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# Decorative cosmetics and skin care products contribute significantly to short-chain perfluoroalkyl carboxylates exposure

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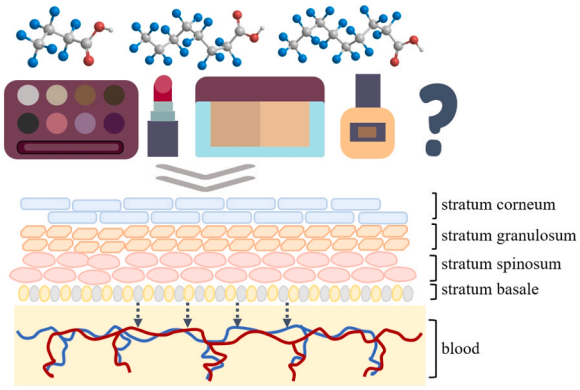
## HIGHLIGHTS

- PFBA and PFTeDA showed the highest and lowest dermal permeation of 14 PFAS.
- Exposure concentration increased from 312.5 to 1562.5 ng/cm$^2$ elevated absorption by 4.4–11.4 %.
- Daily intakes of individual PFAS via dermal exposure were 0.01–0.8 ng/kg/day.
- Dermal uptake of PFOA from decorative cosmetics and skin care products accounts for 40 % of total intake.

## GRAPHICAL ABSTRACT

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## ABSTRACT

Research on dermal exposure of per- and polyfluoroalkyl substances (PFAS) in personal care products is limited. Here, we investigated the permeation of 14 PFAS using *in vitro* 3D-human skin equivalents (3D-HSE). Results revealed that perfluorobutanoic acid (PFBA) exhibited the highest cumulative permeation, while perfluorotetradecanoic acid (PFTeDA) showed the lowest. Increasing the exposure concentration from 312.5 ng/cm$^2$ to 1562.5 ng/cm$^2$ has triggered a growth of 4.4–11.4 % in dermal absorption. The steady-state flux and apparent permeation coefficient ranged from 0.7 to 11.2 ng/cm$^2$·h and $7.0 \times 10^{-5}$-$1.1 \times 10^{-3}$ cm/h, respectively. The estimated absorption using 3D-HSE is close to that using *in vivo* rat model ($p = 0.37$). Subsequently, we summarized the median concentrations of PFAS in various decorative cosmetics and skin care products were 0.6–8.3 ng/g and 0.2–8.0 ng/g, respectively, and thus daily intakes of individual PFAS through dermal exposure ranged from 0.01 to 0.8 ng/kg/day. The total daily intake of short-chain perfluoroalkyl carboxylates via dermal

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pathway, which was estimated based on the sum of dermal exposure from both decorative cosmetics and skin care products, may exceed that from diet. Dermal exposure contributes significantly to PFOA intake for individuals who regularly use decorative cosmetics and skin care products, supporting recent regulation of PFAS used in personal care products.

## 1. Introduction

Human exposure to per- and polyfluoroalkyl substances (PFAS) is associated with many adverse health effects, including cancer, impact on pregnancy metabolism and endocrine function, increased risk of childhood obesity and others [1]. Dietary and drinking water have always been considered as the primary exposure pathways, while a few studies have evaluated the contribution of dermal exposure. As known, PFAS are commonly added to cosmetics as emulsifiers, anti-statics, binders, surfactants, stabilizers, film formers and viscosity agents [2]. Existing studies have illustrated that the total concentration of PFAS in personal care products can be up to μg/g [3]. Meanwhile, The Beauty & Personal Care market worldwide is projected to generate a revenue of US $677.20bn in 2025. The market is expected to grow at an annual rate of 3.37 % (Compound annual growth rate 2025–2030) [4]. This increasing use of cosmetics and widespread occurrence of PFAS in cosmetics make dermal uptake become a potential source, raising concerns about the health risks associated with the use of decorative cosmetics and skin care products.

Understanding PFAS exposure through decorative cosmetics and skin care products requires a comprehensive investigation of their dermal absorption characteristics, using either *in vivo* or *in vitro* approaches. However, only a limited number of studies have addressed this issue. One study using a rat model estimated the dermal permeability of 15 PFAS ranged from 4.1 % to 18.0 % after 6 h exposure [5]. Similarly, a prior study assessed the permeability of sunscreen containing 10 PFAS using *ex vivo* mouse skin, reporting an *in vitro* absorption fraction of 15.2–54.3 % after 36 h exposure [6]. However, neither of the two studies involved human skin, resulting in uncertainties regarding the interspecies exploration when applied to human health risk assessment. Therefore, the human skin equivalents have been considered as a possible alternative. In various types of human skin equivalents, reconstructed epidermis models are commonly used to assess skin penetration, which is *in vitro* reconstructed human epidermis from normal human keratinocytes cultured on a collagen matrix at the air-liquid interface [7]. Reconstructed epidermis models show similar epidermal morphology as native human skin, although slight differences exist in the free fatty acid content and lipid organization [8]. Actually, *in vitro* skin irritation and skin corrosion using the reconstructed human epidermis (RhE) method are included in the Organisation for Economic Cooperation and Development (OECD) Guidelines 439 and 431 [9,10]. Moreover, these *in vitro* models can reduce the reliance on animal testing for product safety assessments [11]. However, only one study based on the 3D-Human Skin Equivalents (3D-HSE) reported that the highest dermal absorbed fraction of some PFAS reached 58.9 % after 36 h exposure to date [12]. Nonetheless, this study utilized only a single exposure dose, while the effects of different exposure concentrations on PFAS permeability remain unclear.

In addition to these legacy PFAS, HFPO-DA (GenX) was first introduced by DuPont in 2010 as a replacement for PFOA, serving as an emulsifying dispersant in the fluoropolymer manufacturing process [13]. Previous studies have reported the concentrations of HFPO-DA ranging from 0.07 to 29.4 ng/g in 29 kinds of cosmetic products [14], raising concerns about its human health risk via dermal absorption. However, no study has reported the skin absorption of HFPO-DA to date.

To address the dermal exposure and associated risk of PFAS including HFPO-DA from decorative cosmetics and skin care products, this study has the following specific objectives: 1) to address the percutaneous penetration of PFAS through human skin, with low and high concentration groups included using 3D-HSE; 2) to estimate the steady-state flux and dermal absorption parameters of PFAS via dermal exposure; 3) to summarize the occurrence of PFAS in cosmetic and skin care products; 4) and finally to calculate the exposure and human health risk assessment. The results may enhance our understanding of dermal exposure risks related to PFAS-containing cosmetics and provide a basis for regulatory considerations.

## 2. Methods and materials

### 2.1. Chemicals and standards

Our study included 14 target PFAS, including perfluorobutanoic acid (PFBA), perfluoropentanoic acid (PFPeA), perfluorobutane sulfonic acid (PFBS), perfluorohexanoic acid (PFHxA), perfluoroheptanoic acid (PFHpA), perfluorohexane sulfonic acid (PFHxS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorooctane sulfonate (PFOS), perfluorodecanoic acid (PFDA), perfluroanoic acid (PFUnDA), perfluorododecanoic acid (PFDoDA), perfluorotetradecanoic acid (PFTeDA) and Hexafluoropropylene oxide-dimer acid (HFPO-DA). The detailed information of these chemicals (e.g., formulas, molecular weight, log $K_{ow}$) is provided in the Supplementary materials (SM) in Table S1 and Text S1.

### 2.2. 3D-human skin equivalent

The 3D-HSE models (EpiKutis) used to examine the PFAS permeation, were purchased from Guangdong BioCell Biotechnology Company (Guangdong, China). Detailed information for Epikutis and its apparent evaluation, tissue viability test, skin barrier function test, and histological structure test was provided in Text S2 and Figure S1. The study protocol received ethical approval (BM20230070) from the Bioethics and Medical Ethics Committee, Beihang University.

