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Dermal bioaccessibility of perfluoroalkyl substances from household dust; influence of topically applied cosmetics

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ABSTRACT

PFAS are known contaminants of indoor dust. Despite the adherence of such dust to skin, the dermal penetration potential of PFAS is not well understood. By applying *in vitro* physiologically based extraction tests, the bioaccessibility of 17 PFAS from indoor dust to synthetic human sweat sebum mixtures (SSSM) was assessed. The composition of the SSSM substantially impacted the bioaccessibility of all target compounds. PFAS bioaccessibility in a 1:1 sweat:sebum mixture ranged from 54 to 92% for perfluorocarboxylic acids (PFCAs) and 61–77% for perfluorosulfonic acids (PFSAs). Commonly applied cosmetics (foundation, sunscreen, moisturiser, and deodorant) significantly impacted the dermal bioaccessibility of target PFAS, e.g., the presence of moisturiser significantly decreased the total bioaccessibility of both PFCAs and PFSAs. Preliminary human exposure estimates revealed dermal contact with indoor dust could contribute as much as pathways such as drinking water and dust ingestion to an adult's daily intake of PFAS. While further research is needed to assess the percutaneous penetration of PFAS in humans, the current study highlights the potential substantial contribution of dermal exposure to human body burdens of PFAS and the need for further consideration of this pathway in PFAS risk assessment studies.

1. Introduction

Per- and polyfluoroalkyl substances (PFAS) have been in production and widely used since the 1940s. Their chemical and thermal stability, as well as their hydrophobic and lipophobic properties make PFAS suitable for use in a broad range of products, such as: aqueous fire-fighting foams (AFFF), textiles and personal care products (Buck et al., 2011; Glüge et al., 2020; Harrad et al., 2019; Whitehead et al., 2021). However, the physicochemical properties of PFAS also result in their global distribution, with perfluorooctane sulfonate (PFOS) being identified in polar bears and other wildlife in remote areas, as far back as the early 2000s (Giesy and Kannan, 2001). Moreover, different PFAS have been identified in human sera from all over the world (Haug et al., 2011; Kim et al., 2019; Sunderland et al., 2019). Consequently, many studies have focused on the possible adverse human health effects of PFAS exposure, with the European Food Safety Authority (EFSA) highlighting the reduced immune response to vaccination (Grandjean et al., 2012, 2017; Abraham et al., 2020), decreased birth weight (Meng et al., 2018; Sagiv et al., 2018), and impaired liver function (Salihovic et al., 2018) leading to a recommended tolerable weekly intake of 4.4 ng/kg bw/week for the sum of four PFAS (perfluorohexane sulfonic acid (PFHxS), PFOS, perfluorooctanoic acid (PFOA) and perfluorononanoic acid (PFNA)) (EFSA CONTAM Panel and (EFSA Panel on Contaminants in the Food Chain), 2020).

Studies on human exposure have found diet and drinking water to be the greatest contributors to total human adult exposure to PFAS, followed by inhalation of indoor air and ingestion of indoor dust (Harrad et al., 2019; Haug et al., 2011; Sunderland et al., 2019). However, despite the known presence of PFAS in indoor dust and the adherence of such dust to skin, dermal uptake arising from indoor dust is poorly understood. Moreover, recent studies have highlighted the huge variety of PFAS applications in products that come in contact with the skin e.g., personal care products and clothing (Glüge et al., 2020; Whitehead et al., 2021; Schultes et al., 2018; Xia et al., 2022). Finally, recent *in vivo* studies on rats and one human subject showed that PFAS are able to penetrate the skin and considerably contribute to total body burdens (Chen et al., 2022; Abraham and Monien, 2022). Despite this, very little is known about the human dermal uptake of PFAS and very few studies have investigated this exposure pathway (Ragnarsdóttir et al., 2022).

The surface of human skin is covered with a skin surface film liquid

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(SSFL) composed of a mixture of sweat and sebum. Sebum is a clear, oily substance secreted by sebaceous glands which are found in most areas of the body. Sweat is an aqueous solution containing various electrolytes, vitamins, amino acids, organic acids, and nitrogenous substances (Nicolaides, 1974; Stefaniak and Harvey, 2008). As a first step in the process via which chemicals present in materials coming into contact with the skin may undergo dermal uptake; chemicals must dissolve from such materials into the SSFL, in order to become available for dermal absorption (i.e. *bioaccessible*) (Luo et al., 2020). Dermal *in vitro* physiologically-based extraction tests have been used to determine the dermal bioaccessibility of various xenobiotics, both inorganic and organic, e.g. sensitising metals, flame retardants, plasticisers, and pesticides (Ertl and Butte, 2012; Pawar et al., 2017; Stefaniak et al., 2014; Zeng et al., 2019).

To differentiate, *bioavailability* is defined as "the fraction of a chemical that reaches the systemic circulation", *bioaccessibility*, on the other hand, refers to the fraction of a chemical that is released into the body's fluids (SSFL for skin) from a matrix (e.g., *dust*) making it available for absorption (Ertl and Butte, 2012; Pawar et al., 2017; Ruby et al., 1996). In other words, a chemical within a matrix (e.g., *dust*) or product (e.g., *fabric*) must become *bioaccessible* first, in order to be available for absorption by the skin. However, it is not guaranteed that all the *bioaccessible* fraction of a chemical will penetrate the skin barrier to reach the systemic circulation (*i.e.,* become bioavailable). A potential oversight therefore is that *in vitro* dermal absorption studies rarely account for chemical release from a source matrix into the fluids on the skin surface, which could be a rate limiting step in dermal absorption (Collins et al., 2015). Thus, a combination of data on bioaccessibility and subsequent percutaneous penetration is necessary to fully understand the extent of human dermal uptake of chemicals (e.g., PFAS) (Pawar et al., 2017; Abdallah et al., 2012).

