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Occurrence of perfluoroalkyl substances in matched human serum, urine, hair and nail

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ABSTRACT

The purpose of this study was to determine perfluoroalkyl substances (PFASs) in human serum, urine, hair and nail from general populations, and to investigate the possibility for human urine, hair and nail used as the biomonitoring sample for PFASs exposure. We detected the concentrations of PFHxA, PFOA, PFNA, PFDA, PFUnDA, PFDoA, PFHxS and PFOS in 39 matched human serum, urine, hair and nail samples from Shenzhen in China. The detection frequency and the median level of PFOS were all higher than that of the other PFASs in four matrices. The median concentration of PFOS in serum, urine, hair, and nail were 9.24 ng/mL, 13.96 ng/L, 0.58 ng/g and 0.63 ng/g, respectively. The results of spearman correlation test indicated that nail was an ideal matrix for biomonitoring PFOS rather than human urine and hair in general populations for the non-invasive sampling.

Introduction

Perfluoroalkyl substances (PFASs) are persistent organic pollutants (POPs) and persist in the environment. They are widely used in consumer and industrial products, such as surfactants, carpets, fire-retarding and food packaging (Hekster et al., 2003; Liu et al., 2009). Due to the multi-organ toxicity and potential health risk to humans (Guruge et al., 2006; Harada et al., 2005; Lau et al., 2006), perfluorooctanesulfonate(PFOS) and its salts had been included in Stockholm Convention on persistent organic pollutants since 2009 (Stockholm Convention on Persistent Organic Pollutants, 2009). As far as we know, PFASs are ubiquitous all over the world, which were frequently detected in environment medium, human foodstuffs, human tissue and various animals, including soils (Wang et al., 2013), surface waters (Cai et al., 2012), tap water (Mak et al., 2009), fish and shell fish (Domingo et al., 2012; Munschy et al., 2013; Shi et al., 2010; Zhao et al., 2011), foods (Guerranti et al., 2013; Zhang et al., 2010), foodstuff packing (Zafeiraki et al., 2014), human blood (Guo et al., 2011; Ji et al., 2012) and human milk (Barbarossa et al., 2013; Liu et al., 2010). Moreover PFASs have been verified associated with breast cancer (Siddique et al., 2016), obesogenic effects (Karlsen et al., 2017), allergic diseases (Goudarzi et al., 2016) and asthma (Humblet et al., 2014) in recent years.

So far, human blood and breast milk are the most common biomonitoring matrices for human exposure to PFASs in

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general populations (Kim et al., 2014; Stubleski et al., 2016). However, the collection of human samples like serum is very difficult from some persons, especially neonates and young children, because of ethics and humanity. Non-invasive samples like nails, hairs are therefore imminently required (Li et al., 2013). Human hair and nail, as the most common non-invasive samples, is easily available, stored, transported and ethically not prioritized, which could be used as a biomonitoring sample for human exposure to some POPs associates with environmental or occupational exposure (Król et al., 2013; Appenzeller and Tsatsakis, 2012; Li et al., 2013; Liu et al., 2011a; 2011b; Schramm, 2008; Xu et al., 2010). Besides, nail and hair are mainly composed of keratin which quite suitable for monitoring the exposure for PFASs. Recently some studies have already developed the method for determining PFASs in human hair and nail with the lower limit of detection (LOD) (Alves et al., 2015; Li et al., 2012; Liu et al., 2011a; 2011b; Perez et al., 2012; Xu et al., 2010). Moreover urine is the primary elimination pathway of PFASs, and the association between blood concentrations and urine concentrations for PFASs has been found by few researches (Zhang et al., 2013a, 2015). Although our laboratory has already discussed the possibility for human urine, hair and nail to be used as the biomonitoring sample of human exposure to PFASs (Li et al., 2013), it is essential to investigate comprehensively in different locations and populations.

In this study, we detected the PFASs concentrations in 39 matched human serum, urine, hair and nail samples from Shenzhen, one of most developed cities in south China. We contrasted the concentrations of PFASs in other countries and assessed the gender and age effect for PFASs in the four matrices. We also validated the possibility again for human urine, hair and nail used as the biomarker of human exposure to PFASs.

