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Importance of Dermal Absorption of Polycyclic Aromatic Hydrocarbons Derived from Barbecue Fumes

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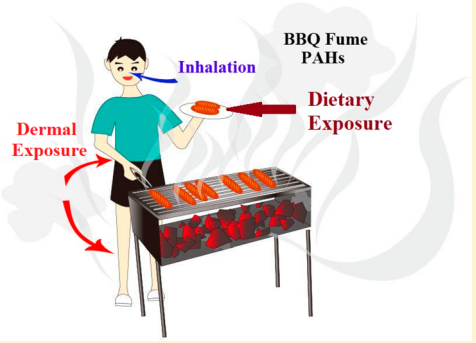
Supporting Information

ABSTRACT: Despite the ubiquity and carcinogenicity of polycyclic aromatic hydrocarbons (PAHs), their dermal absorption for the general population has not been adequately addressed. Aiming to verify the importance of dermal absorption of PAHs, barbecue (BBQ) in Guangzhou, China was chosen as a case study. Urine samples were collected and analyzed for nine hydroxyl (OH)-PAHs. Air, food, and cotton clothing samples were analyzed for 16 PAHs. Dietary exposure was the dominant exposure route with the greatest amounts of OH-PAH excretion and PAH intake. Dermal intake of low molecular-weight PAHs was greater than inhalation intake from the occurrence of atmospheric PAHs. In addition, the net excreted amounts of OH-naphthalene, OH-fluorene, OH-phenanthrene, and OH-pyrene via dermal absorption were 367, 63, 98, and 28 ng, respectively, upon 2.5-h exposure, comparable to those via combined dermal and inhalation exposure, which were 453, 98, 126, and 38 ng. The ratios of excretion to intake via dermal absorption were 0.11, 0.036, and 0.043 for fluorene, phenanthrene, and pyrene, respectively, lower than the ratios from dietary exposure (0.38, 0.14, and 0.060) but higher than the ratios from inhalation (0.097, 0.016, and 0.025). In the case of BBQ fumes, dermal absorption was a more important pathway for intake of low molecular-weight PAHs than inhalation.



INTRODUCTION

Ambient air pollution in both urban and rural areas was reported to cause three million premature deaths worldwide in 2012, and 14% of the deaths were caused by lung cancer.[1] Ambient air quality for 92% of the world's population does not meet the WHO air quality guideline values.[1] Although fossil fuel burning and industrial emissions are mostly responsible for deteriorating ambient air quality, certain special pollution episodes, such as fumes generated from barbeque (BBQ), electronic-waste combustion, wild fire, and waste incineration, should not be overlooked. Incomplete combustion of organic matter often encountered in these events can generate large amounts of contaminants, including polycyclic aromatic hydrocarbons (PAHs) and halogenated flame retardants.[2−4] The general population may not be aware of the potential health risk they are subject to, as these pollution episodes do not happen so often.

Although BBQ may not be a daily activity, it is perhaps one of the most popular outdoor events around the world. Barbeque not only improves the flavor of foods but also provides a venue for get-togethers of families and friends.[5] Seventy-five percent of adults in the United States own a grill or smoker, and nearly half of them grill once or twice a week in summer.[5,6] Eighty-seven percent of Americans grilled on the Fourth of July in 2016.[7] Households in the United Kingdom and Europe barbecue more than 10 times a year with a preference for charcoal as a fuel source.[8] While grilling, people are surrounded by BBQ fumes containing large amounts of PAHs, which can cause respiratory disease (even lung cancer) and are carcinogenic to mouse skins.[9−12] Wu et al.[2] confirmed that bystanders would also be exposed to considerable amounts of PAHs via dermal absorption and inhalation even though they did not eat grilled foods, and dermal absorption with PAHs may be a significant intake pathway.

Diet has been recognized as the most predominant exposure route, whereas inhalation is inevitable and constant. Thus, many studies have focused on dietary ingestion and inhalation in human health risk assessment.[3,6,13−15] However, dermal absorption has been mainly investigated for occupational exposure.[16,17] Dermal absorption of the general population to fumes and related health risk seem to have been largely overlooked. Most previous studies have used models to estimate dermal absorption of PAHs.[18−20] Only a few investigations have been conducted on exposure of firefighters and smokers to PAHs from wild fire and tobacco smoke, respectively, with urinary hydroxyl (OH)-PAHs as target compounds.[21,22] Few studies used human biomonitoring to

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examine internal exposure to PAHs via dermal absorption for the general population.

To help fill this knowledge gap, the present study quantified the intake amounts of light molecular-weight PAHs from external and internal exposure to BBQ fumes via dermal absorption and inhalation, as well as dietary ingestion for comparison. An outdoor BBQ event, participated in by 20 males in Guangzhou, Guangdong Province of China, was chosen as a case study. Sixteen priority PAHs (Supporting Information, SI, Table S1) were measured in gaseous and particulate samples, food items, and clothes, and nine OH-PAHs were measured in the participants' urine samples.