Certain ingredients of cosmetics (e.g., sunscreens and moisturisers) can remain on the skin for a long time and affect the properties of the SSFL. Furthermore, this could alter the skin's hydration or interact with the proteins in the skin barrier, altering the lipid-protein domain of the skin and enhancing the dermal permeability for other chemicals (Lane, 2013). This has been shown in previous studies where sunscreen lotions enhanced the dermal penetration of contaminants such as herbicides and flame retardants (Pawar et al., 2017; Pont et al., 2004). Thus, it is important to investigate the possible effects of topically applied cosmetics when studying the dermal bioaccessibility of PFAS in indoor dust.

In the current study, we investigate for the first time, the dermal bioaccessibility of several PFAS, including C_4–C_{14} perfluorocarboxylic acids (PFCAs) and C_4–C_{10} perfluorosulfonic acids (PFSAs). The bioaccessible fractions of these PFAS from indoor dust to various physiologically relevant mixtures of synthetic human SSFL were quantified and the impact of different topically applied cosmetics on PFAS bioaccessibility was investigated. Finally, the potential for human exposure to PFAS via dermal contact with indoor dust was assessed and compared to other well-studied exposure pathways (*i.e.,* diet and drinking water).

2. Materials and methods

2.1. Materials

The standard reference material (SRM2585, organics in house dust, particle size <100 μm and total moisture content = 2.11 ± 0.06%) was purchased from NIST (Gaithersburg, MD, USA). HPLC grade methanol, ammonium acetate, ammonium hydroxide, Optima LC-MS grade methanol, and Optima LC/MS grade water were obtained from Fisher Scientific (Loughborough, UK). Native and mass labelled PFAS standards were purchased from Wellington Laboratories Inc. (Guelph, Canada). The target compounds are listed in Tables SI–3.

2.2. Synthetic sweat and sebum mixture preparation

Synthetic sweat and sebum mixtures (SSSM) simulating physiological human skin surface film liquid were prepared according to a previously reported US patent (Stefaniak and Harvey, 2008). Artificial sweat and sebum mixtures were prepared separately (See Tables SI–1 for detailed ingredients list), the sweat mixture was pH adjusted to that of normal human skin (5.3 ± 0.1) and both solutions stored at 5 °C. Sweat: sebum mixtures were prepared at different, physiologically relevant ratios (100% sweat, 95:5 sweat:sebum, 1:1 sweat:sebum and 100% sebum), using drops of Tween-80 to prevent phase-separation and simulate naturally secreted SSFL (Stefaniak and Harvey, 2008; Pawar et al., 2017).

2.3. Dermal bioaccessibility in vitro test protocol

The bioaccessibility test was based on protocols reported previously (Ertl and Butte, 2012; Pawar et al., 2017). In brief, 60 mg SRM2585 dust were accurately weighed into a clean, dry test tube. When tested, ca. 6 mg of personal care products (moisturiser, sunscreen, foundation, and deodorant, all tested separately) were accurately weighed into the same test tube. As the dust-to-sweat ratio on human skin can vary, "wet skin conditions" were chosen based on a previous study (Ertl and Butte, 2012). Thus, 1:100 w/v dust:SSSM ratio was used and 6 mL sweat:sebum mixture was added to the test tube. The mixture was gently stirred and kept at physiological skin temperature (32–34 °C) using a heated magnetic stirrer plate. After 1 h the two phases were separated by centrifugation at 3900 RPM for 15 min. All experiments were conducted in triplicate. The resulting dust (solid residue, n = 36) and the SSSM (supernatant, n = 36) samples were analysed separately.

2.4. Sample extraction and clean-up

2.4.1. Dust samples

Dust sample extraction and preparation was based on a previously reported method (Harrad et al., 2020). Triplicate samples (ca. 60 mg each) of unexposed SRM2585 were analysed separately in addition to the exposed dust samples. Briefly, samples were extracted with basic methanol by ultrasonication followed by a clean-up with EnviCarb™ SPE cartridges. A detailed description of the method is provided in the Supporting Information.

2.4.2. SSSM samples

The extraction and preparation of SSSM supernatant samples was based on a method previously reported (Harrad et al., 2019). In short, samples were extracted using a Chromabond™ PFAS (6 mL/300 mg, Chromabond) SPE cartridge followed by clean-up using EnviCarb™ SPE cartridges. A detailed description of the extraction method is provided in the Supporting Information.

2.5. Chemical analysis

Target PFAS were analysed on a Sciex Exion UPLC coupled to a Sciex 5600+ triple TOF MS operated in negative mode based on a previously reported method (Harrad et al., 2019). Detailed instrumental parameters are provided in the Supporting Information.

2.6. Quality assurance and quality control

All experiments were performed in triplicate and one procedural blank prepared for every 6 samples. Additionally, sample blanks containing only SSSM and personal care product were included for each tested personal care product. Identification and quantification of target analytes were performed according to the relative retention times to the corresponding isotope labelled surrogate standard and the accurate mass of each target PFAS. In most blanks, none of the target compounds

were detected. However, a few showed measurable concentrations of some target PFAS (PFDoA in 40% of blanks, PFTrDA in 16% and PFNA, PFOA, PFPeA, PFDoA, PFTrDA, and PFTeDA, in 25% of cosmetics blanks) In such instances, no blank correction was performed when the concentration in the blank was <5% of the average sample concentration from the same sample batch. Blank correction was performed in the instances where the blank concentration was between 5 and 20% of average sample concentrations.