### 2.3. Dosing and dermal exposure experiment

Experiments were conducted according to the operating instructions and the OECD guidelines [15]. Permeation experiments followed previously published protocol [16,17]. In brief, the dosing solutions were prepared in acetone at concentrations of 10 ng/μL (individual PFAS, 312.5 ng/cm$^2$) representing for the low (L) group, and 50 ng/μL (individual PFAS, 1562.5 ng/cm$^2$) representing for the high (H) group. The reasons we chose acetone as the solvent are that PFAS can be dissolved in acetone at a concentration of more than 50 ng/μL and acetone has less effect on the skin barrier functions [18]. Before the permeation experiments, 5 % bovine serum albumin (BSA) was added to the culture medium to enhance the solubility of target PFAS. A 20 μL volume of dosing solutions was applied to the skin surface in the donor compartment. The whole 0.9 mL of receptor fluid in the receptor compartment was collected and replaced with fresh fluid at the following time points: 0.5 h、1 h、2 h、5 h、8 h、12 h、18 h、24 h、30 h、36 h、42 h and 48 h. The experiment was performed under the condition of avoiding light, with triplicate treatments applied. The experimental protocol applied during dermal permeation experiments is shown in Figure S2. After 48 h, the skin surface was thoroughly wiped with cotton buds pretreated with methanol, the skin tissues were collected, and the donor and compartments were rinsed five times with 2 mL methanol to collect the unabsorbed PFAS. All the collected samples were stored in centrifuge tubes at −20 ℃ until analysis.

### 2.4. Sample extraction and chemical analysis

Each dermal exposure experiment generated five different types of samples: receptor fluid (at twelve-time points), skin tissue, cotton buds, donor and receptor compartment washing fluid. The extraction of the collected samples was conducted according to a previously reported method [19,20]. Detailed information for sample pretreatment and instrumental analysis was provided in SM Text S3, Text S4 and Table S2.

### 2.5. Quality assurance/quality control

Recoveries of PFAS were evaluated by spiking blank samples with mixed standards before pretreatment. The average recoveries of target PFAS spiked into samples ranged from 98.1 % to 132.0 % and the relative standard deviations (RSDs) were all less than 9 % (Table S3). PFAS were quantified using internal standard calibration curves comprising eight points of regression (0.05 −200 ng/mL), with all the regression coefficients higher than 0.99. The limits of detection were determined as the concentrations produced a signal-to-noise ratio of 3 (Table S4). Data analysis was performed using Origin 2021 (OriginLab Corporation, MA, USA).

### 2.6. The calculation of steady-state flux and dermal absorption parameters

The steady-state flux ($J_{ss}$) was calculated using an extended form of Fick's first law of diffusion (Eq. 1) [21]:

$$J_{ss} = \frac{\Delta m}{\Delta t \times A} = \frac{D \times K \times \Delta c}{dx} \quad (1)$$

Where $J_{ss}$ is the steady-state flux (ng/cm$^2$·h); $\Delta m$ is the permeated mass (ng); $\Delta t$ is the time interval (hour); $A$ is the area of EpiKutis (0.64 cm$^2$); $D$ is the diffusion coefficient (cm$^2$/h); $K$ is the partition coefficient; $\Delta c$ is the concentration difference across the membrane (ng/cm$^3$); $dx$ is the thickness of membrane (cm).

When using infinite-dose configurations, i.e. in which the donor concentration far exceeds the concentration in the receptor compartment ($C_D \gg C_A$), $\Delta C$ can be replaced by the known donor concentration, $C_D$, and the permeated mass per time assumed constant. Therefore, the $J_{ss}$ (ng/cm$^2$·h) for each target PFAS for the examined skin model (EpiKutis) were estimated using a plot of the cumulative absorbed mass of each target compound (ng/cm$^2$) against time (hours). The steady-state range of the curve was identified according to the method reported by the previous study [21]. In addition to PFTeDA in the L group, at least five data points lay within the linear range. The linear regression is fitted to all data points by using Eq. 2; The apparent permeation coefficient ($P_{app}$, cm per h) and lag time ($t_L$) were calculated using Eqs. 3 and 4:

$$\frac{m}{A} = J_{ss}t + b_0 \quad (2)$$

$$P_{app} = \frac{J_{SS}}{C_D} \quad (3)$$

$$t_L = -\frac{b_0}{J} \quad (4)$$

where $b_0$ describes the y-axis intercept of the regression line; $m$ is the cumulative absorbed mass of each target compound (ng); $t$ is the exposure time (hours), $C_D$ used in this study is 10 ng/μL. Thus, within 48 h, the time-dependent absorption fraction ($AF$, %) was estimated using the following Eqs. 5 and 6:

$$M_i = A(Jt_i + b_0) \quad (5)$$

$$AF_i = \frac{M_i}{TM} \quad (6)$$

where $M_i$ is the mass in receptor fluid after $i$ hours' exposure (ng); $TM$ is the total measured mass after 48 h exposure. In this study, we assumed the average time people wear decorative cosmetics and skin care products is 8 and 12 h, respectively, and thus the dermal exposure for decorative cosmetics and skin care products was estimated based on this assumption.

### 2.7. Dermal exposure assessment and risk assessment from personal care products

Generally, the estimated daily intake (EDI; in nanograms per kilogram BW per day) of each PFAS was calculated using Eq. 7:

$$EDIs = \frac{C_{pj} \times AF \times EDA_j}{BW} \quad (7)$$

where $C_{pj}$ denotes the concentration of different PFAS in decorative cosmetics and skin care products (ng/g); $j$ represents different kinds of products; $EDA_j$ is the estimated daily amount applied (g/d) and the values of EDA of each type of product were referred to the guidance for the safety evaluation of cosmetic ingredients from the Scientific Committee for Consumer Safety (SCCS, 2021) [22], which was detailed in Table S5; BW is the body weight of the adults (kg). BW was determined to be 60 kg in this study. The total daily intake via dermal pathway was calculated as the sum of dermal exposure from both decorative cosmetics and skin care products.

Based on an extensive literature survey, the concentrations of PFAS in decorative cosmetics and skin care products ($C_{pi}$) were obtained. A comprehensive literature survey consisting of four steps was detailed in Figure S3. In short, a broad search was performed using keywords of ('PFASs' or 'per- and polyfluoroalkyl substances' or 'PFAS') and 'cosmetics' across publications existing publications in Web of Science, which yielded about 3000 publications. Then, the title, abstract and full text were examined to exclude irrelevant literature or incomplete data (only analyzed a few PFAS from the 14 PFAS we measured in the experiment), narrowing the selection to around 13 publications. After that, data on concentrations of PFAS in cosmetics were extracted, and articles that only reported the total PFAS concentration without detailing the concentrations of individual PFAS were removed. In step 4, we have standardized the PFAS data to ensure uniformity across studies. Finally, we identified 8 articles, involving different decorative cosmetics and skin care products. Detailed information of the article, sampling location, brand, PFAS concentration and others were all recorded in detail, as presented in SM raw_data.xlsx.

To further clarify the risk of human exposure to PFAS as a result of cosmetic use, hazard quotient (HQ) were calculated based on Eq. 8:

$$HQ = \frac{EDIs}{RfD} \quad (8)$$

$HQ$ is the hazard quotient. The relative potency factor (RPF) approach was applied to achieve a PFOA-equivalent HQ. Fourteen PFAS were included in the RPF calculation, and their corresponding RPF factors are listed in Table S6 [23]. The sum of PFOA-equivalent EDIs can be compared to the reference dose (RfD) of PFOA for subsequent health risk assessment. The RfD of PFOA used in this study is 0.8 ng/kg bw/day, which was provided by the European Food Safety Authority in 2018 [24].

