Journal of Exposure Science and Environmental Epidemiology (2015) 25, 632–638

www.nature.com/jes

ORIGINAL ARTICLE

Distribution of perfluoroalkyl compounds in rats: Indication for using hair as bioindicator of exposure

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Hair analysis is potentially advantageous in exposure assessment of perfluoroalkyl acids (PFAAs) as a non-invasive method, combined with the ability to reflect long-term exposure. The present study aims to assess the feasibility of using hair as an indicator of PFAA exposure. Adult male and female rats were subchronically exposed to selected PFAAs, including perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), and perfluorooctanesulfonate (PFOS), for 90 days. Hair, serum, and other tissues, including liver, kidney, spleen, lung, brain and heart, as well as the urine and feces excretions, were analyzed for PFAA levels. PFOA/PFNA/PFOS were detected in rat hair in a dose-dependent manner, in the order of PFOS > PFNA > PFOA. Hair PFAA concentrations were higher in male rats than the female rats, except for PFOS at low dose. Moreover, significant positive correlations as well as similar PFAA profiles were observed between hair, serum, and other tissues. Besides, hair PFAAs were negatively correlated with the urinary excretion rate. Although the influencing factors in humans still need further investigation, the results suggested that hair is capable of reflecting PFAA exposure, and could be employed as an alternative exposure bioindicator of PFAAs.

Journal of Exposure Science and Environmental Epidemiology (2015) **25,** 632–638; doi:10.1038/jes.2014.54; published online 13 August 2014

Keywords: perfluoroalkyl acids; hair; serum; tissue; urine; feces

INTRODUCTION

Perfluoroalkyl acids (PFAAs) are a family of synthetic perfluorinated chemicals, consisting of high-energy carbon–fluorine bonds. Their commercially advantageous surfactant properties make them widely used in a large amount of industrial and consumer products. These fully fluorinated hydrocarbons are extremely stable and poorly degraded by chemical or biological routes, leading to their ubiquitous presence in air, water, sediments, and accumulation in wildlife and humans.[1–6]

PFAAs were detected in most of the people living in the industrialized world in the blood/serum, indicating a widespread exposure.[1–3,5–7] The production and the application of PFAAs have been reduced or limited, especially after perfluorooctanesulfonate (PFOS) and related compounds were listed under Annex B of the Stockholm Convention in 2009. However, exposure to the precursor compounds such as perfluorooctanesulfonamide (FOSA), and other alternative PFAA products posed humans to a widely, continuous, low-level residual exposure. The most frequently detected PFAAs are PFOS and perfluorooctanoic acid (PFOA). In addition, perfluorononanoic acid (PFNA), a nine-carbon backbone PFAA, has been detected in environment and human blood with increasing levels in recent years.[8,9]

The potential adverse effects of PFAAs on human health have become an increasing concern. It was reported that increased PFOA or PFOS serum concentrations have a negative association with childhood diphtheria, tetanus, and rubella vaccine response.[10,11] Associations between serum PFOS concentration and thyroid disease are observed in patients with thyroid diseases.[12,13] The assessment of human exposure is critical to evaluate the relationship between exposure and health effects. Most of the studies on human exposure assessment to PFAAs have reported the results in whole blood, plasma, or serum.[2,7] However, blood sampling is disadvantageous in invasive collection, limited sample size, and daily variation that restrict the survey for large population, especially for children. Some children studies, most of which were based on pooled samples or blood spot analysis, reported a comparative, sometimes even higher, blood PFAA level as compared with the adults.[14–16]

Non-invasive biological indicator is a valuable tool to facilitate large population survey, as well as for children exposure assessment. Human hair has been employed in assessing trace element deficiency and disease diagnosis.[17,18] Moreover, the relatively high lipid level makes hair a suitable matrix for the hydrophobic persistent organic pollutants analysis.[19] Good correlations between the hair and blood levels of some organic pollutants, such as dichlorodiphenyltrichloroethane (p,p′-DDT), polychlorinated biphenyls (PCBs), polychlorinated dibenzo-p-dioxins (PCDDs), and polychlorinated dibenzofurans (PCDFs), have been reported.[20,21]

Few data are currently available on the use of hair as indicator of PFAA exposure. Meyer et al.[22] revealed a significant positive correlation between the feather and liver PFOS levels in birds. Li et al.[23] reported PFAA levels in human hair and observed a correlation between hair and serum levels. However, further studies including optimization of the analytical methods of hair PFAAs and evaluation of the influencing factors when employing hair analysis for exposure assessment are necessary, which is critical to make it an accurate and applicable bioindicator.