Further details on QA/QC measures including recoveries of internal (surrogate) standards, method accuracy, precision, and limits of quantification, as well as mass balance results for each SSSM composition and cosmetic product studied are provided as Supporting Information (Tables SI-3 and SI-5 to SI-15).

2.7. Assessment of dermal bioaccessibility

Bioaccessibility is expressed as $f_{bioaccessible}$, calculated as the percentage of each target PFAS detected in the supernatant after exposure compared to the unexposed dust (eq. (1)). All experiments were carried out in triplicate, thus average values were used:

$$f_{bioaccessible}(\%) = \frac{Average\ mass\ of\ PFAS\ in\ supernatant}{Average\ mass\ of\ PFAS\ in\ dust} * 100 \quad (1)$$

2.8. Statistical analysis

Statistical analysis of data was conducted using Microsoft Excel (Microsoft Office 365) and SPSS 26 for Windows. Means of various data sets were estimated and compared using ANOVA followed by Tukey's Honest Significant Difference (HSD) *post hoc* test or the Games -Howell test when a test of homogeneity showed no equal variance ($p < 0.05$). P-values of <0.05 were considered significant.

3. Results and discussion

3.1. Dermal bioaccessibility of PFAS in indoor dust

Fig. 1 depicts the $f_{bioaccessible}$ of target PFCAs and PFSAs from indoor dust in the different SSSM. Average $f_{bioaccessible}$ values of target PFAS can be found in Tables SI–7. Our results show that four of the target PFCAs were 100% bioaccessible from dust particles; PFHxA in 100% sweat, PFPeA in 95:5 sweat:sebum, and PFDA and PFTeDA in 100% sebum (Tables SI–6). While the composition of SSSM in real-life varies, 1:1 sweat:sebum is considered the most physiologically relevant ratio (Buckley and Lewis, 1960; Stefaniak and Harvey, 2006). The ratios examined here were chosen to account for different physiologically

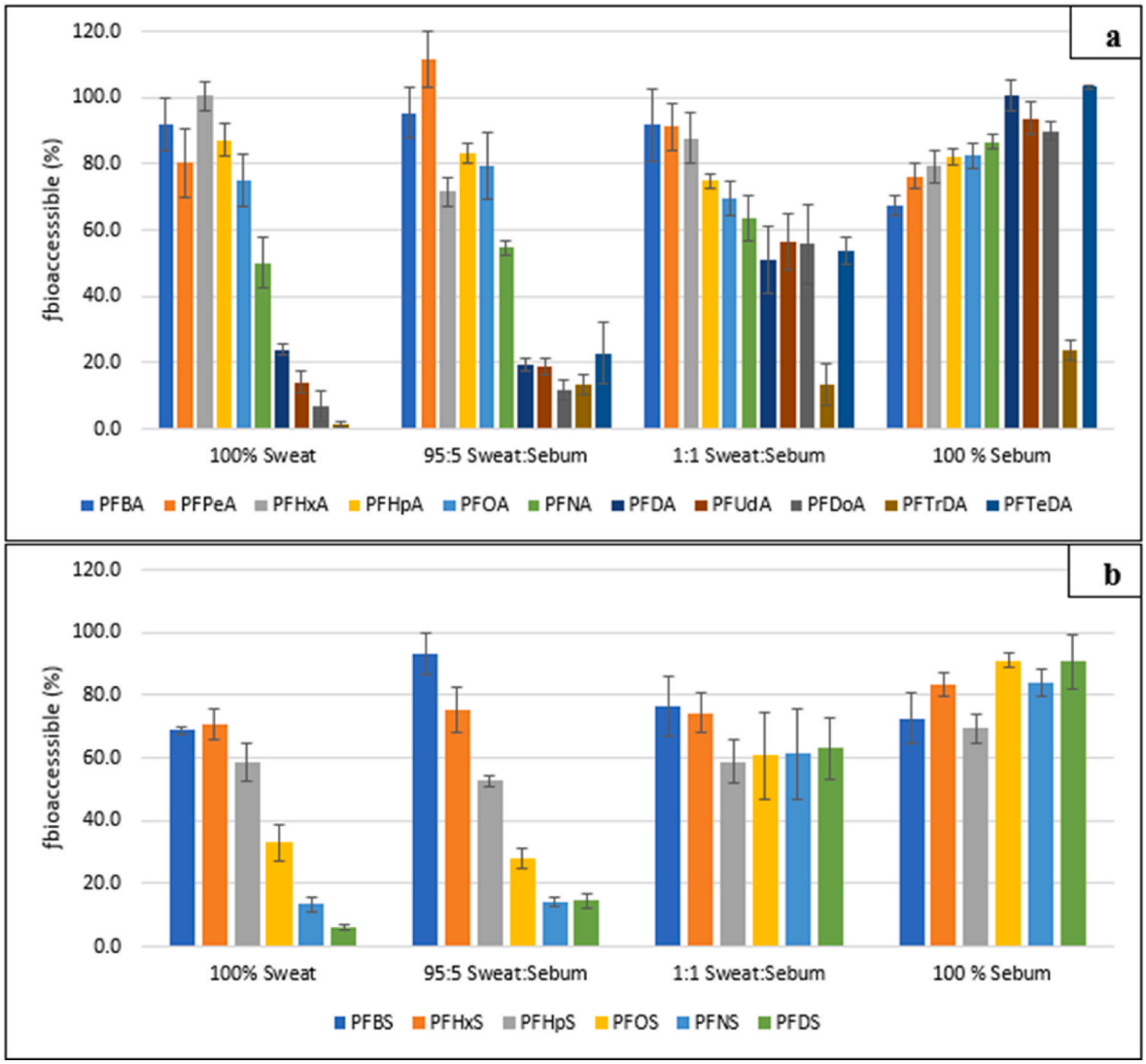

Fig. 1. Dermal bioaccessibility of (a) PFCAs and (b) PFSAs in different composition of synthetic sweat sebum mixtures. Error bars represent the standard deviation (n = 6).