## 3. Results

### 3.1. The time-varying dermal absorbed concentration of PFAS

The mass balance of the penetration experiments was generally calculated using the sum amounts of three parts: a) permeable compartments (accumulation in the receptor fluids and the receptor compartment washing fluids after 48 h experiments), b) accumulated in

skin tissues, c) unabsorbed compartments (accumulation in skin surface wipes and the donor compartment washing fluids after 48 h experiments). Overall, the mass recoveries of target PFAS ranged from 65.7 % to 103.4 % for the L group (312.5 ng/cm$^2$) and from 65.1 % to 120.0 % for the H group (1562.5 ng/cm$^2$). Volatile loss and transformation might explain PFAS reduction in the dermal absorption experiment [25,26].

The accumulation of different PFAS in receptor fluid over time under two different exposure concentrations is illustrated in Fig. 1. For PFAS with perfluorinated carbon chain length of 3–6 in the L group, the accumulation in the receptor fluid ranged from 149.4 to 255.3 ng/cm$^2$ after 48 h. PFAS with perfluorinated carbon chain lengths of 7–13 in L group accumulated between 13.8 and 141.2 ng/cm$^2$. Comparing Fig. 1 (a) and (b), PFAS with chain lengths less than 6 accumulated 1.8–10.8 folds more in the receptor fluid after 48 h than those with chain lengths greater than 7. Additionally, Fig. 1(a) and (c) demonstrated that increasing the exposure concentration by a factor of 5 resulted in a 5.6–6.6 fold increase in accumulation for PFAS with chain lengths of 3–6. Similarly, a 5.9–10.3 fold increase for PFAS with chain lengths of 7–13 was noted, as shown in Fig. 1(b) and (d). The 14 target PFAS showed considerable differences in their ability to penetrate the skin in applied experimental conditions. After 48 h exposure, PFAS in permeable compartment showed the same order in L and H groups: PFBA>PFPeA>PFBS>PFHxA>HFPO-DA>PFHpA>PFHxS>PFOA>PFNA>PFOS>PFDA>PFUnDA>PFDoDA>PFTeDA, which indicated that the permeability of all PFAS except HFPO-DA decreased with perfluorinated carbon chain length, and the permeability of perfluoroalkyl carboxylates (PFCAs) were higher than perfluoroalkyl sulfonates (PFSAs).

### 3.2. Absorbed fractions of PFAS

Fig. 2 demonstrated that only a few fractions of PFAS were present in the permeable compartment during the initial 2 h, especially in the L group. Distribution of target PFAS in the EpiKutis after the 48 h exposure is illustrated in Table S7. In the L group, PFPeA, PFBA, PFBS, PFHxA, and HFPO-DA penetrated the skin rapidly, with approximately 39.5–54.1 % of the total measured mass occurring within 2–18 h, after which the penetration rate gradually decreased. For PFHpA, PFHxS, PFOA, PFNA, PFOS, and PFDA, the period of slow permeability extends up to the initial 8 h, compared to a rapid increase in the 8–24 h. Penetration of PFUnDA increased from 4.5 % per 6 h to 11.5 % within 12–36 h, while PFDoDA penetration rose from 3.0 % per 6 h to 9.7 % within 18–36 h. After that, the penetration rates for both PFUnDA and PFDoDA declined during 36–48 h. However, PFTeDA has not appeared in the receptor fluids until 18 h, and then penetrated about only 2 % every 6 h during 30–48 h.

Similar trends were observed in the H group, but the target PFAS appeared earlier in the permeable compartment than in the L group, and

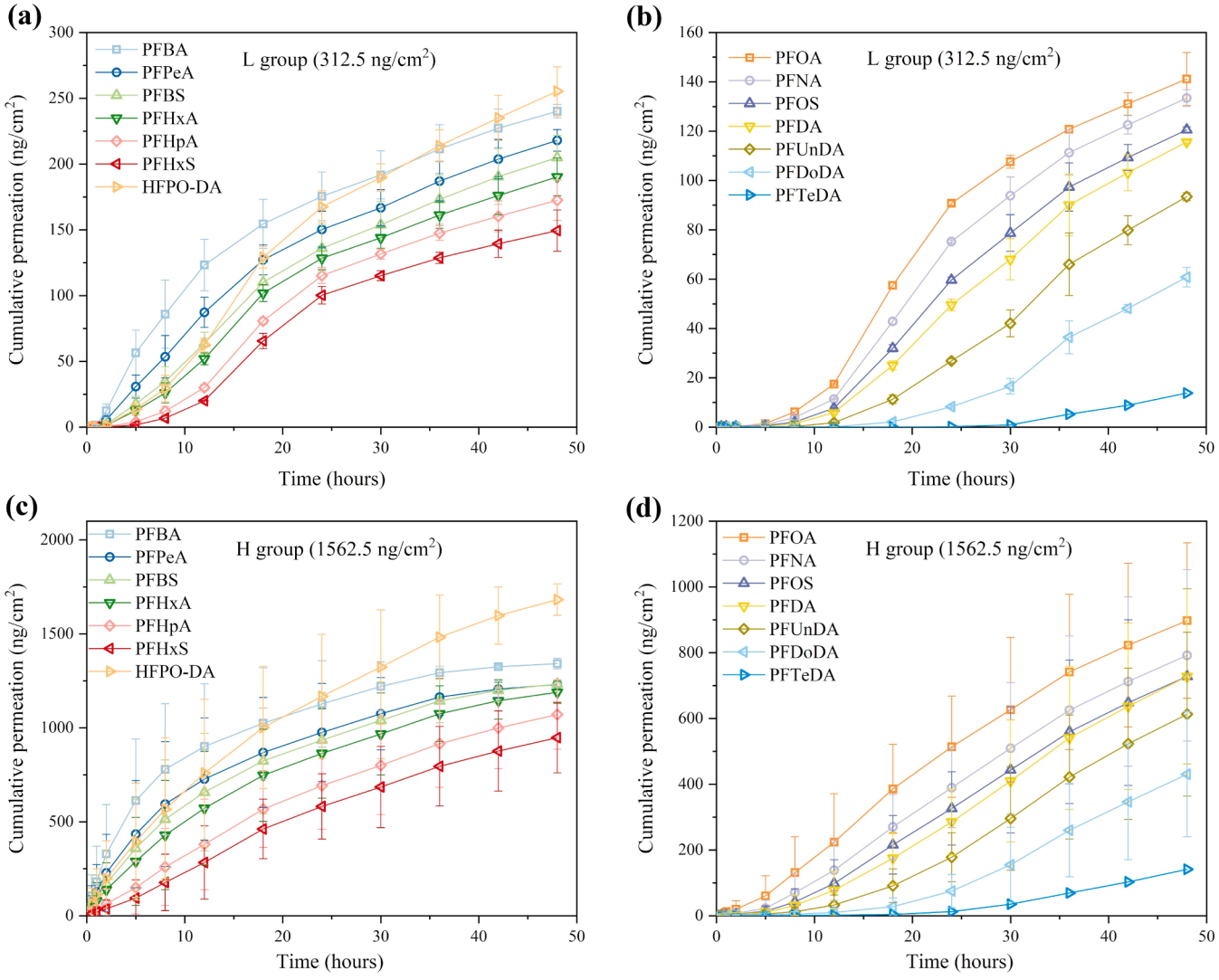


**Fig. 1.** Cumulative permeation (ng/cm$^2$) into the receptor fluid following exposure to 312.5 ng/cm$^2$ and 1562.5 ng/cm$^2$ of target PFAS through 48 h.