The objective of the present study is to assess the use of PFAA measurements in hair as an indicator of exposure to PFAAs. The

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Received 10 January 2014; accepted 5 June 2014; published online 13 August 2014

distribution of PFOA/PFNA/PFOS in rat hair, serum, and main tissues, and the correlation are evaluated. Besides, the relevance to elimination through urinary/fecal excretion is analyzed. The rat experiments are advantageous in a defined exposure and an observation of PFAA distribution in different tissues. However, it should be pointed out that one must be cautious when developing human exposure bioindicator based on animal experiments because of the species difference in elimination kinetics.

MATERIALS AND METHODS

Reagents

PFOA (CAS number 335-67-1, 98% purity), PFNA (CAS number 375-95-1, 98% purity), and PFOS (CAS number 1763-23-1, 98% purity) were purchased from Fluka (Milwaukee, WI, USA). High-performance liquid chromatography (HPLC) grade ammonium acetate, methanol, acetonitrile (ACN), methyl-tert-butyl ether (MTBE), and sodium carbonate were purchased from Sigma-Aldrich (St Louis, MO, USA). HPLC grade tetra-n-butylammonium hydrogen sulfate (TBAHS) was purchased from Fluka (Morris Plains, NJ, USA). Milli-Q water was cleaned using Waters Oasis HLB Plus cartridges (Milford, MA, USA) to remove the potential residue of PFAAs, called PFAA-free water.

Animals and Treatment

Forty Wistar rats (male/female = 1:1), 8 weeks old, were purchased from the Experimental Animal Center of Dalian Medical University (Dalian, China). PFOA/PFNA/PFOS were administered to the rats by drinking water for 90 days, with each compound at doses of 0, 0.05, 0.5, and 5 mg/l. The solvent control group received water with 0.03% Tween-20 only. The daily drinking volumes in each cage containing five rats were recorded, based on which the average total exposure and the daily intake for each rat were estimated.

Sample Collection and Preparation

Urine and feces samples were collected after administration with PFAAs by moving rats to standard metabolism cages overnight for 24 h intervals on day 84 (week 12). Urine samples were stored in polypropylene (PP) vessels and feces in PP plastic bags and frozen at − 20 °C until analysis.

After 90 days of exposure, rat dorsal hair samples were obtained by stainless scissors after anesthesia before dissection. Hair sample were placed in PP plastic bags and stored at room temperature. Then, blood was collected by puncture of the jugular vein, and serum was obtained by centrifugation at 3000 r.p.m. for 10 min and then stored at − 20 °C. Liver, kidney, spleen, lung, brain, and heart were collected and also stored at − 20 °C. Measurement of excretions, hair samples, serum, and tissues were carried out in individual rats. The tissues analyzed in the present study were regarded as representative of most of the body load. All the experimental vessels were washed with methanol before use.

The procedures adopted during hair sample pretreatment are (1) washing, (2) desiccation, (3) digestion, (4) extraction, and (5) cleaning. Hair PFAA concentrations decreased after one wash, suggesting some external contamination was removed (Table 1). However, there was no significant difference between washing two and three times. Therefore, washing two times with 1% solution of the Triton X-100 in an ultrasonic bath for 20 min was employed. The samples were then washed with PFAA-free water once and methanol two times. After drying, the hair samples were sent to digestion and extraction.

Alkaline digestion has been widely used for PFAA extraction from biological samples.[24–26] Approximately 0.1 g of washed hair pieces were placed in 15 ml PP tube, and 2 ml of sodium hydroxide solution (NaOH) was added, digesting in a water bath at 80 °C for 12 h. Then, HCL was added to the resultant digest to adjust pH to neutral. The ion pair extraction method (IPE) was employed, with 1 ml of 0.5 M of TBAHS added as ion-paired reagent, followed by twice extraction with 5 ml of MTBE, 20 min for each time. After centrifuging for 10 min at 3000 r.p.m., the supernatant of MTBE was collected, and the two supernatants were combined in another 15 ml PP tube. The MTBE solvent was evaporated to dryness under a gentle flow of high purity nitrogen, and then redissolved in 1 ml of acetonitrile. The solution was filtered using a 0.45-μm nylon filter, and was adjusted to a 40% acetonitrile/water solution. The resultant solution was then ready for instrumental analysis. The details for the treatment of serum, tissue, and urine/feces samples are presented in Supplementary Information.