relevant SSSM, as well as the two extremes (100% sweat and 100% sebum). When comparing the total PFAS bioaccessibility between the different SSSM compositions; a Games-Howell Post Hoc test revealed that total PFAS bioaccessibility in 100% sebum significantly exceeded that in 100% sweat ($p = 0.01$), and the same was seen when comparing 100% sebum and 95:5 sweat: sebum ($p = 0.028$). Our results show that the target PFAS are bioaccessible at varying levels in all SSSM mixtures, making those PFAS available for absorption through human skin.

Comparison of the bioaccessibility of PFAS in 100% sweat and 100% sebum revealed a clear trend for both PFCAs and PFSAs (Fig. 1). The general trend observed in 100% sweat was that the bioaccessibility decreased with increasing chain length with the $f_{bioaccessible}$ ranging from <LOD (PFTeDA) to 92.0 ± 7.9% (PFBA) for PFCAs ($r = -0.95$, $p \leq 0.001$), and 6.1 ± 0.7% (PFDS) to 68.9 ± 1.1% (PFBS) for PFSAs ($r = -0.92$, $p = 0.008$). The opposite trend was seen in 100% sebum with $f_{bioaccessible}$ values ranging from 103.3 ± 0.54% (PFTeDA) to 67.4 ± 2.8% (PFBA) for PFCAs ($r = 0.91$, $p \leq 0.001$(PFTrDA excluded)). While the same trend appeared for PFSAs, it was not significant ($r = 0.68$, $p =$

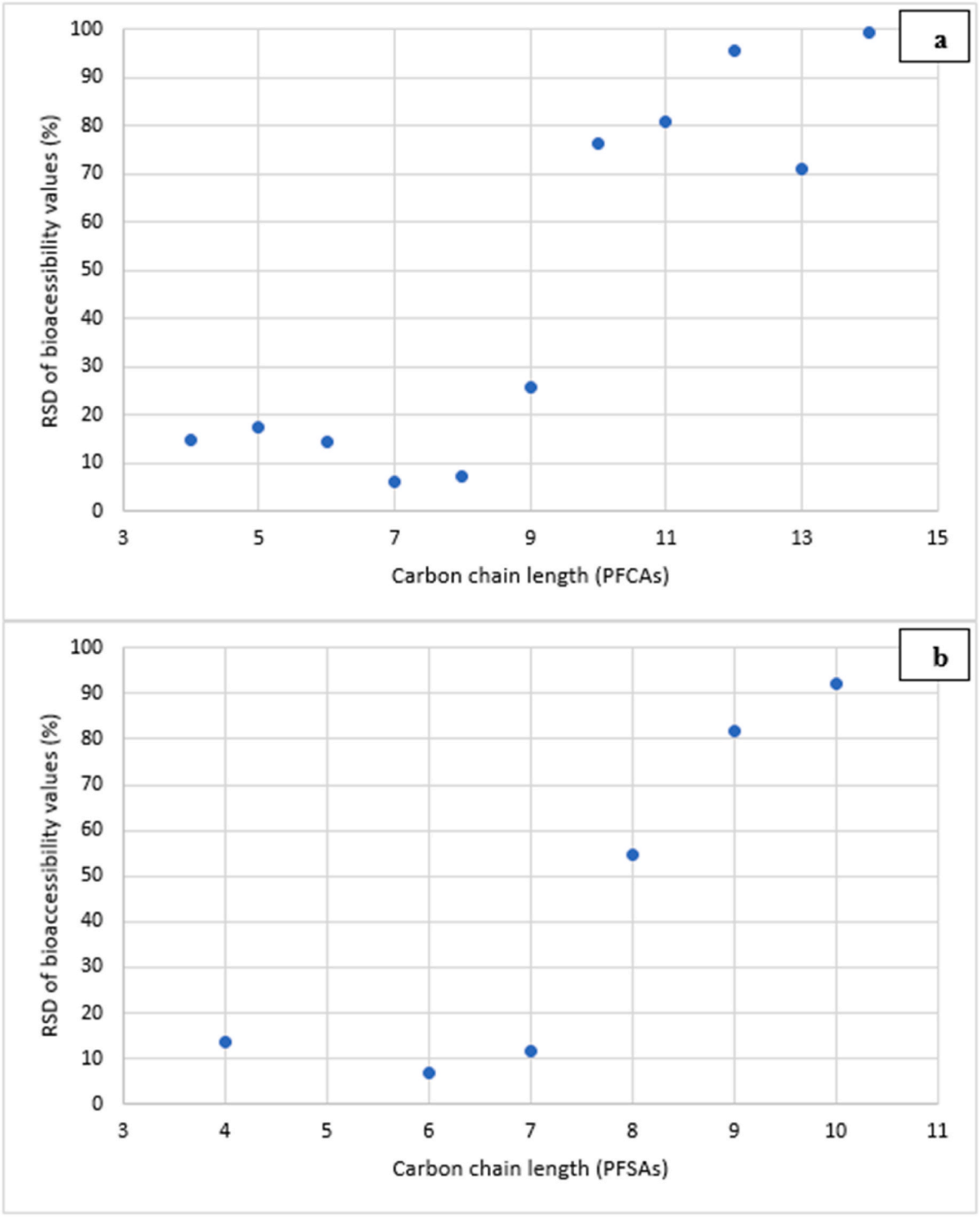

Fig. 2. Plot of PFAS carbon number versus relative standard deviation (RSD) of the bioaccessibility values obtained for individual PFAS across the range of SSSM compositions examined for: (a) PFCAs and (b) PFSAs.

