated for different age groups (i.e., toddlers (2−5 yrs), children and adolescents (6−17 yrs), and adults (≥18 yrs)) through multiplication of the mean PFC concentrations in fish and seafood by the consumption rate reported in a previous survey in China.[31] Furthermore, a questionnaire-based daily consumption rate of fish and seafood by adults from Tianjin was conducted in the current study because this city was not included in the earlier dietary survey.[31] The mean estimated daily consumption amount (grams per person, fresh weight) of fish and seafood by adults from Tianjin (44.8 g/day) was higher than that reported for other Chinese cities (30.3 g/day).[31] The exposure dose of PFCs via drinking water (i.e., tap water) ($EDI_{drinking\ water}$) was estimated for the general population in Tianjin, Nanchang, Wuhan, and Shenyang; the drinking water consumption data were obtained

from a previous report.[32] Details regarding the daily intake calculation and dietary survey are shown in Table S3 (Supporting Information).

Regional Differences in Human Exposure to PFOS. Human exposure to PFOS via drinking water, fish, and seafood consumption has been reported;[3,15,19,22,25] however, these studies only focused on a specific area or country. Studies on the regional differences in human exposure to PFOS have not been conducted. In this study, we modeled the total dietary intake (TDI) of PFOS based on the blood concentrations for adults from four Chinese cities (including Tianjin, Nanchang, Wuhan, and Shenyang) and assessed regional characteristics of human exposure by comparing the $EDI_{fish\&seafood}$ and $EDI_{drinking\ water}$ to TDI. The reason for selecting these cities is because the representativeness of samples collected from these cities and Wuhan and Shenyang are the PFCs-related industrial cities in China.

In previous studies,[3,33−35] pharmacokinetic models were developed for the estimation of daily intake of POPs from biomonitoring data. Ritter et al.[35] established a multi-individual pharmacokinetic model and modeled the daily intake of POPs; however, this model may not be applicable to the Chinese population.[35] A simple one-compartment toxicokinetic model is considered only valid for steady-state conditions[3,34] of blood PFC levels. We assumed that steady-state conditions of PFOS levels exist in adults. The TDI of PFCs by adults was estimated based on the blood PFC concentrations using the following equation. The change in blood concentration (C_p) resulting from a given exposure dose (E) can be described by the following equation:

$$\frac{\Delta C_p}{\Delta t} = E - k \times V_d \times C_p$$

where V_d is the apparent volume of distribution (mL/kg), and k is the first-order rate constant for PFOS elimination per day = $0.693/t_{1/2}$, at steady-state conditions, where $\Delta C_p/\Delta t = 0$,

$$E = k \times V_d \times C_p$$

and

$$E = 0.693/t_{1/2} \times V_d \times C_p$$

For females, the total clearance was corrected by menstrual serum loss. As described by Harada et al.,[36] menstrual serum loss was assumed to be 42 mL/month or 0.025 mL/kg/day, assuming an average body weight of 60 kg.[37] For PFOS, median half-lives were 1661 days (4.55 yrs).[38] In accordance with Thompson et al.,[34] we used a volume distribution of 230 mL/kg for PFOS. This model is unavailable for PFOA and other PFCs;[3,14] therefore, regional difference in human exposure was only conducted for PFOS in this study.

Quality Assurance and Quality Control. Matrix−spike recoveries of individual PFCs through the analytical procedure were determined by the spiking of 10 target compounds into randomly selected samples from each matrix type (5.0 ng each; n = 3−5 for each type of sample) (Table S4, Supporting Information). Two internal standards (MPFOS and M8PFOA) were spiked (2.5 ng each) into all samples prior to extraction. Recoveries of PFCs spiked into sample matrixes ranged from 73 ± 14% (mean ± RSD) to 116 ± 10% for fish and seafood, from 84 ± 10% to 149 ± 16% for human blood, and from 82 ± 4% to 120 ± 2% for water. An exception was noted: perfluorobutane sulfonate (PFBS) recoveries were sometimes below 60%. However, PFBS was not detected in any of the samples analyzed, and the poor recoveries, therefore, did not affect the interpretation of the results. Method precision was good, with relative standard deviations (RSD) for 5 extractions of each sample type ranging from 3 to 20%, for all target compounds (except perfluoroundecanoic acid (PFUnDA) in fish and seafood, RSD = 27%). Recoveries of MPFOS and M8PFOA spiked into each sample type were 84 ± 18% and 100 ± 11% for fish and seafood, 77 ± 4% and 130 ± 17% for human blood, and 88 ± 7% and 100 ± 5% for water, respectively (Table S4, Supporting Information). Therefore, the reported concentrations were not corrected for the recoveries of the respective internal standards.