Table 1. Concentrations of PFAAs in hair sample with different washing times (ng/g; $n = 3$).

Compound	*No wash*	*Wash once*	*Wash two times*	*Wash three times*
PFOA				
Female	486 ± 76.4	467 ± 21.5	264 ± 15.9	266 ± 13.6
Male	990 ± 47.2	887 ± 38.2	458 ± 32.0	453 ± 30.0
PFNA				
Female	582 ± 100	526 ± 71.6	334 ± 13.6	335 ± 14.0
Male	3005 ± 97.8	2787 ± 225	1685 ± 27.8	1689 ± 35.0
PFOS				
Female	2051 ± 61.7	1992 ± 88.7	1843 ± 156	1880 ± 110
Male	3419 ± 250	2951 ± 253	2062 ± 162	2033 ± 278

The hair samples used for evaluating the washing efficiency are mixed samples of administered rats in the 5 mg/l group.

Instrumental Analysis

The samples were analyzed via Agilent 1200 HPLC coupled with Agilent 6410 Triple Quadrupole mass spectrometer (HPLC-MS/MS, Palo Alto and Santa Clara, CA, USA) under optimum instrumental conditions. Briefly, a chromatographic column C_{18} column was heated to 40 °C. A gradient program was employed using 10 mM aqueous ammonium acetate solution and acetonitrile mobile phases and a flow rate of 0.25 ml/min. The gradient started at 40% acetonitrile followed by a 9-min ramp to 90% acetonitrile and maintained at 90% for 3 min. The method then reverted back to initial conditions and an 8-min post time was maintained before the next injection. The triple quadrupole mass spectrometer was operated in the negative electrospray (ESI) mode with multiple reaction monitoring (MRM).

Quality Assurance/Quality Control

In order to minimize the background, use of polytetrafluoroethylene was avoided during the preparation of samples. Washing efficiency was evaluated for the hair samples to avoid the external contamination. Procedure blank was conducted to exclude reagent contamination. Matrix recoveries were evaluated to ensure the reliability of the analytic method. Linear calibration curves were established using matrix-matched standards, obtained by extraction of PFAA standards from control rat hair, aiming to compensate for the matrix effect. Both recovery and reproducibility of the extraction were validated in five replicate analysis by spiking 5 ng of each standard into matrices (0.1 g or 0.1 ml). The limit of detection (LOD) was defined as the analyte peak required yielding a signal-to-noise (S/N) ratio of 3:1. The limit of quantification (LOQ) was defined as the analyte peak required yielding a signal-to-noise (S/N) ratio larger than 10:1 for the PFAAs analyzed. The LOD and LOQ for PFOA, PFNA, and PFOS in different matrices are listed in Table 2. The recovery of the standard-spiked matrix for PFOA/PFNA/PFOS was 86.4–101%, 76.4–109%, 100–108%, 82.1–122%, and 72.5–119% for serum, tissues, hair, and urine and feces, respectively.

Statistical Analysis

All statistical analyses were carried out using SPSS 17.0 (Chicago, IL, USA). Spearman's correlation coefficient was utilized to assess the association between PFAA concentrations in hair, serum, and tissue samples. The Kruskal–Wallis test was used to compare the concentration of PFAAs among different administrated groups in the same kind of matrix. After transforming the rank case, Turkey's test was used as a *post hoc* test. The gender difference was evaluated using Mann–Whitney test. For statistical analyses, the samples with undetectable target compounds were assigned a value of half of the LOQ.

Table 2. The LOD and LOQ for the analytical method for compounds.