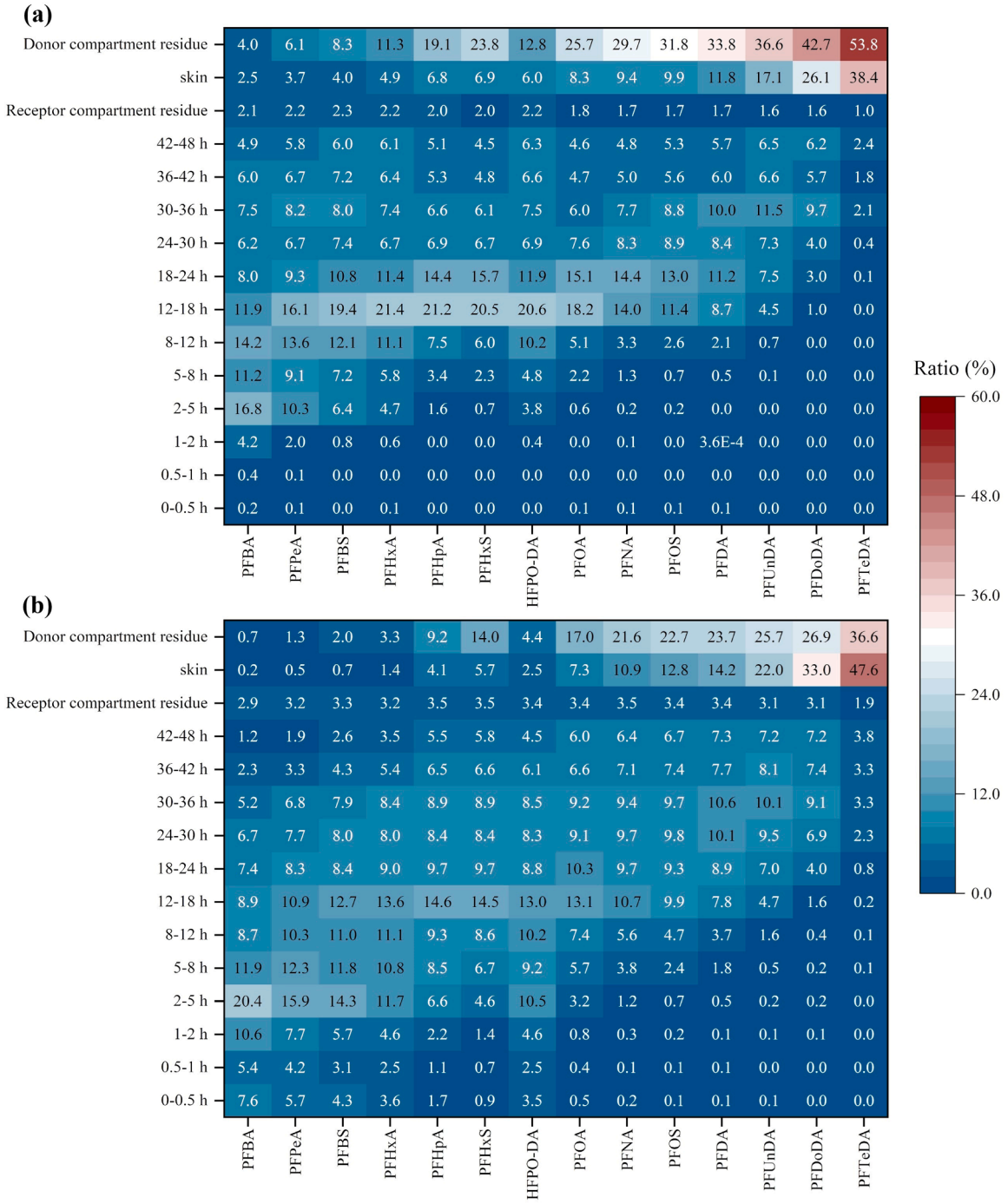


**Fig. 2.** Distribution of target PFAS (expressed as the mean of total measured mass) in the EpiKutis following the 48 h exposure to (a) 312.5 ng/cm$^2$ and (b) 1562.5 ng/cm$^2$. The time points represent the fraction of PFAS accumulated in the receptor compartment during this interval.

showed higher permeability in the initial 18 h of exposure (Fig. 2). Besides, the proportion of PFAS in permeable compartments increased by 4.4–11.4 % in the H group, compared to the L group. This may be because the skin intercepting capacity of the unit surface is limited, and at a higher applied dose, the pressure of the concentration gradient may have a greater effect [19]. Hence, PFBA showed the highest cumulative permeation with 93.7 % and 99.1 % after 48 h experiment in the L and H group, respectively. Contrastingly, PFTeDA displayed the least cumulative permeation with 8.4 % and 15.8 % dermal absorption in the L and H groups, respectively.

For PFAS with the same number of carbon atoms, PFCAs exhibit a bit higher permeability compared to PFSAs. However, comparing PFCAs and PFSAs with the same perfluorinated carbon chain length, it was found that the permeable fractions of PFBS (88.0 % and 97.3 % in the L and H groups) were comparable with those of PFPeA (90.5 % and 98.2 % in the L and H groups) after 48 h experiment. Similar results were found between PFHpA (75.1 % in L group and 86.5 % in H group) and PFHxS (70.6 % in L group and 80.2 % in H group), as well as PFOS (59.8 % in L group and 64.1 % in H group) and PFNA (62.3 % in L group and 67.3 % in H group). On the other hand, although the permeabilities of PFCAs and PFSAs with the same perfluorinated carbon chain length were similar, the permeability of PFCAs remained slightly higher than that of PFSAs (by approximately 0.9–6.3 %).

After 48 h exposure, the accumulated fraction of PFAS in skin tissue

was 2.5–38.4 % and 0.2–47.6 % of the total measured mass for the L and H group, respectively. Compared to the L group, the accumulated fraction of PFBA, PFPeA, PFBS, PFHxA, PFHpA, PFHxS, HFPO-DA and PFOA in skin tissue decreased by 1–3.6 % in the H group, while the accumulated fraction of PFNA, PFOS, PFDA, PFUnDA, PFDoDA and PFTeDA increased by 1.4–9.2 %. In the unabsorbed compartments, PFAS accounted for 4.0–53.8 % and 0.7–36.6 % of the total measured mass in the L and H groups, respectively.

### 3.3. The estimation of steady-state flux and dermal absorption

Generally, $J_{ss}$ quantitatively describes xenogeneic penetration through the skin barrier [18], while $P_{app}$ demonstrated the resistance of human skin *in vitro* to targeted PFAS penetration [21]. As shown in Fig. 3, Table 1 and Figure S4, the $J_{ss}$ and $P_{app}$ values of 14 PFAS ranged from 0.7 to 11.2 ng/cm$^2$·h and 7.0 × 10$^{-5}$-1.1 × 10$^{-3}$ cm/h in the L group. As expected, PFBA and PFTeDA showed the highest and lowest $J_{ss}$ & $P_{app}$ values, respectively, and the $P_{app}$ values of the remaining 12 PFAS were within a similar range. The $t_L$ represents the time of observation of PFAS in the receptor compartment after exposure, with the range of 0.05–28.8 h in the L group. Consistent with the permeability results, the $J_{ss}$, $P_{app}$ and $t_L$ values indicated that long-chain PFAS with larger molecular weight and higher hydrophobic are more difficult to penetrate the skin. Interestingly, the dermal absorption parameters for target PFAS in the L group and H group were slightly different (Table 1). As exposure concentration increases from 312.5 ng/cm$^2$ to 1562.5 ng/cm$^2$, the $J_{ss}$ of the H group increases while $t_L$ decreases. This discrepancy may be attributable to the loading conditions ($N_{derm}$, Text S5). The $N_{derm}$ ranged from 0.6 to 9.2 and 1.4–6.0 in the L group and H group. The generally lower $N_{derm}$ values in H group suggest a delivery-limited state [27]. Under this condition, high fractional absorption is feasible [28], in which higher $J_{ss}$ is expected to occur.