Quantification was performed using linear regression equations (r^2 > 0.99 for all analytes) generated from a ten-point calibration standard prepared in methanol at concentrations ranging from 0.1 to 100 ng/mL. Calibration standards were injected before and after the analysis of a batch of 20 samples, as a check for instrument response. Solvents, blood collection tubes, and method blanks (performance of the blanks are listed in the Supporting Information) were checked for the presence of target PFCs. Blanks contained PFOA at trace concentrations (mean: 0.12 ng/mL for blood, 0.11 ng/L for water, and 0.09 ng/g wet wt for fish and seafood) near the limitation of quantification (LOQ). Reported PFOA concentrations were subtracted from the highest PFOA level found in blanks. The LOQ was determined as the lowest concentration of PFC in the calibration curve, which was measured at a concentration within 70% to 130% of the theoretical concentrations. The LOQ for PFCs was 0.10 ng/mL for blood, 0.10 ng/L for water, and 0.10 ng/g wet wt for fish and seafood.

Statistical Analysis. All statistical tests were performed using the SPSS 17.0 statistical package. The gender-related differences in PFC levels in human blood were assessed using the Student's t test for normally distributed data and the Mann−Whitney U test for log-normally distributed data. The normality of the distribution was tested using a nonparametric test (Kolmogorov−Smironov Z). The differences in PFC levels in surface water and tap water were assessed using one-way ANOVA. Spearman's rank correlation was used to assess the relationships between age and PFC levels in human blood and between age and $EDI_{fish\&seafood}$. Concentrations below the LOQ were assigned half the value of the LOQ for statistical analysis.

RESULTS AND DISSCUSSION

PFCs in Human Blood. Mean and median concentrations of target PFCs in human blood from Tianjin are shown in Table 1. Of the 10 PFCs that were found above the LOQ with varying frequencies of detection in blood samples (Table 1), PFOS (100%), perfluorohexane sulfonate (PFHxS) (84%), PFOA (77%), PFUnDA (74%), perfluorononanoic acid (PFNA) (73%), and perfluorodecanoic acid (PFDA) (51%) were frequently found (>LOQ); perfluorohexanoic acid (PFHxA) and perfluoroheptanoic acid (PFHpA) were only detected in <40% of the blood samples at mean concentrations near LOQ; PFBS and perfluorododecanoic acid (PFDoDA) were not detected (<LOQ) in all blood samples. PFOS was detected at the highest mean concentration in human blood from Tianjin (12.5 ng/mL), followed by PFNA (0.50 ng/mL), PFOA (0.49 ng/mL), and PFHxS (0.34 ng/mL). The mean concentration of the sum of 10 PFCs for Tianjin subjects was 14.7 ng/mL, and the greatest contribution was from PFOS (85%).

The mean concentration of PFOA (0.49 ng/mL) in adult blood from Tianjin was lower than those reported for adults from other countries (1.70−6.20 ng/mL) (i.e., Australia, Canada, Norway, and Germany);[2,4,7,39] however, the blood PFOS level (12.5 ng/mL) in adults from Tianjin is similar to that reported in Germany,[39] Norway,[4] Canada,[2] and several Asian countries (9.10−16.0 ng/mL)[5] but less than that reported in Australia (20.5 ng/mL).[7]

Across all Tianjin donors (18−90 yrs), a significant increase in PFOS (r = 0.447, p < 0.01) concentration with age was found. Age-dependent accumulation of PFOS in adults from Tianjin suggests that PFOS has bioaccumulative properties similar to those of other POPs such as polychlorinated biphenyls (PCBs). PFOS is a persistent chemical with a human serum half-life of

Table 1. Perfluorinated Compound Concentrations in Human Blood, Freshwater Fish, and Seafood from China[a]