	LOD/LOQ		
	PFOA	*PFNA*	*PFOS*
Hair (ng/g)	0.04/0.14	0.04/0.13	0.07/0.22
Serum (ng/ml)	0.01/0.03	0.06/0.21	0.05/0.16
Liver (ng/g)	0.01/0.04	0.05/0.18	0.04/0.12
Kidney (ng/g)	0.02/0.07	0.01/0.04	0.19/0.64
Heart (ng/g)	0.04/0.16	0.03/0.09	0.11/0.37
Brain (ng/g)	0.01/0.05	0.05/0.16	0.09/0.29
Spleen (ng/g)	0.01/0.04	0.01/0.03	0.13/0.44
Lung (ng/g)	0.01/0.04	0.01/0.02	0.26/0.97
Urine (ng/ml)	0.07/0.22	0.07/0.22	0.06/0.19
Feces (ng/g)	0.05/0.17	0.05/0.15	0.05/0.18

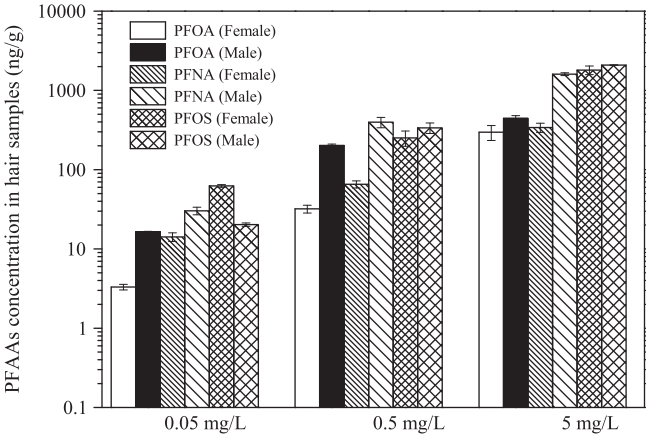

Figure 1. PFAA concentration in hair samples (ng/g).

RESULTS

Hair PFAA Concentrations

The total intake for each compound, calculated from drinking volume multiplied by water concentration of 0.05, 0.5, and 5 mg/l, was estimated to be 0.15 and 0.12 mg/kg bw, 1.52 and 1.22 mg/kg bw, and 13.6 and 17.7 mg/kg bw for female and male rats, respectively. PFOA, PFNA, and PFOS were detected in all the hair samples of treated groups (Figure 1). The mean hair concentrations of PFOA, PFNA, and PFOS ranged from 3.31 to 444 ng/g, 14.2 to 1604 ng/g, and 20.3 to 2086 ng/g, respectively, in different dosage groups. The PFAA profiles in rat hair present similar pattern in different dosage groups (Figure 2; Supplementary Figures S1 and S2). Hair PFAA levels were detected in an order of PFOS > PFNA > PFOA, except that PFNA was the highest in male rats from the 0.05 and 0.5 mg/l groups.

PFOA and PFNA concentrations in hair exhibited similar sex-related tendency, where male rats have a significantly higher hair concentrations than female rats ($P < 0.01$). Hair PFOS levels in male rats were also higher than the female in the 0.5 and 5 mg/l groups, with no significant difference ($P > 0.05$). However, male hair PFOS level was lower than the female in the 0.05 mg/l group.

Correlation between Hair, Serum, and Tissue PFAAs

PFOA, PFNA, and PFOS were detected in all the serum and tissue samples collected from the administration group, except that PFOS was not detected in the brain in the 0.05 mg/l male group (Supplementary Table S1). The PFAA profiles in tissues are dominated by liver, kidney, and lung. The average PFOA, PFNA, and PFOS concentrations in multiple hair, serum, and tissues samples collected from administered groups were compared (Table 3). The concentrations of PFOA, PFNA, and PFOS in hair were significantly correlated with that in serum and other tissues for both females and males.

In addition, the major body compartments for PFOA, PFNA, and PFOS distribution were estimated according to the total intake and individual load of each tissue (Figure 3a and b). The tissue load of PFAAs was calculated from the tissue weight multiplied by corresponding tissue PFAA concentration. Significantly, male rat tissues accumulated more PFAAs than female rat tissues. The accumulation was observed in the order of PFOS > PFNA > PFOA.

The relative abundance ratio of the three PFAAs is similar between serum and hair samples (Figure 2). Moreover, it also should be pointed out that hair has its own unique PFAA distribution, not directly reflecting the distribution of PFAAs in serum. For female rats, based on the mean of ratios calculated from each subject, the hair PFOA, PFNA, and PFOS levels amounted to 1.34-, 0.07-, and 0.04-fold, respectively, of the serum level, whereas the values in male rats, are 0.07, 0.03, and 0.05, respectively. PFOS and PFOA were distributed mainly in serum and liver.[2] The mean hair to liver ratios of PFOA, PFNA, and PFOS are 6.87, 0.30, and 0.04 for female rats, and 0.85, 0.06, and 0.03 for male rats.