MATERIALS AND METHODS

Materials. A standard solution containing 16 PAHs (Table S1) was obtained from AccuStandard (New Haven, CT). 1-Naphthol (1-OH-Nap), 2-naphthol (2-OH-Nap), 1-hydroxyphenanthrene (1-OH-Phe), 2-hydroxyphenanthrene (2-OH-Phe), 3-hydroxyphenanthrene (3-OH-Phe), 4-hydroxyphenanthrene (4-OH-Phe), and 9-hydroxyphenanthrene (9-OH-Phe) were purchased from Dr. Ehrenstorfer GmbH (Augsburg, Germany). 2-Hydroxyfluorene (2-OH-Flu), 2-naphthol-d_7, and 1-hydroxyphenanthrene-d_9 (1-OH-Phe-d_9) were purchased from Toronto Research Chemicals (Ontario, Canada). 1-Naphthol-d_7 (1-OH-Nap-d_7) was purchased from C/D/N Isotopes (Quebec, Canada). 1-Hydroxypyrene-d_9 (1-OH-Pyr-d_9) was purchased from Chiron AS (Trondheim, Norway). 3-Hydroxyphenanthrene-$^{13}C_6$ and 6-hydroxychrysene-$^{13}C_6$ were purchased from Cambridge Isotope Laboratories (Andover, MA). Detailed information about the standard materials of PAHs was presented in a previous study.[2]

Target Population and Sampling Strategy. Outdoor barbecue heating by charcoal was conducted from 17:00 to 19:30 on November 5, 2016 in Guangzhou. Twenty males aged 22 to 25 participated in the sampling campaign, and were divided into three groups. The first group (group A) consisted of seven participants subjecting to dietary, dermal, and inhalation exposures. The second group (group B) consisted of seven participants with dermal and inhalation exposures. The third group (group C) consisted of six participants with dermal absorption only, who wore hoods to avoid inhaling barbecue fumes. Each hood is composed of a tightly sealed mask and a gas cylinder of 9 L volume filled with compressed air. The participants in groups B and C were allowed to eat boiled foods only. Pre-exposure urine samples were collected three times, at approximately 17 h before barbecue, in the morning but before lunch, and immediately before the beginning of barbecue. Postexposure samples were collected in 35 h after barbecue. The participants recorded collection time and total urine sample volume for every urination of postexposure period, and completed a questionnaire (Text S1). The urine samples were collected in polypropylene centrifuge tubes and stored at −80 °C until analysis.

Atmospheric samples were collected at approximately 2 and 10 m away from BBQ stoves at 1.2 m above the ground, and four BBQ stoves were arranged in a rectangle formation. Gaseous samples were stored in polyurethane foam, whereas particulate samples were taken on 47 mm diameter glass microfiber filters (Whatman International, Maidstone, England) at a constant flow rate of 30 L min^{-1} by Micro-Orifice Uniform Deposit Impactor (MOUDI) (MSP Corporation, Shoreview, MN). Particulate samples were segregated into 11 size fractions, i.e., >18, 10−18, 5.6−10, 3.2−5.6, 1.8−3.2, 1.0−1.8, 0.56−1.0, 0.32−0.56, 0.18−0.32, 0.10−0.18, and 0.056−0.10 μm. All participants wore their own clothes but had a 20 × 20 cm^2 cotton cloth hanging in front of their chests from the beginning of the BBQ event to the end, and dispersedly sat in a circle around the BBQ stoves. The participants were asked to grill BBQ food with the help of volunteers, but they could not move without permission. The clothing samples were collected in aluminum foil after 2.5 h exposure. Barbecue foods were collected with aluminum foil. All these samples were stored at −20 °C until analysis.

To further confirm the dermal absorption of PAHs from BBQ fumes was not compromised by other exposure routes, we conducted a separate indoor BBQ event, and collected and analyzed silicone wristband and skin-wipe samples (Text S6).

Measurement of OH-Polycyclic Aromatic Hydrocarbons. Urine samples were taken out from a freezer and thawed at a dark place. Two milliliters of each sample was spiked with the surrogate standards, 1 mL of ammonium acetate buffer, 50 μL of β-glucuronidase/sulfatase, and 30 μL of mercaptoethanol. The homogenized sample was incubated at 37 °C for 16 h and extracted with a solid phase extraction method.[23] Briefly, each cartridge was activated with 5 mL methanol, 5 mL water, and 10 mL 25 μmol L^{-1} monopotassium phosphate buffer, respectively. Each hydrolyzed urine sample was added to the cartridge at a flow rate of <1.0 mL min^{-1}, which was then washed with 4 mL monopotassium phosphate buffer and 5 mL water, dried in vacuum, and finally eluted with 12 mL methanol. The eluate was concentrated to 500 μL with a rotatory evaporator, filtered through a 0.22 μm nylon filter, and spiked with the internal standards before instrumental analysis. Urinary creatinine in each urine sample was determined at Guangzhou Overseas Chinese Hospital with a 7600−020 automatic biochemical analyzer (Hitachi, Japan).