locations		PFHxS	PFOS	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA
					Human Blood (ng/mL)					
Tianjin (n = 50)	D[b](%)	84	100	39	23	77	73	51	74	0
	M[c](M)	0.34 (0.28)	12.5 (12.2)	0.27 (0.25)	0.16 (<0.10)	0.49 (0.22)	0.50 (0.36)	0.14 (<0.10)	0.22 (0.12)	<0.10
	range	<0.10−1.22	0.25−29.8	<0.10−2.25	<0.10−1.07	<0.10−3.49	<0.10−2.36	<0.10−2.48	<0.10−2.17	<0.10
					Freshwater Fish and Seafood (ng/g wet wt)					
total (n = 72)	D (%)	1	62	3	25	70	19	22	57	9
	M (M)	0.05 (<0.10)	0.92 (0.21)	0.07 (<0.10)	0.09 (<0.10)	0.28 (0.23)	0.08 (<0.10)	0.10 (<0.10)	0.26 (0.11)	0.06 (<0.10)
	range	<0.10−0.13	<0.10−26.2	<0.10−0.97	<0.10−0.32	<0.10−1.99	<0.10−0.49	<0.10−1.44	<0.10−2.94	<0.10−0.39
					By Sampling Location[d]					
Shulan (n = 7)	M (M)	<0.10	0.42 (0.57)	0.27 (<0.10)	0.08 (<0.10)	0.24 (0.23)	<0.10	<0.10	0.08 (<0.10)	<0.10
	range	<0.10	<0.10−0.92	<0.10−0.97	<0.10−0.18	0.11−0.38	<0.10	<0.10	<0.10−0.32	<0.10
Shenyang (n = 9)	M (M)	<0.10	0.46 (0.27)	<0.10	0.17 (0.15)	0.47 (0.33)	0.13 (<0.10)	0.09 (<0.10)	0.32 (0.15)	0.09 (<0.10)
	range	<0.10	<0.10−1.94	<0.10	<0.10−0.32	<0.10−1.68	<0.10−0.49	<0.10−0.23	<0.10−0.85	<0.10−0.31
Tianjin (n = 12)	M (M)	<0.10	1.37 (0.40)	<0.10	0.06 (<0.10)	0.37 (0.22)	0.09 (<0.10)	<0.10	0.21 (0.11)	<0.10
	range	<0.10	<0.10−6.85	<0.10	<0.10−0.13	<0.10−1.99	<0.10−0.24	<0.10	<0.10−0.91	<0.10
Cangzhou (n = 2)	M (M)	<0.10	<0.10	<0.10	<0.10	0.14 (0.14)	<0.10	<0.10	<0.10	<0.10
	range	<0.10	<0.10	<0.10	<0.10	<0.10−0.22	<0.10	<0.10	<0.10	<0.10
Guangan (n = 3)	M (M)	<0.10	<0.10	<0.10	0.15 (0.20)	0.11 (<0.10)	<0.10	<0.10	0.16 (0.15)	<0.10
	range	<0.10	<0.10	<0.10	<0.10−0.21	<0.10−0.24	<0.10	<0.10	<0.10−0.29	<0.10
Kunming (n = 3)	M (M)	<0.10	<0.10	<0.10	<0.10	0.19 (0.11)	<0.10	<0.10	<0.10	<0.10
	range	<0.10	<0.10	<0.10	<0.10	<0.10−0.40	<0.10	<0.10	<0.10	<0.10
Zhengzhou (n = 3)	M (M)	<0.10	0.09 (<0.10)	<0.10	0.15 (0.17)	0.21 (0.20)	<0.10	<0.10	0.10 (0.12)	<0.10
	range	<0.10	<0.10−0.16	<0.10	<0.10−0.23	0.12−0.31	<0.10	<0.10	<0.10−0.15	<0.10
Nanchang (n = 10)	M (M)	<0.10	0.19 (0.24)	<0.10	0.15 (0.16)	0.32 (0.30)	0.08 (<0.10)	0.13 (0.11)	0.38 (0.35)	0.08 (<0.10)
	range	<0.10	<0.10−0.85	<0.10	<0.10−0.29	0.14−0.74	<0.10−0.14	<0.10−0.31	0.10−0.72	<0.10−0.22
Wuhan (n = 11)	M (M)	0.06 (<0.10)	3.13 (0.23)	<0.10	0.06 (<0.10)	0.25 (0.29)	0.07 (<0.10)	0.14 (0.14)	0.40 (0.15)	0.09 (<0.10)
	range	<0.10−0.13	<0.10−26.2	<0.10	<0.10−0.23	<0.10−0.46	<0.10−0.41	<0.10−0.82	<0.10−2.94	<0.10−0.39
Tianmen (n = 3)	M (M)	<0.10	0.09 (<0.10)	<0.10	<0.10	0.08 (<0.10)	<0.10	<0.10	0.14 (0.10)	<0.10
	range	<0.10	<0.10−0.18	<0.10	<0.10	<0.10−0.13	<0.10	<0.10	<0.10−0.27	<0.10
Xuzhou (n = 3)	M (M)	<0.10	0.12 (<0.10)	<0.10	0.12 (<0.10)	0.07 (<0.10)	0.11 (<0.10)	0.51 (<0.10)	0.38 (<0.10)	<0.10
	range	<0.10	<0.10−0.27	<0.10	<0.10−0.25	<0.10−0.12	<0.10−0.24	<0.10−1.44	<0.10−1.05	<0.10
					By Fish and Seafood Species					
crucian carp (n = 26)	M (M)	<0.10	1.22 (<0.10)	0.08 (<0.10)	0.08 (<0.10)	0.18 (0.19)	<0.10	0.06 (<0.10)	0.10 (<0.10)	<0.10
	range	<0.10	<0.10−26.2	<0.10−0.97	<0.10−0.23	<0.10−0.46	<0.10	<0.10−0.14	<0.10−0.27	<0.10
common carp (n = 6)	M (M)	<0.10	0.36 (0.16)	0.15 (<0.10)	0.09 (<0.10)	0.24 (0.26)	0.07 (<0.10)	0.10 (<0.10)	0.24 (<0.10)	<0.10
	range	<0.10	<0.10−0.92	<0.10−0.65	<0.10−0.17	<0.10−0.38	<0.10−0.12	<0.10−0.31	<0.10−0.67	<0.10
grass carp (n = 3)	M (M)	<0.10	0.07(<0.10)	<0.10	0.08 (<0.10)	0.19 (0.25)	0.08 (<0.10)	0.08 (<0.10)	0.10 (<0.10)	<0.10
	range	<0.10	<0.10−0.10	<0.10	<0.10−0.14	<0.10−0.26	<0.10−0.14	<0.10−0.13	<0.10−0.20	<0.10
silver carp (n = 3)	M (M)	<0.10	1.35 (0.13)	<0.10	<0.10	0.12 (<0.10)	<0.10	0.07 (<0.10)	0.10 (<0.10)	0.09 (<0.10)
	range	<0.10	<0.10−3.89	<0.10	<0.10	<0.10−0.27	<0.10	<0.10−0.11	<0.10−0.19	<0.10−0.16
snakehead (n = 6)	M (M)	<0.10	0.23 (0.28)	<0.10	0.11 (<0.10)	0.18 (0.13)	0.10 (<0.10)	0.44 (0.24)	0.31 (0.13)	0.06 (<0.10)
	range	<0.10	<0.10−0.31	<0.10	<0.10−0.26	<0.10−0.34	<0.10−0.24	<0.10−1.44	<0.10−1.05	<0.10−0.11
catfish (n = 9)	M (M)	<0.10	0.18 (<0.10)	<0.10	0.08 (<0.10)	0.19 (0.20)	0.06 (<0.10)	0.06 (<0.10)	0.15 (0.13)	<0.10
	range	<0.10	<0.10−0.58	<0.10	<0.10−0.20	<0.10−0.38	<0.10	<0.10−0.15	<0.10−0.20	<0.10
yellow croaker (n = 3)	M (M)	<0.10	2.32 (<0.10)	<0.10	0.08 (<0.10)	0.16 (0.12)	0.08 (<0.10)	0.07 (<0.10)	0.15 (0.16)	<0.10
	range	<0.10	<0.10−6.85	<0.10	<0.10−0.13	<0.10−0.30	<0.10−0.13	<0.10−0.11	<0.10−0.18	<0.10
hairtail (n = 3)	M (M)	<0.10	0.12 (0.27)	<0.10	0.09 (<0.10)	0.15 (0.11)	<0.10	0.07 (<0.10)	0.58 (0.59)	<0.10
	range	<0.10	<0.10−0.27	<0.10	<0.10−0.18	<0.10−0.29	<0.10	<0.10−0.11	<0.10−0.91	<0.10
greasyback (n = 4)	M (M)	<0.10	0.12 (<0.10)	<0.10	0.08 (<0.10)	0.15 (0.12)	0.11 (<0.10)	0.11 (0.13)	0.40 (0.27)	0.07 (<0.10)
	range	<0.10	<0.10−0.27	<0.10	<0.10	<0.10−0.28	<0.10−0.22	<0.10−0.22	<0.10−0.75	<0.10−0.13
swimming crab (n = 4)	M (M)	0.07 (<0.10)	0.97 (0.93)	<0.10	0.14 (0.11)	0.66 (0.45)	0.29 (0.28)	0.33 (0.23)	1.11 (0.70)	0.23 (0.25)
	range	<0.10−0.13	<0.10−1.94	<0.10	<0.10−0.32	<0.10−1.68	<0.10−0.49	<0.10−0.81	<0.10−2.94	<0.10−0.37