1. Materials and methods

1.1. Chemicals and reagents

PFAC-MXB and MPFAC-MXA were purchased from Wellington Laboratories with purities ≥98%. PFAC-MXA is a mixture standard, which consists of perfluorohexanoic acid (PFHxA), perfluoroctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUnDA), perfluorododecanoic acid (PFDoA), perfluorohexanesulfonate (PFHxS) and perfluorooctanesulfonate (PFOS). As well as MPFAC-MXA is a mixture internal standards of above mentioned PFASs. Methanol (LC–MS grade) and acetonitrile (HPLC grade) were obtained from Fisher Scientific (USA), while acetone was purchased by J.T. Baker (Phillipsburg, USA). Tetra-*n*-butylammonium hydrogen sulfate (TBA) was obtained from J&K chemical company, and methyl-tert-butyl ether (MTBE) and ammonium hydroxide (analytical grade) was achieved from Sigma-Aldrich. Moreover ammonium acetate (HPLC grade) and formic acid (HPLC grade) were supplied from Dikma Pure (Richmond Hill, USA). Sodium carbonate (analytical grade) was purchased from the Jinke Institute of Fine Chemicals. Weak anion exchange solid phase extraction (SPE) cartridges (Oasis®Wax, 150 mg, 6 mL, 30 μm) were provided by Waters (Milford, Ireland).

1.2. Sample collection

We collected matched human serum, urine, hair and nail samples from 15 males and 24 females in 2015 with non-occupation exposure in Shenzhen, China. The ages of the donors ranged from 20 to 53 years old with the average age of 38 years old. All the donors were fully told the purpose and content of this investigation and signed the consent forms. According to the sampling method used in our laboratory, about 2 mL serum, 50 mL urine, 0.5 g hair and 0.5 g nail samples for each donor were gathered (Li et al., 2012). The individual samples were then stored in a polypropylene centrifuge tube pre-cleaned by water and methanol successively. The serum and urine samples were frozen at −20°C immediately until the analysis (Li et al., 2012, 2013).

1.3. Sample preparation

The sample preparation methods were described in detail in our previous publications (Li et al., 2012, 2013). To remove the external contamination, about 20 mL of water was added to each of the individual hair or nail sample and let soaked for 10 min to remove any surface dirt that may have interfered with the analysis. The water was then discarded and the samples were washed twice with acetone, and then air-dried. Before extraction, the hair and nail samples were ground to powder employed a Mini-mill Grinder (FRITSCH, "Pulverisette 23", Germany). The serum samples were extracted by ion-pair extraction developed by Hansen et al. (2001). For urine, hair and nail samples, PFASs were extracted by various organic solvent. Then the extracts were all cleaned by the WAX cartridge. After that the target were eluted with 9% ammonium hydroxide in methanol, which was concentrated to dryness under nitrogen gas and reconstituted by 200 μL solution of water/methanol (V/V; 1/1). Finally the particles were removed by filtration using 0.2 μm nylon filter.

1.4. Instrumental analysis

The instrumental analysis methods were also depicted in detail in our previous studies (Guo et al., 2011; Li et al., 2012, 2013; Liu et al., 2009, 2010, 2011a; Wu et al., 2012). PFASs were performed employing ultra-performance liquid chromatography coupled with tandem mass spectrometry in negative-ion pattern with electrospray ionization source and multiple-reaction- monitoring mode. A 20-μL extract was injected to a 50°C ACQUITY UPLC BEH C18 column (2.1 mm i.d. × 50 mm length, 1.7 μm; Waters, USA) in full loop model. Methanol and 2 mM ammonia acetate were used for the gradient program, with the flow rate of 0.4 mL/min. The particular mass transitions are summarized in Appendix A Table S1.