Relevance between Hair and Urinary/Fecal PFAAs

PFOA, PFNA, and PFOS concentrations increased in urine and feces with increasing exposure level (Supplementary Figure S3). The urine concentrations were observed in an order of PFOA > PFNA > PFOS, except that urine PFNA concentration was the highest in the 0.5 mg/l female group. In contrast to the relatively high urinary PFOA level, fecal PFOA concentrations are the lowest among the three target PFAAs. The hair PFAA concentrations increased with the decreasing urine PFAA levels.

DISCUSSION

The washing procedure in the present study proved to be efficient for removing external PFOA, PFNA, and PFOS from hair sample surface. The substantial weakness of hair analysis is lack of the ability to distinguish endogenous from exogenous origin,[27] as is necessary in evaluating internal doses of the substance of interest. The efficient washing could remove the external contamination without loss of internal PFAAs. In addition, some researchers may also argue that the exogenous chemicals from the atmosphere could not only deposit on the surface of hair, but also enter into the hair where the contaminants could not be removed completely by washing. It has been proved that dietary exposure is the dominant intake pathway of PFAAs, among various routes including inhalation of air and ingestion of dust.[28–30] Therefore, the potential combination of airborne PFAAs into the hair matrix, if exist, is expected to pose no significant effects on the endogenous hair PFAA accumulation.

The positive correlation between hair PFAAs and the external exposure level and the serum and tissue analysis suggest that hair PFAAs are capable of reflecting exposure accurately. Moreover, PFAAs depositing in hair is an elimination route of rats as well as humans. In contrast to the external elimination, accumulation in tissues could lead to a variety of organ poisoning. Concentrations of PFAAs have been measured mainly in human blood and to a much lesser extent in liver. Very few data are currently available on the distribution of PFAAs in other human tissues such as lung, brain, kidney, and so on. Future research is warranted to develop the correlation between human hair and tissues in order to facilitate using hair samples to estimate the burden in tissues for human health.

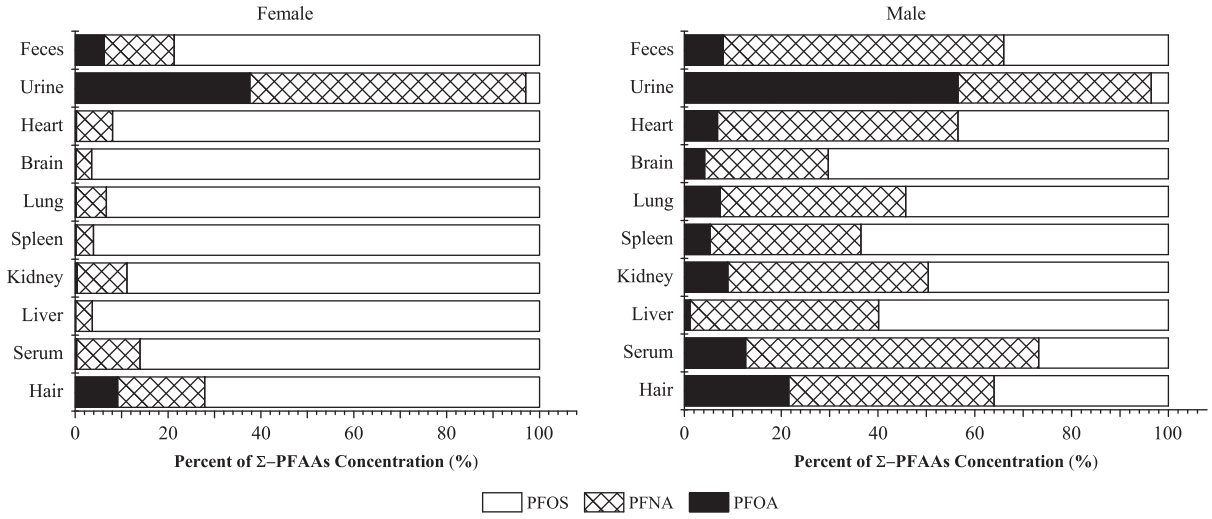

Figure 2. Percent compositions of ∑-PFAA concentrations in hair, serum, tissues, and excretions of administered rats in the 0.5 mg/l group.