Table 1. Continued

locations		PFHxS	PFOS	PFHxA	PFHpA	PFOA	PFNA	PFDA	PFUnDA	PFDoDA
oyster (n = 1)	M (M)	<0.10	1.07 (1.07)	<0.10	<0.10	0.22 (0.22)	0.12 (0.12)	<0.10	0.11 (0.11)	<0.10
squid (n = 2)	M (M)	<0.10	1.69 (1.69)	<0.10	<0.10	0.13 (0.13)	<0.10	0.09 (0.09)	0.38 (0.38)	0.14 (0.14)
	range	<0.10	0.32−3.05	<0.10	<0.10	<0.10−0.21	<0.10	<0.10−0.12	<0.10−0.72	<0.10−0.22
mentis shrimp (n = 1)	M (M)	<0.10	0.40 (0.40)	<0.10	0.13 (0.13)	1.99 (1.99)	0.24 (0.24)	<0.10	0.49 (0.49)	<0.10

[a] PFBS was not detected (<LOQ) and was not shown. [b] D = frequency detection. [c] M (M) = mean (median) concentration. [d] The PFC concentrations in the fish and seafood samples from Taian (n = 3) and Langfang (n = 3) were not detected (<LOQ) and were not shown.

4.6 yrs.[38] However, concentrations of PFOA ($r = -0.362$, $p < 0.05$) exhibited a significant negative relationship with age, although serum elimination half-life of PFOA is also long (3.5 yrs);[38] the reason for the negative trend of PFOA with age may be due to the high rate of exposures in children relative to that in adults. Concentration of PFOA in Chinese indoor dust was 205 ng/g and much higher than other PFCs (<15 ng/g);[14] the daily intake of PFOA via dust ingestion for children was 5 times higher than that for adults in China.[14] In Sweden, percent contribution of dust to human PFC exposure was reported to be in the range of 0.4 to 5% for adults and 5 to 55% for toddlers.[12] Child-specific exposure sources (dust ingestion) of PFOA may result in the intake not reaching a steady-state in age groups <18 yrs, while PFOA in human blood is eliminated at ages >18 yrs due to relatively smaller doses of exposures from diet.