1.5. Quality assurance/quality control (QA/QC)

The blanks of various solvents in the experiment are firstly examined, and no PFAS solvents were used for sample preparation and instrumental analysis. Two method blank samples were extracted with each batch of samples to examine the background concentrations (Li et al., 2013; Wu et al., 2012). The five-point standard calibration was run before and after instrumental analysis to affirm the accuracy of each sample, which

also showed the strong linearity ($r^2 > 0.99$) (Li et al., 2013; Wu et al., 2012). The limit of detection (LOD) and limit of quantification (LOQ) of the target PFASs were individually defined as the concentration needed to produce a signal–noise ratio of 3:1 and 10:1 in human serum, urine, hair and nail respectively and listed in Appendix A Table S1. The reference material of human serum (SRM1957 and SRM1958) from National Institute of Standards and Technology were successfully used to validate the accuracy of our experiments. However there were no reference material for human hair, nail and urine. For PFASs in human hair, nail and urine, the recovery tests were employed to validate the accuracy and precision of methods. The recovery values ($n = 6$) ranged from 90% to 114% in hair and 91% to 112% in nail with the spiked level of 1 ng/g, as well as 85% to 103% in urine with the spiked level of 20 ng/L. And the corresponding RSD ranged from 4.4%–18% in hair, 2.6%–11% in nail and 4.6%–17% in urine respectively.

1.6. Statistical analysis

Due to the skew distribution of the data, Mann–Whitney U test was employed to compare the levels of PFASs in different matrices from gender and age groups, and Spearman correlation test was used to show the correlations among different matrices employing the software of SPSS 19.0. Levels for the samples below LOD were set to be LOD/√2 and lower than LOQ but above LOD were set to be LOQ for statistical analysis (Li et al., 2013; Zhang et al., 2013a).

2. Results and discussion

2.1. Levels and composition profiles of PFASs in human serum, urine, hair and nail

PFHxA was only detected in nail with the detection frequency (DF) of 12.82%. PFDoA was found in urine, hair and nail with low frequencies (<15%), and detected in serum at trace levels with the DF of 66.67%. Consequently we only discussed six PFASs, which consist of PFOA, PFNA, PFDA, PFUnDA, PFHxS and PFOS.

The levels and DF of six PFASs in human serum, urine, hair and nail are summarized in Table 1. The six PFASs were found in all serum samples. PFOS was detected with high DF in hair (92.31%) and nail samples (87.18%). While, in urine samples, PFOS was detected with DF of 76.92%. PFOA was detected in 71.79% hair samples, while in a few urine (33.33%) and nail samples (17.95%). Besides, the DF of PFNA, PFDA and PFUnDA in nail was much higher than that in urine and hair. Moreover PFHxS was not detected in hair samples. In general, the DF of PFOS was higher than that of other PFASs in four matrices.

In addition, the median concentration of PFOS was also higher than that of other PFASs in four matrices. The median concentration of PFOS in serum, urine, hair and nail were 9.24 ng/mL, 13.96 ng/L, 0.58 ng/g and 0.63 ng/g, respectively. Compared with other studies in China, for the serum matrix, the median levels of PFOA and PFOS in serum in this study were higher than that in Shanxi (Li et al., 2013), Liaoning (Liu et al., 2009), and some cities around Bohai Sea (Guo et al., 2011). The median concentrations of PFHxS and PFOS in this study in serum were lower than that in Hebei province, while the median levels of PFOA, PFNA, PFDA and PFUnDA were slightly higher than that in Hebei province (Zhang et al., 2013b). The results indicated that the PFASs concentrations of Shenzhen were at a relative higher level in China. Zhao et al. (2014) measured the PFASs concentrations of sediment and biota in the Pearl River Delta of South China. Their results indicated that the PFASs levels in Shenzhen are much higher than other region, which is similar to our study. Compared with the studies reported in other countries, the median concentrations of the six PFASs in serum from Shenzhen were much lower than that in South Korea (Kim et al., 2014), but the mean levels of six PFASs in serum were much higher than that in Spain (Ericson et al., 2007) except PFHxS. Moreover the median levels of PFOA, PFNA and PFHxS in serum were much lower than that in HK and Korea, while the PFOS level was a slightly higher than that in HK

Table 1 – Concentrations of the primary PFCs in human serum, urine, hair and nail.