### 3.4. The concentration of PFAS in decorative cosmetics and skin care products

We have summarized the PFAS concentrations in 211 samples, including different kinds of decorative cosmetics and skin care products, and only PFAS with a sample size greater than 10 are considered. The tested products covered Canada, France, China, South Korea, Japan, Sweden, and the United States, including nearly 20 different brands. As shown in Fig. 4 and SM raw_data.xlsx, the concentrations of each PFAS varied substantially, ranging from 0.01 to 4640.0 ng/g and 0.07–29300.0 ng/g in decorative cosmetics and skin care products, respectively. Notably, higher PFAS concentrations were mainly observed in decorative cosmetics. The median concentrations of each PFAS in decorative cosmetics ranged from 0.6 ng/g to 8.3 ng/g, which is comparable to the levels found in skin care products (0.2–8.0 ng/g).

**Table 1**
Estimated flux of the steady-state flux ($J_{ss}$), apparent permeation coefficient ($P_{app}$), and lag time ($t_L$) from the exposure of EpiKutis for target PFAS.

| PFAS | $J_{SS}$ (ng/cm$^2$·h) | $P_{app}$(cm/h) | $N_{derm}$ | $t_L$(h) |
|---|---|---|---|---|
| exposed to 312.5 ng/cm$^2$ (L group) | | | | |
| PFBA | 11.19 | 1.12 × 10$^{-3}$ | 0.58 | 0.60 |
| PFPeA | 6.82 | 6.82 × 10$^{-4}$ | 0.96 | 0.47 |
| HFPO-DA | 5.89 | 5.89 × 10$^{-4}$ | 1.11 | 0.51 |
| PFBS | 4.96 | 4.96 × 10$^{-4}$ | 1.31 | 0.05 |
| PFHxA | 4.68 | 4.68 × 10$^{-4}$ | 1.39 | 0.62 |
| PFHpA | 4.17 | 4.17 × 10$^{-4}$ | 1.56 | 2.03 |
| PFHxS | 3.73 | 3.73 × 10$^{-4}$ | 1.74 | 3.15 |
| PFOA | 3.55 | 3.55 × 10$^{-4}$ | 1.84 | 3.66 |
| PFNA | 3.40 | 3.40 × 10$^{-4}$ | 1.91 | 5.33 |
| PFOS | 3.17 | 3.17 × 10$^{-4}$ | 2.06 | 7.24 |
| PFDA | 3.13 | 3.13 × 10$^{-4}$ | 2.08 | 9.12 |
| PFUnDA | 2.83 | 2.83 × 10$^{-4}$ | 2.30 | 14.16 |
| PFDoDA | 2.28 | 2.28 × 10$^{-4}$ | 2.86 | 21.04 |
| PFTeDA | 0.70 | 7.04 × 10$^{-5}$ | 9.24 | 28.75 |
| exposed to 1562.5 ng/cm$^2$ (H group) | | | | |
| PFHxS | 23.05 | 4.61 × 10$^{-4}$ | 1.41 | 0.01 |
| PFOA | 20.05 | 4.01 × 10$^{-4}$ | 1.62 | 0.42 |
| PFNA | 18.60 | 3.72 × 10$^{-4}$ | 1.75 | 3.69 |
| PFOS | 17.75 | 3.55 × 10$^{-4}$ | 1.83 | 5.70 |
| PFDA | 18.17 | 3.63 × 10$^{-4}$ | 1.79 | 7.40 |
| PFUnDA | 16.96 | 3.39 × 10$^{-4}$ | 1.92 | 11.85 |
| PFDoDA | 13.96 | 2.79 × 10$^{-4}$ | 2.33 | 17.54 |
| PFTeDA | 5.43 | 1.09 × ×10$^{-4}$ | 6.00 | 22.67 |

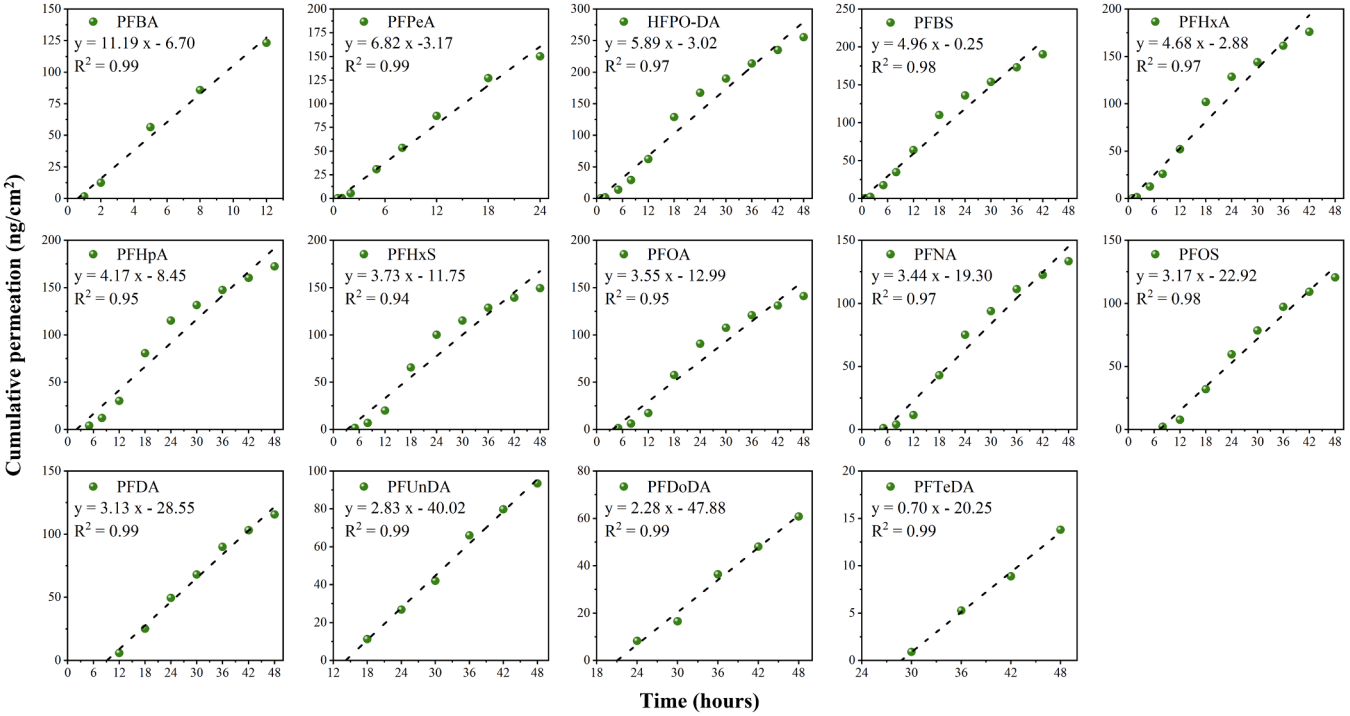


**Fig. 3.** Cumulative permeation (ng/cm$^2$) of target PFAS through the EpiKutis following exposure to 312.5 ng/cm$^2$ for 48 h.