Furthermore, no significant association between age and concentrations of PFHxS was found; and no gender-related differences in the concentration of PFCs were found ($p > 0.05$) in the present study.

PFCs in Freshwater Fish and Seafood. The mean, median, and range of concentrations of PFCs in freshwater fish and seafood samples are presented in Table 1. Nine of the 10 PFCs at concentrations above the LOQ were found in at least one sample. PFOA (70%), PFOS (62%), and PFUnDA (57%) were detected frequently. Other PFCs were detected in <30% of the samples analyzed. The mean concentration of PFOS was the greatest among target PFCs in all fish and seafood samples, at 0.92 ng/g wet wt (<0.10−26.2 ng/g), followed by PFOA at 0.28 ng/g wet wt (<0.10−1.99 ng/g) and PFUnDA at 0.26 ng/g wet wt (<0.10−2.94 ng/g).

PFC concentrations in fish and seafood varied depending on the location. The mean concentration of PFOS was the highest in Wuhan (3.13 ng/g wet wt), followed by Tianjin (1.37 ng/g wet wt) and Shenyang (0.46 ng/g wet wt); PFOS was not detected (<LOQ) in fish samples collected from Taian, Langfang, Cangzhou, Guangan, and Kunming (Table 1). The highest PFHpA, PFOA, PFNA, and PFDoDA concentrations in fish and seafood were found in samples from Shenyang (Table 1). Fish and seafood collected from Wuhan contained the highest mean concentration of PFOS; this is due to the peripheral areas of Wuhan having several PFOS and related chemical manufacturing facilities[40] and to the fact that the current production of PFOS in China is mainly from this area. Recently, Wang et al.[40] reported a very high concentration of PFOS in wastewater (>100 μg/L) in Wuhan and demonstrated that the production site is the primary source of PFCs in this region. Therefore, PFOS-contaminated environmental waters is a reason for the elevated concentrations of this compound found in Wuhan. Further, we need to evaluate the relative contributions of the manufacturing of PFOS-containing products to the ecological exposure of PFOS. Furthermore, Shenyang in Liaoning Province has the largest perfluorinated carboxylate (PFCA) manufacturing operations in China,[41] and this explains the highest concentrations of several PFCAs in fish from this city.

The highest mean concentrations of all detected PFCs (except PFHxA) were found in marine species (Table 1). Mean concentrations of PFOA, PFNA, PFUnDA, and PFDoDA in seafood samples were 2 to 4 times higher than the levels in freshwater fish (Table S5, Supporting Information). PFOS concentrations were higher in carnivorous fish (i.e., crucian carp, common carp, snakehead, and catfish at 1.24 ng/g wet wt) than in herbivorous fish (silver carp and grass carp at 0.52 ng/g wet wt). A similar trend was found for PFOA, PFDA, and PFUnDA (Table S5, Supporting Information). This indicates a food chain transfer of PFCs to higher trophic level organisms as reported earlier.[11] In general, concentration of PFOS increased with the trophic level, as has been observed for fish blood from Beijing, China,[42] and in food chain samples from the US Great Lakes.[43] However, concentration of PFOS was higher in lower trophic level marine fish from two cites in China.[23]

PFCs in Water. The mean concentrations of 10 PFCs in tap water and surface water are shown in Table S6 (Supporting Information). PFOA was detected in all tap water samples (>LOQ) at a concentration range of 0.10 to 0.92 ng/L, followed by PFOS (0.24−0.35 ng/L) and PFHpA (0.14−0.21 ng/L); other PFCs were not detected (<LOQ) in tap water, except for PFBS, which was detected at 18.0 ng/L in a tap water sample from Wuhan.

The PFC concentrations in surface water were significantly higher ($p < 0.01$) than those in tap water from each city. The PFOA and PFOS levels in surface water ranged from 0.84−14.7 ng/L and 0.50−3.74 ng/L, respectively. Surface water is the source of drinking water as the samples were collected from the major water body in each city, and our finding indicates that PFCs are partly removed by drinking water treatment processes in China. However, no discernible difference in PFC levels was found between the influent and effluent of drinking water plants in the U.S. [44]

The PFC concentrations in tap water from Shenyang were also reported in two earlier studies.[19,22] The mean concentrations of PFOS and PFOA in tap water from Shenyang were 0.60 and 1.20 ng/L in 2002[22] and 0.39 and 2.60 ng/L in 2006,[19] respectively. The mean concentration of PFOS in tap water decreased during 2002−2011 (0.24 ng/g, present study) in Shenyang. PFOA concentration in tap water from Shenyang was the highest in 2006, followed by that in 2002 and in 2011 (0.92 ng/g, present study). Potential PFOA precursors, such as polytetrafluoroethylene (PTFE), have been widely used in industrial and consumer products in Liaoning Province (where Shenyang is located) since 2004;[41] a previous study[41] showed PFOA emissions from the PTFE production facilities. Therefore, the reason for the decreasing of PFOA concentration in drinking water from Shenyang is unknown.