Table 3. Correlation between mean PFAA concentrations in hair, serum, and tissue samples collected from different administrated doses of rats.

	PFOA		*PFNA*		*PFOS*	
	Female	*Male*	*Female*	*Male*	*Female*	*Male*
Hair/serum						
R	0.90[a]	0.85[a]	0.82[a]	0.88[a]	0.93[a]	0.92[a]
Median ratio	1.23	0.07	0.06	0.03	0.03	0.05
Mean ratio (95% CI)	1.34 (0.93–1.75)	0.07 (0.07–0.08)	0.07 (0.04–0.10)	0.03 (0.02–0.03)	0.04 (0.03–0.05)	0.05 (0.05–0.06)
Hair/liver						
R	0.75[a]	0.86[a]	0.84[a]	0.90[a]	0.87[a]	0.92[a]
Median ratio	2.50	1.01	0.18	0.05	0.03	0.03
Mean ratio (95% CI)	6.87 (2.82–10.9)	0.85 (0.63–1.07)	0.30 (0.18–0.41)	0.06 (0.05–0.06)	0.04 (0.03–0.05)	0.03 (0.02–0.03)
Hair/heart						
R	0.85[a]	0.91[a]	0.88[a]	0.89[a]	0.89[a]	0.93[a]
Median ratio	6.56	0.89	0.46	0.28	0.13	0.24
Mean ratio (95% CI)	6.16 (5.31–7.00)	0.89 (0.69–1.08)	0.92 (0.01–1.83)	0.28 (0.28–0.30)	0.15 (0.12–0.18)	0.24 (0.21–0.27)
Hair/brain						
R	0.63[b]	0.84[a]	0.86[a]	0.90[a]	0.93[a]	0.89[a]
Median ratio	70.2	14.1	9.24	3.15	1.04	0.87
Mean ratio (95% CI)	85.2 (1.25–45.2)	15.9 (10.4–21.6)	9.91 (7.78–12.0)	4.23 (2.69–5.76)	1.84 (1.04–2.64)	1.09 (0.49–1.69)
Hair/spleen						
R	0.84[a]	0.90[a]	0.86[a]	0.89[a]	0.95[a]	0.90[a]
Median ratio	7.68	1.10	0.64	0.41	0.10	0.15
Mean ratio (95% CI)	18.8 (8.00–29.6)	1.11 (0.97–1.23)	1.06 (0.66–1.46)	0.39 (0.33–0.44)	0.14 (0.10–0.17)	0.16 (0.14–0.18)
Hair/lung						
R	0.89[a]	0.90[a]	0.88[a]	0.90[a]	0.87[a]	0.92[a]
Median ratio	4.09	0.55	0.30	0.18	0.08	0.12
Mean ratio (95% CI)	4.26 (3.08–5.46)	0.53 (0.43–0.64)	0.40 (0.26–0.53)	0.16 (0.12–0.19)	0.10 (0.07–0.12)	0.12 (0.10–0.14)
Hair/kidney						
R	0.89[a]	0.84[a]	0.91[a]	0.93[a]	0.89[a]	0.89[a]
Median ratio	0.96	0.26	0.08	0.09	0.03	0.06
Mean ratio (95% CI)	2.12 (1.09–3.15)	0.23 (0.17–0.29)	0.11 (0.08–0.13)	0.08 (0.06–0.10)	0.04 (0.03–0.05)	0.06 (0.05–0.07)

[a]Extremely significant correlation ($P < 0.01$). [b]Significant correlation ($P < 0.05$).