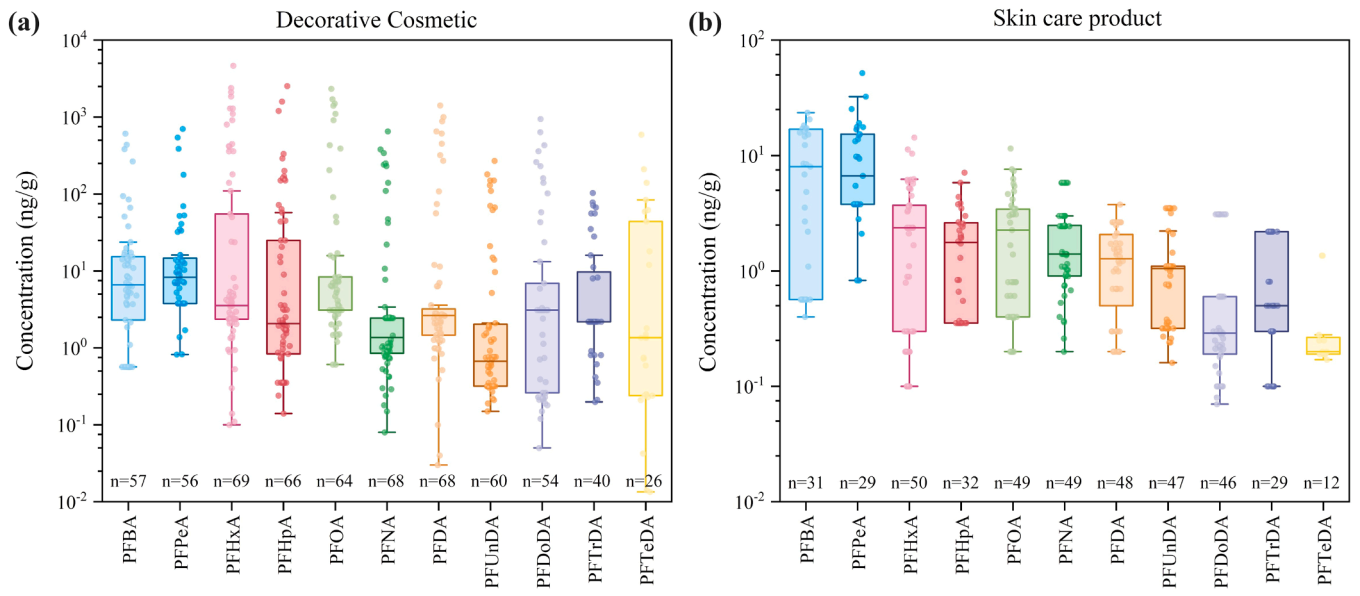


**Fig. 4.** The boxplot of PFAS concentration in (a) decorative cosmetics and (b) skin care products. The n marked in each panel represents the sample size.

PFCAs were the most commonly detected PFAS in decorative cosmetics and skin care products, especially PFBA, PFPeA, PFHxA and PFHpA.

### 3.5. The exposure and human health risk assessment

Using Eq. (6), the AF for the 11 target PFAS ranged from 0 % to 31.6 %, and 0–48.6 % after 8 and 12 h of exposure, respectively. Subsequently, the EDIs of PFAS through dermal exposure are tabulated in Table 2. Overall, EDIs of target PFAS through dermal exposure ranged from 0.46 to 22.8 pg/kg bw/day for decorative cosmetics, with a median of 3.2 pg/kg bw/day and an average of 7.7 pg/kg bw/day. EDIs for skin care products were generally higher than those for decorative cosmetics, ranging from 11.0 to 815.7 pg/kg bw/day, with a median of 64.0 pg/kg bw/day and an average of 112.6 pg/kg bw/day. PFBA and PFPeA dominated the dermal daily intakes of PFAS, followed by PFHxA, PFHpA, PFOA and PFNA. EDIs of skin care products were much higher than cosmetics, which is possibly due to the estimated daily amount applied of skin care products being about 19 times that of cosmetics, even though concentrations of PFAS were close [22].

**Table 2**
Median concentrations of PFAS in decorative cosmetics and skin care products and EDI (pg/kg/day) of dermal exposure.

| Category | PFAS | Medians (ng/g) | AF (%) | EDI (pg/kg/day) | PFOA-equivalent intake (pg/kg/day) |
|---|---|---|---|---|---|
| **Decorative Cosmetics:** include BB/CC cream, bronzer, concealer, eye liner, eye shadow, foundation, lipstick, mascara [3,14,30,37,55–57] | PFBA | 6.60 | 31.55 | 22.80 | 1.14 |
| | PFPeA | 8.27 | 20.73 | 18.78 | 0.19 ≤EDI≤ 0.94 |
| | PFHxA | 2.53 | 14.81 | 4.10 | 0.04 |
| | PFHpA | 1.91 | 10.41 | 2.18 | 0.02 ≤EDI≤ 2.18 |
| | PFOA | 3.10 | 6.99 | 2.37 | 2.37 |
| | PFNA | 1.05 | 4.03 | 0.46 | 4.63 |
| **Skin care products:** include cream, cleanser, exfoliator, mask, shaving cream [14,30,37,56–58] | PFBA | 8.02 | 48.61 | 815.66 | 40.78 |
| | PFPeA | 6.67 | 31.74 | 442.98 | 4.43 ≤EDI≤ 22.15 |
| | PFHxA | 2.37 | 22.83 | 113.19 | 1.13 |
| | PFHpA | 1.77 | 17.38 | 64.37 | 0.64 ≤EDI≤ 64.37 |
| | PFOA | 2.26 | 13.44 | 63.53 | 63.53 |
| | PFNA | 1.40 | 10.07 | 29.48 | 294.84 |
| | PFDA | 1.28 | 4.11 | 11.01 | 44.03 ≤EDI≤ 110.07 |

Abbreviations: AF, the absorption fraction of PFAS by skin; EDI, the estimated daily intake.

Using the RPF method, we first estimated the PFOA-equivalent risk of individual PFAS is 2.7 × $10^{-5}$-0.006 and 8.1 × $10^{-4}$-0.4 for decorative cosmetics and skin care products, respectively. Among the seven PFAS (PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA and PFDA) analyzed, PFNA contributes the most to the total PFOA-equivalent risk, accounting for 41.0–55.2 % in decorative cosmetics and 49.4–65.6 % in skin care products, followed by PFOA (21.0–28.3 % and 10.6–14.1 %, respectively) and PFBA (10.1–13.6 % and 6.8–9.1 %, respectively). However, the classification of PFNA as a high-risk substance still carries significant uncertainties, as the RPFs in risk assessment are recommended for situations involving oral exposure [23].

It should be noted that the RfD of 0.8 ng/kg bw/day for PFOA provided by the European Food Safety Authority in 2018 was adopted [24]. However, in 2024 April, the U.S. EPA released an updated reference dose of 0.03 ng/kg bw/day, which is much lower than the estimated daily intake from dermal exposure, indicating that dermal exposure may result in higher human health risk [29].

## 4. Discussion

One of the widely known uses of PFAS is additives in cosmetics that come into contact with the skin [2]. In a study of 45 cosmetic products, target PFAS measurements were performed for 15 of 45 cosmetic products purchased from local stores in Stockholm, which contained measurable concentrations of at least one PFAS [30]. Another latest study estimated the total mass of PFAS contained in cosmetics sold in California, the results indicate that it cumulatively contains 650–56000 kg of total PFAS, 370–37000 kg of organic fluorine, and 330–20000 kg of fluorinated side chains associated with PFAA precursors during one year [31]. This has raised concerns about PFAS exposure in cosmetics and prompted inquiries into whether PFAS in cosmetics may impact health.