Source Analysis Based on PFC Profiles. The relative proportions of 7 frequently detected PFCs in human blood from Tianjin

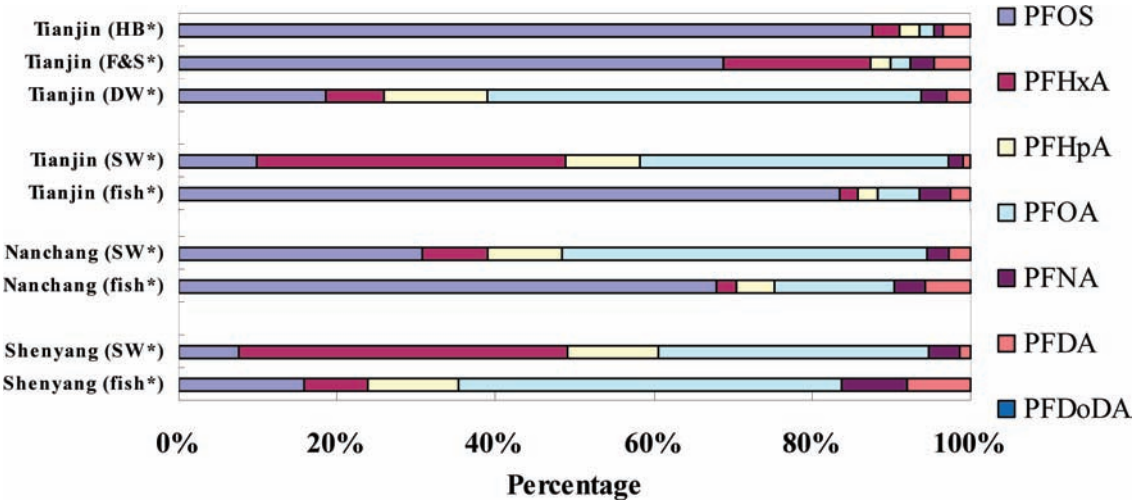

Figure 1. Composition profiles of perfluorinated compounds found in human blood, water, fish, and seafood samples collected from China. HB* = human blood, F&S* = fish and seafood, fish* = freshwater fish, DW* = drinking water, and SW* = surface water; the PFC profiles in surface water and freshwater fish from Wuhan are not shown due to the differences in sampling period.

adults are shown (Figure 1). PFOS, PFHxA, and PFOA accounted for 85%, 3%, and 2%, respectively, of the total PFC concentrations. In comparison with the profiles of PFOS (60%), PFHxA (16%), and PFOA (2%) in fish and seafood from Tianjin, a similar PFC profile was found in human blood, suggesting that fish and seafood consumption is a major exposure source of PFCs in adults in this city. On the contrary, drinking water is a minor source of PFCs in adults from Tianjin, which is also noted from the differences in PFC profiles between blood and drinking water (Figure 1). In our earlier study,[14] we showed that fish and seafood (79%) consumption is a major source of PFOS in Chinese adults.

The composition profiles of PFCs in surface water were compared among the cities (Figure 1). The profiles of PFCs in surface water and freshwater fish for Wuhan are not shown in Figure 1 due to the differences in sampling periods (surface water was collected in 2004, while freshwater fish were obtained in 2010). PFOS and PFOA accounted for 39% of the total PFC concentrations in surface water from Tianjin; this composition profile is similar to that found in the surface water from Shenyang. However, PFC profiles in surface waters between Tianjin and Nanchang exhibited different patterns, suggesting different exposure sources of and/or pathways of PFCs in the surface waters of each city. As mentioned above, Shenyang has PFC-related industrial activities; however, the PFC concentrations in surface water from this city were not higher than those found in Nanchang and Tianjin (Table 1). In the present study, fish and seafood collected from Wuhan contained the highest PFOS concentration, whereas the highest PFHpA, PFOA, PFNA, and PFDoDA concentrations were found in samples from Shenyang (Table 1).

The profiles of relative concentrations of PFCs measured in surface water and freshwater fish were compared for each city (Figure 1). In surface water, PFOA was the major PFC, accounting for 34%−84% of the total PFCs for all cities, while PFOS was the dominant PFC in freshwater fish (59%−83% of total PFCs) from Tianjin and Nanchang; this is because of the higher bioaccumulation factor (BAF) of PFOS than that of PFOA.[28]