0.14) with the $f_{bioaccessible}$ ranging from 90.8 ± 8.9% (PFDS) to 72.6 ± 8.1% (PFBS). These trends are indicative of the physicochemical properties of the PFAS examined, *i.e.,* the more ionic character of the short-chain PFAS that leads to low $logK_{ow}$ and high water solubility and the less ionic character of the long-chain PFAS has the opposite effects (Tables SI–4).

In general, PFAS $f_{bioaccessible}$ values were more similar for the shorter chain compounds (Carbon number ≤7 for PFCAs and ≤6 for PFSAs) in the different SSSM compositions with no significant differences noted. For longer chain compounds however, the $f_{bioaccessible}$ in 1:1 sweat:sebum significantly exceeded those in 100% sweat ($p = 0.001$ (PFTrDA excluded). The, $f_{bioaccessible}$ trends in 95:5 sweat:sebum were akin to those in 100% sweat, with no significant differences in bioaccessibility seen for neither short-chain or long-chain compounds ($p = 0.990$). The $f_{bioaccessible}$ in the most physiologically relevant SSSM (1:1 sweat:sebum) (Stefaniak and Harvey, 2006) exceeded 50% for all studied PFAS (except PFTrDA, 10.2 ± 6.3), ranging from 51.3 ± 10.1% (PFDA) 91.7 ± 10.8 (PFBA) for PFCAs and 60.7 ± 13.7% (PFOS) 76.6 ± 9.4 (PFBS) for PFSAs.

As PFAS chain length increased, the dependence of bioaccessibility on the SSSM composition increased, with the shorter chain compounds less affected by the SSSM composition. This is illustrated in Fig. 2 which plots the relative standard deviation of the $f_{bioaccessible}$ of a given PFAS across the range of SSSM compositions examined, against PFAS carbon number for both PFCAs and PFSAs.

The overall trends seen for both PFCAs and PFSAs can be attributed to the different properties of the aqueous-based sweat compared to the oily sebum and the varying physicochemical properties of our target PFAS based on chain length (e.g., $logK_{OW}$ and water solubility (Tables SI–4)). There is a significant negative correlation between $f_{bioaccessible}$ and $logK_{ow}$ in 100% sweat for both PFCAs ($r = -0.95$, $p \leq 0.001$) and PFSAs ($r = -0.93$, $p = 0.006$). In 100% sebum however, the $f_{bioaccessible}$ and the $logK_{ow}$ PFCAs did not show a correlation ($r = 0.06$, $p = 0.85$), while PFSAs showed a moderate positive correlation although not significant ($r = 0.68$, $p = 0.14$). In the most physiologically-relevant SSSM (1:1 sweat:sebum) a significant negative correlation was seen for PFCAs for the $f_{bioaccessible}$ and the $logK_{ow}$ ($r = -0.86$, $p \leq 0.001$). While a negative correlation was also seen for PFSAs in the 1:1 mixture, it was not significant ($r = 0.76$, $p = 0.08$). Figs. SI–1, which shows the $f_{bioaccessible}$ values of each individual PFAS averaged across all 4 SSSMs further supports this overall trend, where the PFAS average $f_{bioaccessible}$ decreased with increasing chain length.

When calculating the correlation between $f_{bioaccessible}$ and water solubility, no clear correlation was seen in 100% sweat ($r = 0.32$, $p = 0.54$ and $r = 0.36$, $p = 0.76$ for PFCAs and PFSAs, respectively). Similarly, in the 1:1 sweat:sebum mixture, no correlation was seen ($r = 0.53$, $p = 0.28$ (PFCAs) and $r = 0.60$, $p = 0.59$ (PFSAs)). In 100% sebum a negative correlation was seen between $f_{bioaccessible}$ and water solubility ($r = -0.88$, $p = 0.02$) for PFCAs, while this trend was not seen for PFSAs ($r = -0.29$, $p = 0.14$). It is worth noting that a unified single experimental and/or modelled approach that provides accurate values of physicochemical properties for all the studied PFAS could not be found in the available literature, which may affect the reliability of the statistical analysis conducted because the reported values for e.g., $logK_{ow}$ and water solubility of different PFAS were obtained from different sources using different approaches for their estimation.

3.2. Effects of cosmetics on the dermal bioaccessibility of PFAS from indoor dust

The topical application of personal care products or cosmetics may either enhance or diminish the release of a chemical ($f_{bioaccessible}$) from particles adhering to the skin (Pawar et al., 2017). To evaluate the effect of cosmetics on the dermal bioaccessibility of PFAS in indoor dust, we estimated the $f_{bioaccessible}$ of target PFAS from dust into 1:1 sweat:sebum mixture in the presence of four different, widely used personal care products (each tested separately). The 1:1 sweat:sebum mixture was used as the control as it is considered the most physiologically relevant composition (Buckley and Lewis, 1960). The products evaluated were sunscreen lotion, moisturising cream, deodorant stick, and foundation. As the aim of our study was to investigate the impact of cosmetics on the bioaccessibility of PFAS from indoor dust, rather than the release of PFAS from cosmetics; none of the chosen cosmetic products contained PFAS. Sample blanks containing a personal care product and SSSM mixture not exposed to dust were included for each tested product.