Our study revealed functional groups and carbon chain length play a

key role in dermal absorption. Therefore, we explore the effect of physicochemical parameters (hydrophobicity and molecular weight) on dermal absorption, which is associated with functional groups and carbon chain length. The similar hydrophobicity between PFOA (log $K_{ow}$ = 5.30) and PFHxS (log $K_{ow}$ = 5.17) may have contributed to their consistent permeable fractions (PFOA:67.2 % in L group and 75.4 % in H group; PFHxS:70.6 % in L group and 80.2 % in H group), suggesting that hydrophobicity is also a primary factor influencing dermal permeability of PFAS [5,32]. Besides, the comparable MW between PFHxA (MW = 314) and HFPO-DA (MW = 330) may explain their consistent permeable fractions (PFHxA: 84.2 % in L group and 95.2 % in H group; HFPO-DA: 81.8 % in L group and 93.2 % in H group). Thus, the correlation analysis between permeable compartments of the target PFAS and their corresponding physicochemical parameters (log $K_{ow}$ and MW) was analyzed (Figure S5). Spearman correlation analysis showed that the dermal permeability of PFAS was inversely ($p < 0.05$) proportional to log $K_{ow}$ and MW of L and H group, which indicated that PFAS with larger molecular weight and higher hydrophobicity were more difficult to enter the body through the skin [33].

To further explore the correlation between *in vitro* experiment and *in vivo* experiment, we have used Eqs. (1)-(6) to calculate the penetration of 13 PFAS after 6 h, 8 h and 12 h exposure in the L group (Fig. 5), and compared with the permeability observed in a previous animal study [5]. The results showed that the permeability of PFBA was approximately twice as high *in vitro* compared to *in vivo*. Meanwhile, the permeability of PFPeA, PFHxA, PFHpA, PFOA, PFBS, and PFHxS showed similar or slightly lower results in vitro. The in vitro permeability of PFNA was only 0.14 times that of the *in vivo* data, and no permeability was observed for PFDA, PFUnDA, PFDoDA, PFTeDA, and PFOS after 6 h of in vitro exposure, while relatively low permeability (5.3 %-7.8 %) was observed in the *in vivo* studies. The permeability of most PFAS *in vitro* and *in vivo* experiments had a good correlation ($R^2$ = 0.41–0.51, $p < 0.05$), indicating that the *in vitro* experiment could reflect the real situation of *in vivo* exposure to a certain extent. Particularly, a paired *t*-test was performed to compare the permeability of 8 PFAS (PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFBS and PFHxS) after 6 h in 3D-HSE experiment with that observed in animal studies with 6 h exposure. The resulting *p*-value of 0.37 suggests an insignificant difference in dermal permeability between *in vivo* and *in vitro* conditions for these PFAS, suggesting that 3D-HSE models may be alternative to estimate the dermal absorption of chemicals.

Actually, several studies have used skin equivalents to investigate the

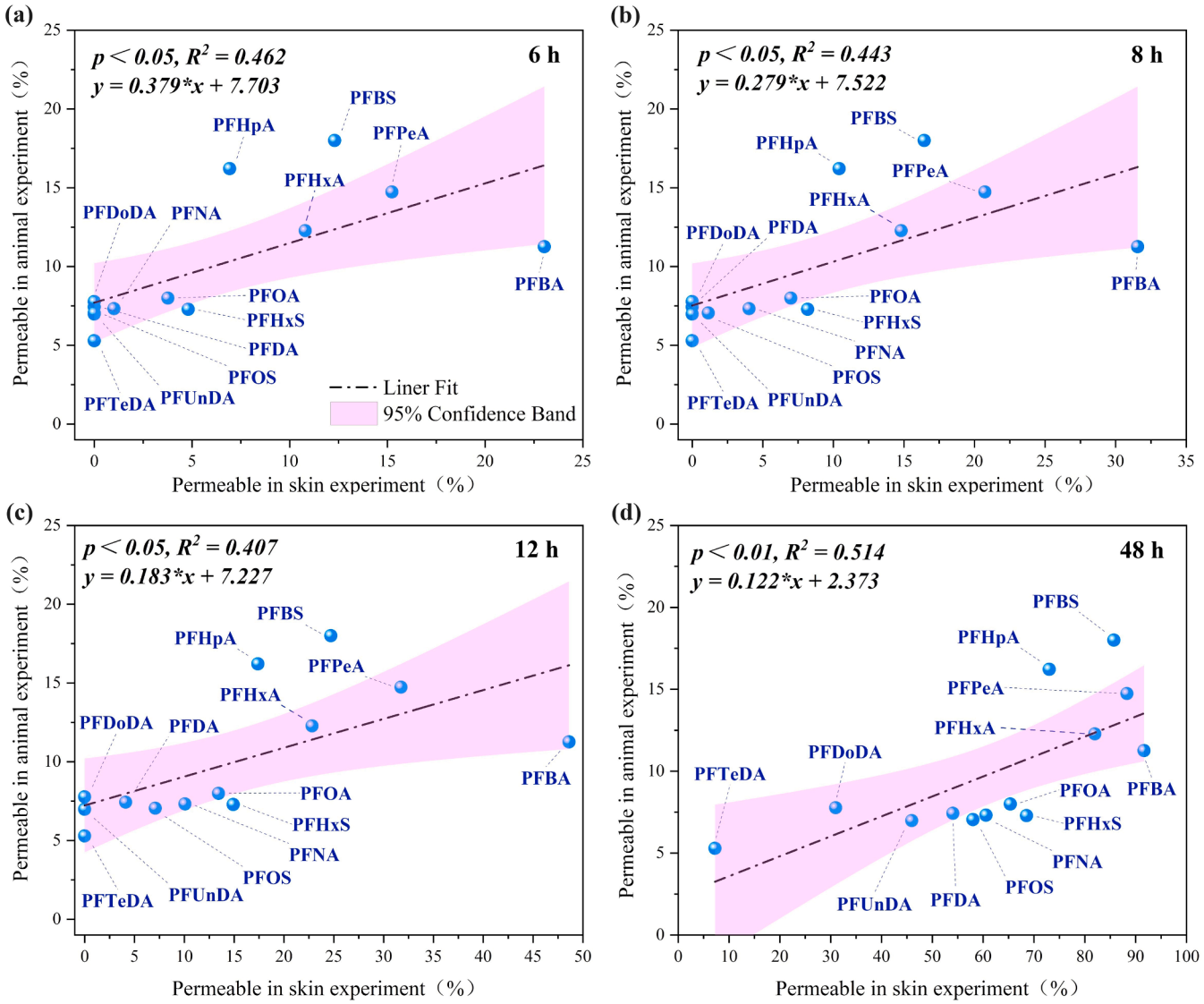


**Fig. 5.** Correlation of permeable in animal experiment after 6 h exposure with (a) calculated permeable (% of total measured mass present in the receptor compartment) following the 6 h exposure, (b) calculated permeable following the 8 h exposure, (c) calculated permeable following the 12 h exposure and (d) the permeable after the 48 h exposure (of the applied 312.5 ng/cm$^2$ dose).

dermal absorption of various substances, such as flame retardants, plasticizers and chlorinated paraffins (Table S8). As shown, our results are higher than that previous study on PFAS using EPISKIN RHE/L/13 model after 36 h exposure [12]. Differences can be affected by different parameters applied in these studies, such as exposure duration, solvent types, and the specific 3D-HSE models used. Therefore, comparisons should be made with caution. Meanwhile, the permeability of PFAS after 9 h of exposure was lower compared to phthalate and alternative plasticizers [34]. After 24 h of exposure, the permeability of PFAS ranged from 0.1 % to 67.1 %, with most target PFAS exhibiting higher permeability than brominated flame retardants (3.82–6.78 %) and polybrominated diphenyl ethers (ND to 24.92 %) [18,20].