		PFOA	PFNA	PFDA	PFUnDA	PFHxS	PFOS
Serum (ng/mL)	Detection frequency	100%	100%	100%	100%	100%	100%
	Range	0.72–6.40	0.35–2.05	0.11–1.39	0.11–1.63	0.12–2.67	2.39–31.65
	Mean	2.37	0.79	0.69	0.69	0.70	9.77
	Media	1.96	0.76	0.69	0.69	0.50	9.24
Urine (ng/L)	Detection frequency	33.33%	5.13%	7.69%	10.26%	10.26%	76.92%
	Range	<1.07–36.17	<0.56–1.89	<0.44–1.75	<0.83–< 2.14	<1.41–104.23	<2.09–80.74
	Mean	4.61	0.46	0.39	0.75	6.91	18.71
	Media	<1.07	<0.56	<0.44	<0.83	<1.41	13.96
Hair (ng/g)	Detection frequency	71.79%	23.08%	5.13%	17.95%	–	92.31%
	Range	<0.03–0.96	<0.04–0.48	<0.06–0.22	<0.06–0.33	–	<0.03–1.60
	Mean	0.25	<0.12	<0.06	<0.20	–	0.60
	Media	0.26	<0.04	<0.06	<0.06	–	0.58
Nail (ng/g)	Detection frequency	17.95%	51.28%	56.41%	92.31%	17.95%	87.18%
	Range	<0.04–0.46	<0.02–3.38	<0.07–0.47	<0.04–0.70	<0.09–3.39	<0.05–1.89
	Mean	<0.14	0.27	<0.24	0.23	0.44	0.69
	Media	<0.04	<0.07	<0.24	0.21	<0.09	0.63

PFOA: perfluoroctanoic acid; PFNA: perfluorononanoic acid; PFDA: perfluorodecanoic acid; PFUnDA: perfluoroundecanoic acid; PFHxS: perfluorohexanesulfonate; PFOS: perfluorooctanesulfonate.

(Wan et al., 2013) and Korea (Ji et al., 2012). For the urine matrix, the median PFOS concentration is similar with the result determined by Zhang et al. (2013a), and much lower than Li et al. (2013), while PFOS was not found in 30 samples by Perez et al. (2012). For PFOA in urine, the median level in our study is much lower than some researches (Li et al., 2013; Perez et al., 2012; Zhang et al., 2013a, 2015), and PFHxs is also much lower than the study published by Perez et al. (2012). With regard to PFOA and PFOS in human hair, the levels detected by Perez et al. (2012) and Li et al. (2013) are much higher than our result, while PFOS was not found by Alves et al. (2015). Moreover the concentrations of PFOA and PFOS in nail samples is much lower than that in Dalian (Liu et al., 2011a; 2011b), Shanxi (Li et al., 2013), Shenyang and Liaoyang (Xu et al., 2010). In a word, compared with other studies, PFASs concentrations of human urine, hair and nail in our research were at a relative lower level.

As shown in Fig. 1, PFOS was the leading PFAS found in four matrices. The percentage contribution of PFOS in hair (61.01%) and nail (50.68%) were close to that in serum (66.8%). However the value increased to 96.86% in urine, which indicated that urine is a probable way for human to excrete PFOS. Moreover the percentage of PFOA in hair (27.29%) was much higher than that in other matrices (range of 0.78%–14.15%), which was also observed in our previous study (Li et al., 2013). This result suggested that hair was a special carrier for PFOA bioaccumulation. In addition, the percentage of PFDA (18.85%) and PFUnDA (16.92%) in nail was also much higher than that in other matrices. Besides, the percentage of PFHxS in urine (21.73%) and nail (23.50%) were much higher than that in serum (4.69%) and hair (0%), which indicated that PFHxS may be more easily occurring in urine and nail.

2.2. Gender and age effect

In the present study, we only discussed the gender and age effect for the PFASs with the DF more than 30%. The median concentrations in male and female groups are shown in Table 2. Mann–Whitney U test showed that there were significant differences in concentrations for PFOA and PFHxS in serum between male and female groups ($p < 0.01$). The concentrations of PFOA and PFHxS in male groups were much higher than that in female groups. The studies in Wenzhou (Zhang et al., 2011), HK (Wan et al., 2013), Taiwan (Hsu et al., 2013) and Korea (Ji et al., 2012) showed that the PFOS level in serum or blood was significantly higher in males than in females, which were not found in this study. However the studies in HK (Wan et al., 2013), Korea (Ji et al., 2012) and Spain (Ericson et al., 2007) indicated that the levels of PFOA and PFHxS in serum or blood were significantly higher in men than in women, the study of South Korea (Kim et al., 2014) showed no gender effect for ∑PFASs. Moreover in this study, the statistical difference of PFASs was not observed between male and females in urine, hair and nail, which was different from our previous study (Li et al., 2013).