3.2.1. Influence of topically applied cosmetics on the dermal bioaccessibility of PFAS

The effects of the application of cosmetics on the overall $f_{bioaccessible}$ of PFCAs from indoor dust was compared to the $f_{bioaccessible}$ in the control SSSM mixture, and the statistical significance of the observed differences were determined using a paired *t*-test. Two products significantly affected the overall $f_{bioaccessible}$ of PFCAs: sunscreen ($p = 0.04$) and moisturising cream ($p = 0.03$), both of which decreased PFCAs bioaccessibility from dust (Fig. 3). This is especially evident for the longer chain PFCAs (PFDoA, PFTrDA and PFTeDA) which were not detected in the SSSM (*i.e., were not bioaccessible*) after the addition of sunscreen. For PFDA and PFUdA however, the addition of sunscreen seemed to increase their $f_{bioaccessible}$ values, while no difference was seen for PFHxA, PFOA and PFNA. The inclusion of deodorant increased the $f_{bioaccessible}$ values for selected PFCAs (PFHxA, PFHpa, PFNA, PFDA, PFUdA and PFTeDA) while the $f_{bioaccessible}$ for $\sum$PFAS was not significantly increased.

All but one of the personal care products examined, significantly affected the overall $f_{bioaccessible}$ of PFSAs compared to the 1:1 sweat:sebum mixture (Fig. 3). The $f_{bioaccessible}$ values of PFSAs decreased in the presence of foundation ($p = 0.01$) and moisturiser ($p = 0.03$). While all compounds showed a decrease in $f_{bioaccessible}$ with the inclusion of foundation, the effects of moisturiser were less apparent for PFOS and PFNS compared to other PFSAs. However, a significant increase in $f_{bioaccessible}$ was seen when deodorant was included ($p = 0.04$), although PFDS had a lower $f_{bioaccessible}$ in the presence of deodorant. The decrease in $f_{bioaccessible}$ seen for both PFSAs and PFCAs has been reported previously for the dermal bioaccessibility of flame retardants (FRs) and polychlorinated biphenyls in the presence of sun- and moisturising creams (Ertl and Butte, 2012; Pawar et al., 2017). This could be explained by a possible retention of the more lipophilic compounds by skin cream lipids. Our results are consistent with previous reports that certain ingredients in cosmetics can alter the composition of the SSSM and thus affect the dermal bioaccessibility of PFAS from dust. The magnitude and nature of the these effects are compound-specific and are dependent on the composition of the personal care products (Pawar et al., 2017; Pont et al., 2004; Walters et al., 1997). Other factors that are hypothesised to affect the bioaccessibility of PFAS from indoor dust are: skin contact time, as well as lipid content and ionic strength of the tested cosmetics. Further studies are needed to investigate the bioaccessibility of PFAS from other sources e.g. from PFAS containing fabrics and cosmetics as well as their subsequent dermal uptake and the effects of different personal care products.

3.3. Preliminary estimates of human dermal exposure to PFAS from indoor dust

In the absence of an experimentally determined value, a conservative value of 50% is suggested for dermal absorption by the EU's Scientific Committee of Consumer Safety (SCCS) (SCCS, 2021). Thus, using 50% of the $f_{bioaccessible}$ values obtained for the most physiologically relevant sweat:sebum mixture (1:1), human dermal exposure to target PFAS via contact with indoor dust was estimated (eq. (2))[38] for both adults and toddlers.