In this study, the EDIs of seven PFAS (PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA and PFDA) through dermal exposure were estimated to be 0.46–22.8 pg/kg bw/day in decorative cosmetics and 11.0–815.7 pg/kg bw/day in skin care products. For decorative cosmetics, the EDIs of seven PFAS are relatively minimal, approximating 0.01–0.27 times the dietary exposure of the European population [35], and comparable to house dust ingestion of adults from Norway [36]. Contrastingly, the EDIs from skin care products are notably higher, especially for short-chain PFCAs. For instance, the dermal exposure of PFBA and PFPeA was 2.5 and 6.3 times greater than dietary exposure, respectively [35].

As known, manufacturers have shifted towards using shorter chain PFAS ($<C_8$), such as PFBA, PFBS, and PFHxA as alternatives. These compounds are commonly found in carpets, other textiles, and food packaging [37–39], which have triggered increasing biomonitoring in recent years. For example, between 1996 and 2010, the levels of PFBS and PFHxS in the blood of Swedish women increased by approximately 11 % and 8.3 % per year, respectively [40]. The detection frequencies of several short-chain perfluoroalkyl acids (PFBA, PFBS, PFHxA, PFHpA and PFPeA) have also been rising in breast milk globally, with a doubling time of about four years from 1996 to 2019 [41]. If short-chain PFCAs are used as substitutes in cosmetics, the total dermal exposure of short-chain PFCAs of would increase continually, which may elevate the biomonitoring and non-negligible health risk.

On another aspect, the intake of PFHxA, PFHpA, PFOA, PFNA, and PFDA from decorative cosmetics and skin care products ranges from 0.22 to 0.73 times that of dietary exposure [35]. Using PFOA as an instant, based on the median PFOA serum concentration data from the U.S. 2017–2018 NHANES database (1.37 ng/mL), the EDI of PFOA is approximately 0.16 ng/kg bw/day (Text S6). PFOA exposed from dermal uptake in decorative cosmetics and skin care products contributes approximately 0.066 ng/kg bw/day (median), accounting for 40 % of the total intake. More importantly, the half-life based on dermal exposure was generally longer than that from oral exposure. For example, the half-lives for total and free serum d6-BPA through dermal application are 21.4 and 17.6 h, over 3 times greater than oral application [36]. Typically, a longer half-life can lead to lower toxicity thresholds and higher risk, indicating the contribution of human health risk from dermal exposure calculated above may be markedly underestimated [42].

Over the past decade, the implementation of regulatory policies has led to a decline in temporal trends for PFAS in diet, resulting in decreased serum concentrations of PFAS [43,44]. If PFAS concentrations in cosmetics remain constant or decline slowly, the relative contribution of dietary intake to total daily PFAS exposure may diminish, underscoring the increasing importance of dermal exposure in assessing total PFAS intake. Besides, as the production and application of legacy PFAS face increasing regulatory scrutiny, new alternatives are emerging. HFPO-DA, a substitute for PFOA, has an annual production volume of 10–100 tons [45]. Compared to PFOA (7.0 % for 8 h exposure), the significantly higher dermal permeability of HFPO-DA (13.7 % for 8 h exposure) may lead to potential health risks. However, to date, the investigations on HFPO-DA in personal care products are quite limited, only one study has reported that the median levels of HFPO-DA in decorative cosmetics and skin care products are 1.54 ng/g [14].

Recently, many countries have begun to focus on the regulation of PFAS in cosmetics. Up to now, the European Union already prohibited the use of PFOS, PFOA, PFNA, PFHpA, and PFDA as cosmetic and personal care product ingredients under Annex II of the Regulation on Cosmetic Products [46]. In the United States, nine states have adopted 15 policies about PFAS in personal care products [47]. For example, California has passed two policies regarding PFAS in cosmetics. AB-2771 of 2022 prohibits all PFAS from being intentionally added to cosmetic products manufactured or sold in California [48]. AB-2762 of 2020 prohibits any cosmetic product containing any of several specified intentionally added ingredients (including 13 PFAS), except under specified circumstances [49]. Both of these bills took effect on January 1, 2025. Enhanced regulations are critical to eventually address the issue of PFAS contamination in decorative cosmetics and skincare products. Our study has well illustrated that dermal exposure contributes significantly to the total exposure for some PFAS, supporting the development of such policies.

Using the 3D-HSE model, we estimated the dermal exposure risk of PFAS. However, several uncertainties should be noted. In particular, the *in vitro* model was employed rather than the *in vivo* model in this study. Both methods have their advantages and limitations. The 3D-HSE model may allow more penetration compared to real human *ex vivo* skin, due to its relatively insufficient stratum corneum barrier function [50]. For instance, the permeability of the 3D-HSE model is approximately 1.1 times that of *ex vivo* skin in brominated flame retardants [18]. To address the reliability of the *in vitro* model, we correlated the *in vitro* results with existing *in vivo* data, revealing no significant differences across the eight out of the fourteen PFAS tested. Nonetheless, the use of acetone as a solvent for PFAS introduces an additional layer of uncertainty, as it may act as a mild barrier disrupter [6]. This may result in discrepancies between the permeability of PFAS observed in the experiment and that associated with real application products. Despite this, acetone remains a widely used solvent in *in vitro* dermal absorption studies involving environmental contaminants, such as brominated flame retardants [18], liquid crystal monomers [19], polybrominated diphenyl ethers [20] and chlorinated paraffins [51]. Compared to other solvents (e.g., methanol and hexane), acetone has shown minimal effect on skin barrier functions [52].

Furthermore, we adopted infinite-dose conditions to obtain key parameters of dermal absorption in alignment with previous research [20,51]. This approach was necessary given that the concentrations of individual PFAS (especially some long-chain PFAS) in commercial cosmetics are generally low. Consequently, using real products for exposure would likely result in PFAS levels falling below analytical detection limits. It is also important to note that our investigation focused on 14 of the target PFAS. Other intentional PFAS ingredients (e.g., fluorotelomer alcohols and fluorotelomer phosphate diester) may also be absorbed through the skin and metabolized into these target PFAS [53,54]. As a result, we may have underestimated the dermal exposure of these PFAS from cosmetics in real scenarios.

## 5. Conclusions

This study highlights the critical health risks of PFAS in cosmetics and skin care products via skin contact. In addition, our findings reveal that the permeability of PFAS varies significantly with carbon chain length and chemical structure, with shorter-chain PFAS exhibiting higher dermal absorption. As manufacturers increasingly utilize these shorter-chain alternatives, the potential for human exposure through cosmetic products escalates, raising urgent public health concerns. Furthermore, the calculations of estimated daily intakes suggest that dermal exposure can contribute significantly to some PFAS (for example, short-chain PFCA, PFOA) exposure. These results may provide support for legislative measures regarding PFAS in cosmetics and skin care products.

## CRediT authorship contribution statement

**Guanxiang Yuan:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Mengxin Sun:** Writing – review & editing, Investigation. **Wenhong Fan:** Writing – review & editing, Investigation. **Xiarui Fan:** Methodology, Investigation. **Ziwei Wang:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Baiyu Lai:** Methodology, Investigation. **Xinrui Leng:** Methodology, Investigation. **Guomao Zheng:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Zhaomin Dong:** Writing – review & editing, Investigation, Conceptualization.

## 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.

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## Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jhazmat.2025.138846.

## Data Availability

Data will be made available on request.

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