We divided the 39 donors to younger (<38 years old, $n = 18$) and older groups (≥38 years old, $n = 21$). The median concentration of the two groups is shown in Table 2. No statistically significant difference was observed in PFASs concentrations between the younger and older groups in four matrices ($p > 0.05$). Some studies (Wan et al., 2013; Zhang et al., 2011) also observed that no statistically significant difference for PFASs between the older and younger people in blood, whereas Ericson et al. (2007) found that the PFHxS level in the younger group (25 ± 5 years) was higher than that in the older group (55 ± 5 years) in blood ($p < 0.05$). However Kim et al. (2014) observed that the blood levels of PFOA and PFOS in older people were statistically significant higher than that in younger people. Moreover any correlation between the PFASs levels and age could not be found in four matrices in the present study, while Ji et al. (2012) found that the blood concentrations of PFOA, PFNA, PFDA, PFUnDA, PFHxS and PFOS were elevated with age ($p < 0.01$) for people under 60 years old. Hsu et al. (2013) also observed that the PFOS level in serum increased with age. The inconsistent results mentioned above for gender and age effect are most probably due to the sampling populations, sampling sites, the number of samples and the concentration levels.

2.3. Correlation analysis

The Spearman correlation test showed that PFOA, PFNA, PFDA, PFUnDA, PFHxS and PFOS were significantly correlated in human serum, ranged from 0.419 to 0.942 ($p < 0.01$), which suggested that these PFASs probably had a common pollution source, and a similar result was found in Spain (Ericson et al., 2007). In addition, due to the low DF of PFASs in urine, hair and nail, we only discussed the correlation between PFOA and PFOS in urine and hair, and PFNA, PFDA, PFUnDA and PFOS in nail. The results only showed that PFUnDA and PFOS were significantly correlated in nail, with the Spearman correlation coefficient of 0.359 ($p < 0.05$).

One of the leading characteristics of suitable matrices for biomonitoring is the relationship between chemical concentrations in the matrices and the real body burden which was usually expressed by concentration in serum or blood (Li et al., 2013). The Spearman correlation test showed that PFOS level in serum and nail were significantly correlated ($r = 0.579$, $p < 0.001$), which indicated that the PFOS level in nail could substitute for the serum concentration of PFOS to monitor the human exposure level. Besides, the median concentrations trend of PFOS in serum and nail for the gender and age group is similar. A significant correlation was also found for PFUnDA level in serum and nail ($r = 0.624$, $p < 0.001$). Besides, W. Liu et al. (2011) also observed that fingernail and toenail PFOS

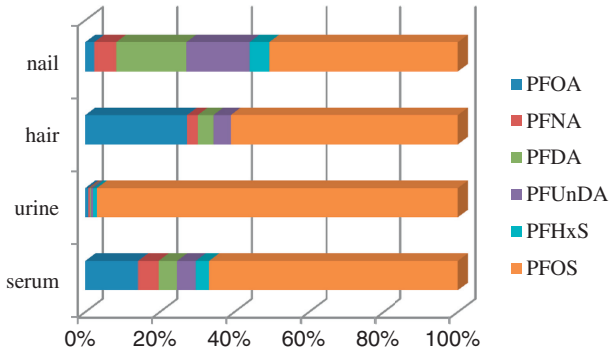

Fig. 1 – Composition profiles of six PFCs in human serum, urine, hair and nail.

Table 2 – Media concentrations in human serum, urine, hair and nail for gender and age groups.