$$DED = \frac{C_{dust} * BSA * DAS * F_A * IEF}{BW} \quad (2)$$

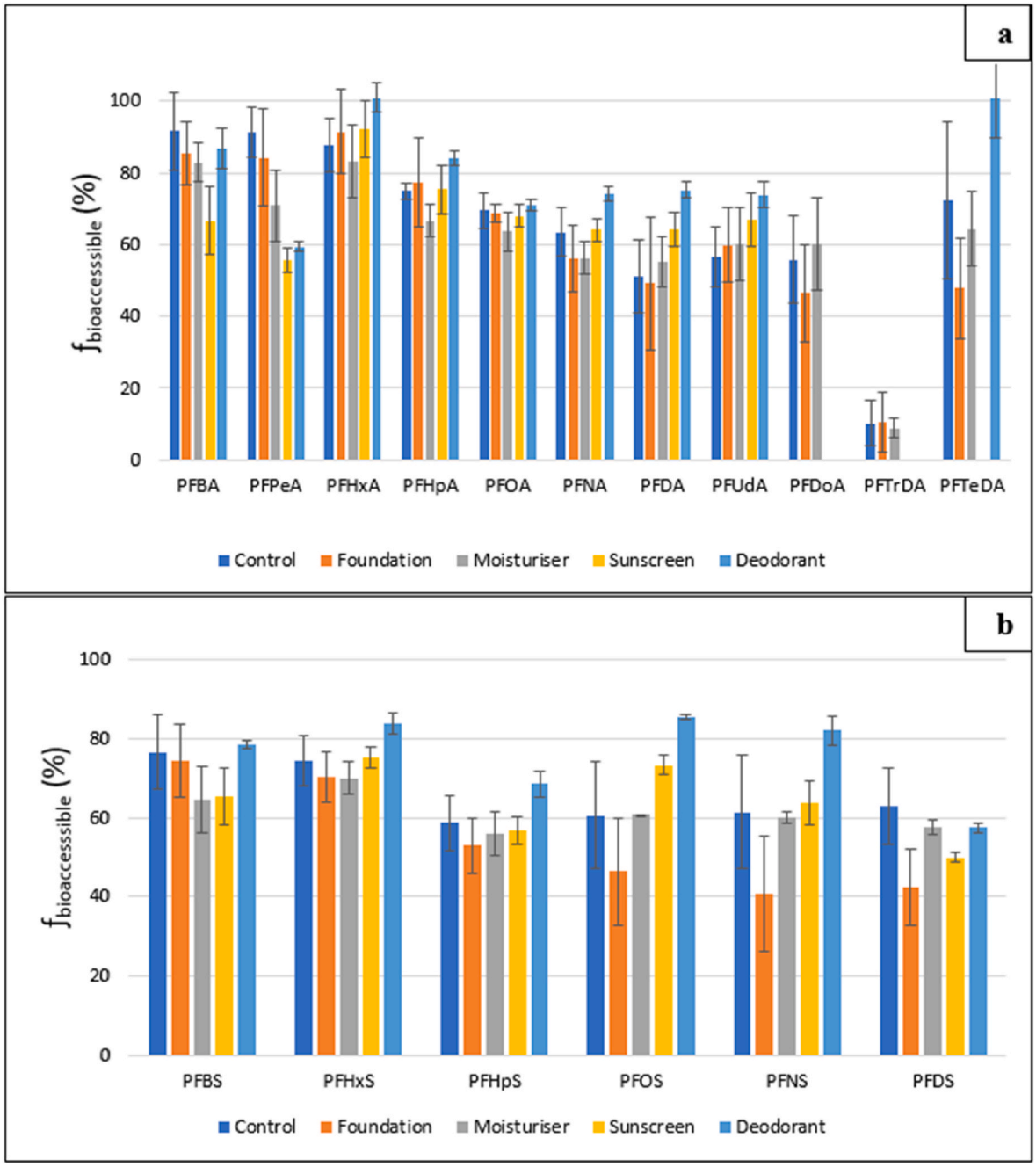

Fig. 3. Comparison of the effects of applied cosmetics on the bioaccessibility of (a) PFCAs and (b) PFSAs. Error bars represent the standard deviation (n = 3).

where *DED* = daily exposure dose (ng/kg bw/day), C_{dust} = PFAS concentration in dust (ng/g), *BSA* = body surface area exposed (cm^2), *DAS* = dust adhered to skin (mg/cm^2), F_A = fraction absorbed by the skin (unitless) (here F_A = 50% of $f_{bioaccessible}$), *IEF* = indoor exposure fraction (hours spent over a day in an indoor environment) (unitless), BW = body weight (kg).

The exposure parameters applied in eq. (2) were obtained from the USEPA exposure factors handbook (USEPA, 2011) and are summarised in Tables SI–16. Two exposure scenarios were applied:

i) **Summer:** assuming head, forearms, hands, thighs, lower legs and feet were exposed to dust (i.e., person wearing shorts and t-shirt).
ii) **Winter:** Assuming head and hands exposed to dust (i.e. person wearing full-length trousers, long-sleeve top and socks).

The dermal exposure of two age groups (adults and toddlers) were estimated based on previously reported concentrations of PFAS in household dust by Gebbink et al. (2015). Data from this study were chosen as information on other major pathways of exposure were provided alongside PFAS concentrations in dust. Our estimates (Table 1) highlight the potentially high dermal exposure to PFAS from contact with indoor dust, particularly in summer. When our dermal exposure values are compared to the EFSA recommended tolerable weekly intake of 4.4 ng/kg bw/week (for the sum of PFOS, PFOA, PFHxS, and PFNA), the exposure during summer can be up to 0.8 ng/kg bw/week for just two out of the four PFAS (PFOS and PFOA) via the dermal pathway alone. For toddlers, the EFSA limit is almost exceeded with PFOS and PFOA accounting for up to 3.2 ng/kg bw/week via dermal exposure to dust. The paper by Gebbink et al. did not include PFHxS and PFNA in their study and thus the dermal exposures to PFHxS and PFNA were not

Table 1
Estimated human daily exposure dose (DED in pg/kg bw/day) to selected PFAS via the dermal pathway from household dust based on contact with 1:1 sweat: sebum mixture.

PFAS	DED (pg/kg bw/day)			
	Adult Summer	Toddler Summer	Adult Winter	Toddler Winter
PFOS	69.6	284.1	24.1	86.7
PFBA	2.0	8.4	0.7	2.5
PFHxA	6.2	25.1	2.1	7.7
PFOA	43.0	175.6	14.9	53.6
PFDA	2.0	8.1	0.7	2.5
PFDoDA	2.0	8.3	0.7	2.5

calculated.