Estimated Daily Intakes of PFCs. On the basis of the representativeness of analyzed samples, we calculated $EDI_{fish\&seafood}$ and $EDI_{drinking\ water}$ for residents from Tianjin, Nanchang, Shenyang, and Wuhan. The $EDI_{fish\&seafood}$ and $EDI_{drinking\ water}$ of PFOS and PFOA (the two most frequently detected PFCs), stratified by age and sampling locations, are shown in Table 2. Across all studied sites, the $EDI_{fish\&seafood}$ of PFOS and PFOA, on a body weight basis, ranged from 0.10 (Nanchang adults) to 2.51 ng/kg bw/day (Wuhan toddlers), and 0.13 (Wuhan adults) to 0.38 ng/kg bw/day (Shenyang toddlers), respectively (Table 2). Furthermore, the values of $EDI_{fish\&seafood}$ for PFOS and PFOA decreased ($p < 0.05$) with age. For adults, the $EDI_{fish\&seafood}$ values for PFOS varied depending on the city, and the highest value was found for Wuhan (1.58 ng/kg bw/day), followed by Tianjin, Shenyang, and Nanchang (Table 2); the values for PFOA were similar among selected cities, with a range of 0.13 to 0.28 ng/kg bw/day. The differences in the $EDI_{fish\&seafood}$ values among age groups and among sampling

Table 2. Estimated Daily Intake (EDI) on a Body Weight Basis (ng/kg bw/day) of Selected Perfluorinated Compounds via Consumption of Freshwater Fish and Seafood and Drinking Water by Chinese, as Stratified by Sampling Location and Age (>1 yrs)

	toddlers (2 to 5 yrs)		C & A[a] (6 to 17 yrs)		adults (≥18 yrs)	
locations	PFOS	PFOA	PFOS	PFOA	PFOS	PFOA
			$EDI_{fish\&seafood}$			
Tianjin	NA[b]	NA	NA	NA	1.02	0.28
Nanchang	0.15	0.26	0.13	0.22	0.10	0.16
Shenyang	0.37	0.38	0.31	0.32	0.23	0.24
Wuhan	2.51	0.20	2.11	0.17	1.58	0.13
			$EDI_{drinking\ water}$			
Tianjin	0.009	0.027	0.007	0.021	0.007	0.021
Nanchang	0.008	0.013	0.007	0.010	0.007	0.010
Shenyang	0.007	0.028	0.006	0.022	0.006	0.021
Wuhan	0.014	0.159	0.007	0.106	0.007	0.106

[a] C & A = children and adolescents group. [b] NA = not available; the data on the fish consumption rate by toddlers and children and adolescents were not available in Tianjin.

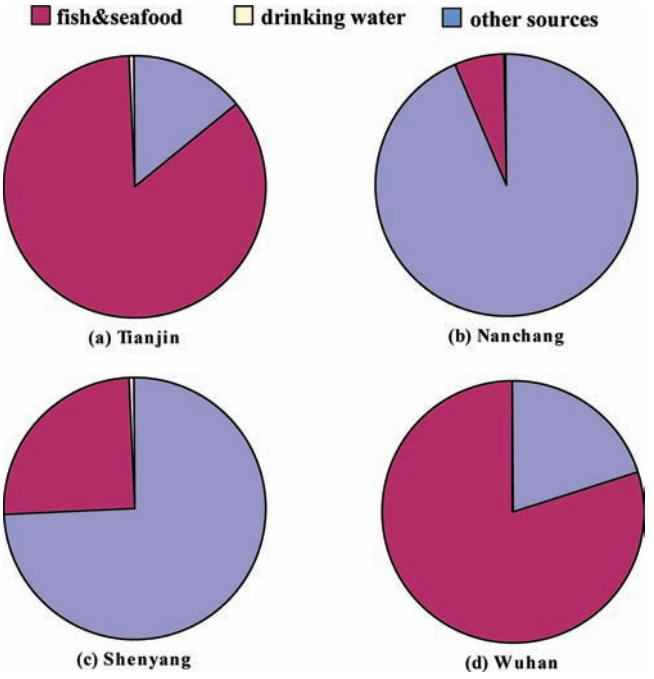

Figure 2. Contribution of drinking water, fish, and seafood consumption to the total dietary intake (TDI) (ng/kg bw/day) of PFOS by adults in Tianjin (a), Nanchang (b), Shenyang (c), and Wuhan (d), China. The modeled daily intake of PFOS based on the blood PFC level has been assumed as the TDI for adults.

locations are related to the amounts of fish and seafood consumed as well as PFC levels measured in fish samples from each city.

The $EDI_{fish\&seafood}$ for PFOS and PFOA in adults (Table 2) from Tianjin, Nanchang, Wuhan, and Shenyang were lower than that reported[23] for Guangzhou and Zhoushan in China. Gulkowska et al.[23] reported an $EDI_{fish\&seafood}$ for PFOS and PFOA at 9.28 and 1.16 ng/kg bw/day in Guangzhou and at 4.24 and 0.94 ng/kg bw/day in Zhoushan, respectively. This is because of the greater daily intake of fish and seafood in both coastal cities (Guangzhou and Zhoushan > 250 g/day) than the intake values in the four studied cities (44.8 g for adults in Tianjin (Table S3, Supporting Information) and 30.3 g for adults in Nanchang, Wuhan, and Shenyang[31]). The $EDI_{fish\&seafood}$ values for PFOS by adults in Tianjin (1.02 ng/kg bw/day) and Wuhan (1.58 ng/kg bw/day) were similar to the values reported for Norway[17] but higher than those reported for Spain[15] and Sweden.[45] However, the $EDI_{fish\&seafood}$ values for PFOS by adults in Nanchang and Shenyang were similar to those reported for Spain[15] and Sweden.[45] The $EDI_{fish\&seafood}$ values for PFOA and PFUnDA by Chinese adults (Table 2) were similar to those reported for Norway.[17] The $EDI_{drinking\ water}$ values (Table 2), were in the range of 0.006 to 0.014 ng/kg bw/day for PFOS and 0.010 to 0.159 ng/kg bw/day for PFOA; these values were much lower than the respective $EDI_{fish\&seafood}$ values (Table 2).