		PFOA	PFNA	PFDA	PFUnDA	PFHxS	PFOS
Serum (ng/mL)	Male	2.84	0.82	0.73	0.70	0.80	11.54
	female	1.52	0.69	0.67	0.68	0.46	8.05
	<38	2.03	0.73	0.62	0.68	0.50	7.80
	≥38	1.96	0.77	0.72	0.70	0.50	10.36
Urine (ng/L)	Male	<1.07	–	–	–	–	19.54
	female	<1.07	–	–	–	–	12.51
	<38	<1.07	–	–	–	–	19.968
	≥38	<1.07	–	–	–	–	12.492
Hair (ng/g)	Male	0.17	–	–	–	–	0.54
	female	0.29	–	–	–	–	0.66
	<38	0.29	–	–	–	–	0.56
	≥38	0.20	–	–	–	–	0.58
Nail (ng/g)	Male	–	<0.02	<0.07	0.19	–	0.66
	female	–	0.07	0.24	0.22	–	0.61
	<38	–	<0.02	0.24	0.21	–	0.57
	≥38	–	0.14	0.24	0.23	–	0.66

PFOA: perfluoroctanoic acid; PFNA: perfluorononanoic acid; PFDA: perfluorodecanoic acid; PFUnDA: perfluoroundecanoic acid; PFHxS: perfluorohexanesulfonate; PFOS: perfluorooctanesulfonate.

concentrations significantly correlated with the serum concentration. The plots of the correlation of PFOS and PFUnDA level in nail are shown in Fig. 2. No correlation was observed for other PFASs between serum and urine and hair and nail. Zhang et al. (2013a) observed the strong correlations between most PFASs levels in urine and blood, whereas only the significant correlation of PFOA between whole blood and urine was found in another study (Zhang et al., 2015).

The method sensitivity is another key factor for the suitable biomonitoring matrices. Due to the trace level of PFASs in urine, hair and nail, the requirements on the sensitivity of the methods for these matrices are higher than that for serum. In this study low DF for urine, hair and nail impacted the correlation analysis of PFASs levels between serum and these non-invasive samples. Even using the state-of-the-art method, increasing the urine, hair and nail sample amount for analysis may be a proper approach, especially for the general population.

3. Conclusions

We detected the PFASs concentrations of 39 matched human serum, urine, hair and nail samples from Shenzhen in China. The DF and the median level of PFOS were all higher than that of other PFASs in four matrices. Besides, PFOS was also the leading PFAS found in four matrices. The Mann–Whitney U test showed that there were significant differences in concentrations for PFOA and PFHxS between male and female group ($p < 0.01$) in serum. However there was no statistically significant difference in PFASs concentrations between the younger and older groups in four matrices ($p > 0.05$). Furthermore, the Spearman correlation tests showed that PFOS and PFUnDA levels in serum and nail were significantly correlated ($r = 0.579$ for PFOS, $r = 0.624$ for PFUnDA, $p < 0.001$). The results of present study suggested nail could be better than other non-invasive matrixes for PFASs, especially for PFOS, biomonitoring in general populations.

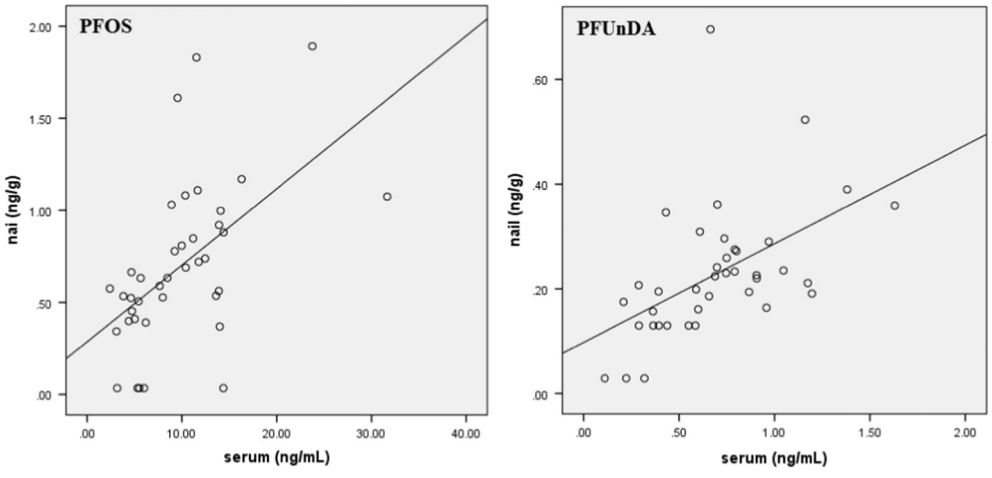

Fig. 2 – Correlation plots of PFOS and PFUnDA level in nail.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jes.2017.08.017.

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