The assumption that all $f_{bioaccessible}$ will proceed to penetrate the skin barrier, can be considered a worst-case scenario, as it is highly unlikely that all the bioaccessible fraction will be absorbed, thus a more conservative value of 50% $f_{bioaccessible}$ was used (Pawar et al., 2017; SCCS, 2021). The two factors governing human dermal uptake of chemicals from house dust to the general circulation are: bioaccessibility and the percutaneous penetration rate. The outermost layer of human skin, the *stratum corneum* presents the main barrier to dermal penetration of organic chemicals. There, the major transport mechanism involved in the dermal uptake of organic chemicals is passive diffusion, which is regulated by compound-specific physicochemical properties. For compounds bound to particulate matter i.e. household dust however, the chemical's release from particles into the fluids on the skin surface can have a bigger impact on the resulting dermal uptake. A compound's physicochemical properties would, in theory, make it suitable for dermal uptake, however, if the dermal bioaccessibility is low, the resulting dermal uptake will be minimal (Luo et al., 2020; Pawar et al., 2017; Zeng et al., 2019). Part of the bioaccessible fraction of a chemical could then pass through the *stratum corneum* where it could either be metabolised *in situ* or enter the systemic circulation ($f_{bioavailable}$) through the viable epidermis and dermis layers by diffusion (Ragnarsdóttir et al., 2022). Further studies are needed to determine the subsequent percutaneous penetration rate of various PFAS. Importantly, we highlight that dust is not the only possible source of dermal exposure to PFAS. Dermal uptake from PFAS-containing fabrics and/or cosmetics (Schultes et al., 2018; Xia et al., 2022), could make a substantial additional contribution to exposure that is not accounted for in our estimates and studies of dermal exposure to PFAS arising from such materials are urgently needed.

The calculated dermal exposure of adults was compared to that arising from other pathways as reported previously (Gebbink et al., 2015) (Fig. 4). Given our assumption that all the dermal bioaccessible fraction will reach the bloodstream (worst-case scenario), our results were compared to the high exposure scenario reported (95th percentile of each input parameter) (Gebbink et al., 2015).

The comparison reveals that under the specific scenarios considered here, diet is the most significant exposure pathway for most of our target PFAS. However, for PFOS and PFOA the possible daily exposure via dermal exposure via indoor dust was significant. Furthermore, dermal exposure via indoor dust during summer exceeded that via air for all compounds except PFDA. While assuming 50% of the bioaccessible fraction will reach the bloodstream could be an overestimation, we are only accounting for one source of dermal exposure (indoor dust) when many other potential such sources are known i.e. fabrics and cosmetics (Schultes et al., 2018; Xia et al., 2022). Given recent studies have shown positive correlations between the use of personal care products and serum PFAS levels (Thépaut et al., 2021; Serrano et al., 2021); it is clear that further studies are needed to better understand the dermal uptake of PFAS and subsequently the potential contribution of dermal exposure to human body burdens of PFAS.

Study limitations

It is difficult to exactly mimic *in vivo* situations e.g., the friction on a person's skin surface when they move, so while we tried to closely mimic this *in vitro* by stirring the dust/SSSM/cosmetics test mixtures, we recognise that this does not necessarily accurately reflect real-life dermal exposure conditions and introduces uncertainties into our estimations of possible dermal uptake of PFAS.

CRediT authorship contribution statement

Oddný Ragnarsdóttir: Investigation, Data curation, Writing – original draft, Visualization. **Mohamed Abou-Elwafa Abdallah:** Supervision, Writing – review & editing. **Stuart Harrad:** Supervision, Writing – review & editing.

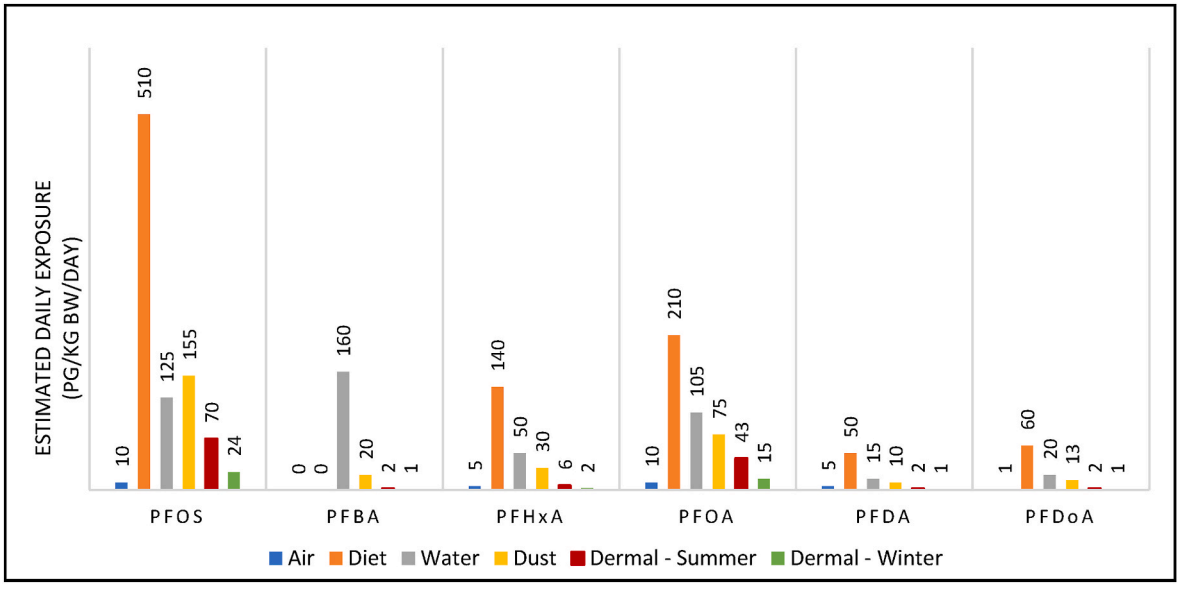

Fig. 4. Comparison of estimated adult human dermal exposure via contact with dust and other pathways of exposure to target PFAS (high exposure scenario) (Gebbink et al., 2015).

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data can be seen in the Supplementary Information

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2023.117093.

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