The gender difference observed in the hair PFAAs was consistent with previous reports in both animal experiments and human exposure assessment because of the gender difference in elimination half-lives. Marked sex differences have been observed in the rats, particularly with perfluorocarboxylic acids. Most notably, the half-lives of PFNA and PFOA in female rats are 20 and 50 times shorter than those in males, respectively.[31,32] Testosterone is considered to be a key determinant of the sex

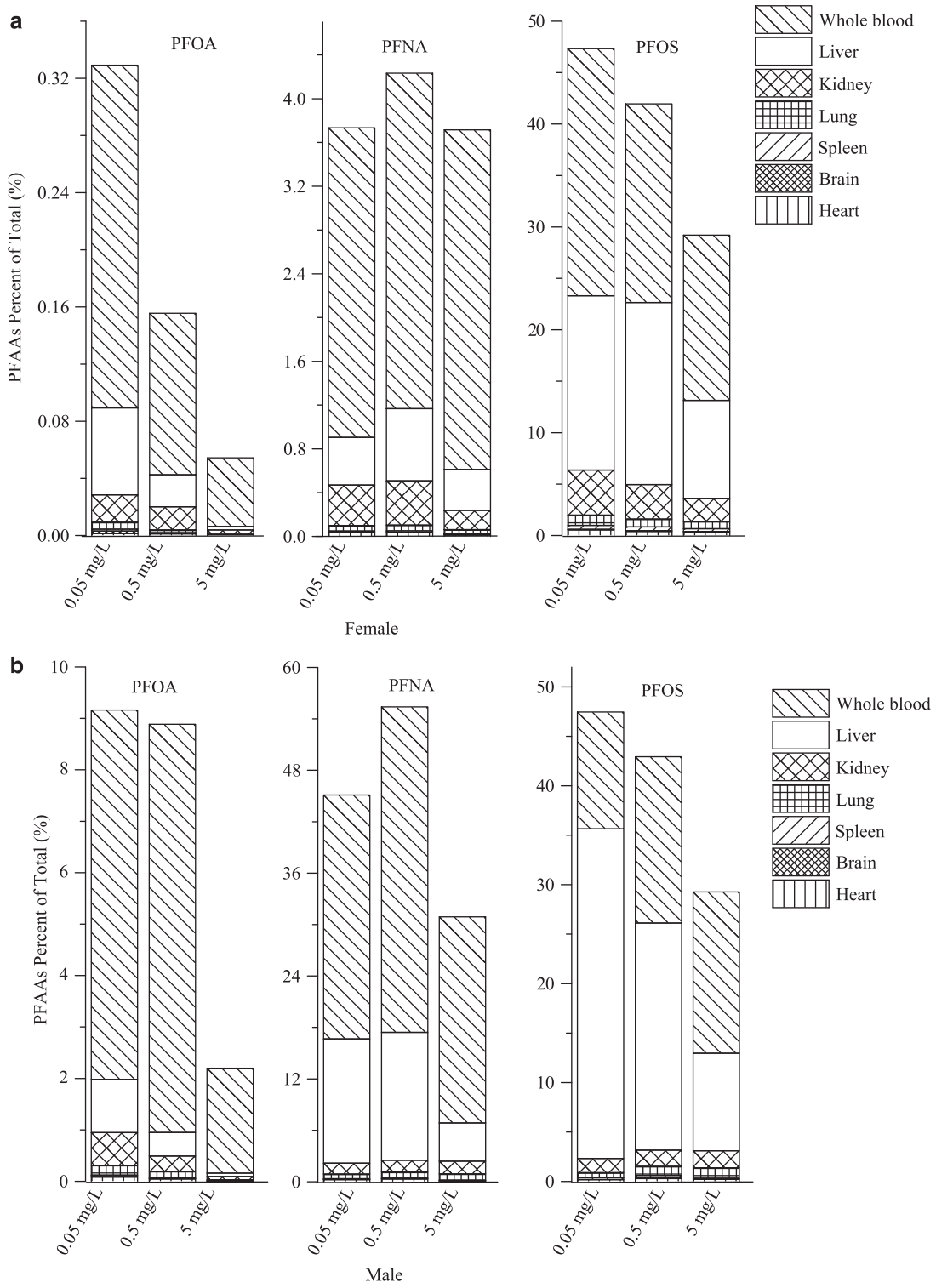

Figure 3. (**a**) The tissue and whole blood PFAA percent of total administrated dose in female rats. (**b**) The tissue and whole blood PFAA percent of total administrated dose in male rats.

difference in PFOA elimination that poses an inhibitory effect on renal excretion in male rats.[33] These differences may be also related to the actions of organic anion transporters (OATs) in the kidney as several transporter proteins expressed differently in male and female adult rats.[34,35] The gender difference in PFAA hair levels possibly is related to the difference in elimination rate and transfer rate from serum to hair.