Comparison of Exposure to PFCs via Fish and Seafood and Other Sources. When compared with other exposure sources, the $EDI_{fish\&seafood}$ values of PFOA for all four cities (Table 2) were similar to the EDI of PFOA via dust ingestion (0.19 ng/kg bw/day)[14] but much lower than intakes from meat and eggs (including meat, meat products, and eggs at 9.16 ng/kg bw/day).[14]

$EDI_{fish\&seafood}$ value of PFOS varied depending on location (Table 2). Therefore, in order to compare with other sources, four selected cities were grouped according to $EDI_{fish\&seafood}$ values calculated for PFOS. Tianjin and Wuhan are grouped as high $EDI_{fish\&seafood}$ of PFOS (Group #1), whereas Nanchang and Shenyang were grouped as low $EDI_{fish\&seafood}$ of PFOS (Group #2). The $EDI_{fish\&seafood}$ values of PFOS by adults in Group #1 were higher than those calculated via meat and egg consumption (0.16 ng/kg bw/day) and dust ingestion (0.004 ng/kg bw/day). However, for Group #2, the $EDI_{fish\&seafood}$ values of PFOS were similar to those calculated for meat and eggs.

Regional Differences in Human Exposure of PFOS. Except for $EDI_{fish\&seafood}$ and $EDI_{drinking\ water}$ of PFOS, no region-specific data are available for our studied cities; therefore, we modeled TDI of PFOS by adults from Tianjin, Nanchang, Shenyang, and Wuhan based on human blood concentrations. The blood PFOS levels in adults from Tianjin (12.5 ng/mL) and Nanchang (15.5 ng/mL) were determined in the current study and our earlier study.[9] The concentrations of PFOS in blood from adults in Shenyang (9.57 ng/mL) and Wuhan (20.7 ng/mL) have been reported in previous studies.[6,8] The modeled dietary intake (i.e., TDI) based on blood measurements of PFOS by adults in Tianjin, Nanchang, Shenyang, and Wuhan were 1.20, 1.49, 0.92, and 1.99 ng/kg bw/day, respectively, and the contribution of drinking water and fish and seafood to the TDI of PFOS for these four cities is shown in Figure 2. Drinking water was a minor source of PFOS (<1%) in adults from all studied cities (Figure 2). However, the contribution of fish and seafood to TDI of PFOS varied depending on the locations. The contribution to TDI of PFOS between fish and seafood and other sources was 84% vs 15%, 7% vs 93%, 24% vs 75%, and 80% vs 20% for adults from Tianjin, Nanchang, Shenyang, and Wuhan, respectively. Therefore, fish and seafood were the most important source of PFOS for adults in Tianjin and Wuhan. This finding indicates regional differences in the sources of human exposure to PFOS in China.

Risk Assessment. To assess potential public health risks, hazard indices (HI) were calculated by dividing the daily intake dose of PFCs by the reference dose (RfD). The HI value being greater than unity would indicate that the exposure dose exceeds RfD, and thus a potential risk may exist. Detailed information on HI calculation is shown in the Supporting Information.

We calculated the daily intake of PFOS and PFOA via the sources examined in this study (drinking water, fish, and seafood) and other exposure sources (i.e., meat, meat products, egg, and dust) investigated in our earlier study.[14] The calculated HIs (<0.001−0.11) were far less than unity for all age groups from each city. These estimates suggest that the risk of PFOS and PFOA associated with diet, drinking water, and dust ingestion to the Chinese general population is low.

In summary, concentrations of 10 PFCs were measured in human blood, water, and fish and seafood fillet samples from China. Regional differences in the sources of human exposure to PFOS were evident; our results indicated that fish and seafood are the most important sources (>80%) of PFOS exposure in adults from Wuhan and Tianjin, whereas fish and seafood are minor sources (<30%) in adults from Nanchang and Shenyang. The risk associated with the intake of PFCs via diet (fish and seafood, meat, meat products, and eggs), drinking water, and dust ingestion is minimal.

■ ASSOCIATED CONTENT

Supporting Information. Reagents and chemicals, sample extraction, instrumental analysis, daily intake calculation and

dietary survey, risk assesment, blanks and matrix spikes experiment, and additional tables and figures. This material is available free of charge via the Internet at http://pubs.acs.org.

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