The generally lower rat hair PFAA level than the rat serum level was different from the results of our previous study, where a higher human nail PFAA concentrations than the serum was observed, suggesting the preferred PFAA accumulation in human nails.[36] A significant difference in the hair/nail to serum ratio between humans and rats is expected because of a remarkably higher excretion rate through urine and feces in rats than that in

human body. Furthermore, the background body burden of PFAAs also affects the hair/nail-to-serum ratio. As observed in the present study, the higher PFAA exposure leads to a higher hair PFAAs, accompanied by lower hair-to-serum ratio. One possible reason may be the limited binding sites in hair matrix for PFAAs. The environmental PFAA exposure usually occurs at low level, possibly far below the saturation level of PFAA accumulation in the hair matrix.

The increase in urine excretion rate of PFOA > PFNA > PFOS is in accordance with the decreasing body load. Moreover, gender difference observed in urine levels also correspond to that in the body load. It seemed that urine excretion affects the body load more than the fecal excretion. Although higher fecal concentrations are observed than urinary concentrations, the larger urine volume than feces possibly make it a major excretion route for rats. Hence, hair PFAA profile is rather consistent with the internal body load than external excretion, which would verify its application in the exposure assessment.

The presence of PFOS and PFOA in serum, liver, and other tissues have been shown to be associated with proteins such as serum albumin, β-lipoproteins, and fatty acid binding proteins.[37–39] Keratin protein is the main component of hair. The occurrences of PFOA, PFNA, and PFOS in hair, and the similar profile to that in the main tissues, suggested that the affinity of PFAAs to keratin possibly play a dominant role in the hair PFAA accumulation. Further research is warranted on the binding of PFAAs to keratins that will possibly give a better explanation for the hair PFAA analysis.

Furthermore, based on the serum PFAA levels, the PFAA dosage employed in the present study is relevant to some heavily PFAA-contaminated areas. The residents exposed to PFOA-contaminated drinking water in Arnsberg, Germany, had plasma PFOA levels above 30 ng/ml.[40] Wang et al.[41] reported that the median levels of serum PFOA and PFOS were 284.34 and 34.16 ng/ml in residents living near fluorochemical plant in Changshu, China, and 1635.96 and 33.46 ng/ml in occupational participants. Olsen et al.[42] reported that the serum PFOS and PFOA range of values for the employees were 91.0–10 600 and 21.0–6160 ng/ml, respectively, from 3M Decatur manufacturing site. Therefore, the dosage in the present study, especially the low dose, is comparable to some heavy environmental exposure, supporting the employment of hair analysis in human exposure assessment.

It should be pointed out that the present study has some limitations. First, the results from the rats could not be simply used in humans because of the significant difference in the elimination kinetics. Second, whether the combined exposure to the three target PFAA compounds will influence each other is unknown.

In summary, the accumulation of PFOA/PFNA/PFOS in rat hair was in a dose-dependent manner after subchronic exposure. The good correlation between hair PFAA levels and serum/tissue levels was observed, along with similar PFAA profile in hair to those in serum and tissues. In addition, the gender difference of higher male hair PFAA levels than female is in accordance to that in serum and other tissues. Furthermore, the hair PFAA levels increased with decreasing urinary excretion rate. Taken together, it is suggested that hair analysis is capable of reflecting internal body burden accurately and could be employed as an alternative bioindicator of exposure. The underlying mechanism might be related to the binding affinity of PFAAs to some tissue proteins, whereas keratin probably acts as a key factor in nail/hair PFAA accumulation. Moreover, it is expected that higher PFAA accumulation would occur in human hair because of the much lower excretion rate in human body than the rats.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

The paper is to commemorate late Professor Dr Yihe Jin (1959–2013) who devoted his whole life to the scientific research and who contributed greatly to the present research. This study is financially supported by National Nature Science Foundation of China (81102096, 21177020) and the Fundamental Research Funds for the Central Universities (DUT12LK13). We also appreciate the 123 Project of Liaoning environment education research supported by Geping Green Finance (CEPF2011-123-2-14).

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Supplementary Information accompanies the paper on the Journal of Exposure Science and Environmental Epidemiology website (http://www.nature.com/jes)