The concentrations of OH-PAHs were determined with an LC-20A high performance liquid chromatography (Shimadzu, Japan) coupled to a Triple Quad 5500 mass spectrometer (AB SCIEX, Redwood City, CA). Chromatographic separation was provided by a Zorbax Eclipse Plus-C18 column (100 × 2.1 mm^2; 1.8 μm thickness). The mobile phases were methanol and water mixture (2:3 in volume) for solvent A and methanol for solvent B, at a flow rate of 0.27 mL min^{-1}. Injection volume was 5 μL. The gradient conditions were as follows: 0−1 min, 5% B; 1−3 min, 5−30% B; 3−5 min, 30% B; 5−10 min, 30−40% B; 10−15 min, 40−80% B; 15−16 min, 80−70% B; 16−20 min, 70−5% B; and 20−24 min, 5% B. The column and ion source temperatures were maintained at 40 °C and 450 °C, respectively. Sample analysis was conducted with multiple-reaction monitoring in negative ion electrospray ionization under −4500 V spray voltage.

Measurement of Polycyclic Aromatic Hydrocarbons. Each sample was spiked with the surrogate standards before extraction. Gaseous samples (polyurethane foams) were Soxhlet extracted with 200 mL of hexane, dichloromethane, and acetone mixture (2:2:1 in volume) for 48 h. Particle and food samples were extracted and cleaned up with the methods described previously.[2] For 20 × 20 cm^2 cotton cloth samples, each was Soxhlet extracted with 200 mL of hexane for 48 h, and the extract was concentrated to 1 mL with a Zymark TurboVap 500 (Hopkinton, MA). The concentrated extract was purified and fractionated with a glass column filled with 6 cm alumina, 12 cm neutral silica gel, and 1 cm anhydrous sodium sulfate from bottom to top. The fraction containing PAHs was eluted with 50 mL of hexane and dichloromethane mixture (1:1 in

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volume), concentrated and solvent-exchanged to hexane, and further concentrated to 50 μL in vial under a gentle stream of N_2. The extract was spiked with the internal standards before instrumental analysis. Pretreatment and extraction procedures for silicone wristband and skin-wipe samples are presented in Text S6. All extracts were analyzed with a Shimadzu GCMS-2010 Plus with a DB-5MS capillary column (30 m × 0.25 mm i.d. with 0.25 μm film thickness).[2]

Quality Assurance and Quality Control. A procedural blank, a spiked blank, a matrix sample, and a matrix-spiked sample were analyzed for each batch of 20 urine samples. The recoveries of the surrogate standards, i.e., 1-OH-Nap-d_7, 1-OH-Phe-d_9, and 1-OH-Pyr-d_9, were 91 ± 6%, 93 ± 4%, and 68 ± 10% in blank samples, 89 ± 10%, 90 ± 8%, and 84 ± 14% in field samples, and 89 ± 5%, 86 ± 6%, and 87 ± 3% in matrix-spiked samples. For atmospheric, food, and clothing samples, the recoveries of the surrogate standards, i.e., naphthalene-d_8, acenaphthene-d_{10}, phenanthrene-d_{10}, chrysene-d_{12}, perylene-d_{12}, and benzo[*ghi*]perylene-d_{12}, were 51 ± 11%, 64 ± 12%, 79 ± 18%, 90 ± 24%, 82 ± 19%, and 84 ± 16%. Only low levels of 2-OH-Nap and 1-OH-Nap were detected in procedural blanks; therefore they were not subtracted from the measured concentrations in urine samples. Concentrations of PAHs in field samples were corrected by those in corresponding procedural blanks within the same batch. The lowest calibration concentrations divided by the actual sample volumes were defined as the reporting limits in the present study.

Data Analysis. Net excreted amounts of OH-PAHs were calculated based on personal urine volumes and OH-PAH concentrations for a 24-h period. As 1-OH-Phe and 9-OH-Phe were not separable by the chromatographic column, they were combined in data analysis and designated as 1 + 9-OH-Phe. The sum of 2-OH-Nap and 1-OH-Nap is defined as OH-Nap, whereas the sum of 1-OH-Phe, 2-OH-Phe, 3-OH-Phe, 4-OH-Phe, and 9-OH-Phe is defined as OH-Phe.

Dermal intake of PAHs was assessed using the formula proposed by Weschler and Nazaroff,[24,25] with body surface area estimated using a formula by Stevenson[26] (Text S2). Exposed dermal fractions of 15−30% body surface area were adopted from the bare-skin fractions of the participants, estimated based on previously reported results.[27,28] The model by the simplified equations from the International Commission on Radiological Protection was adopted for assessing inhalation intake of PAHs[29] (Text S3). Intake amounts of PAHs via dermal and inhalation pathways were estimated for an exposure period of 2.5 h. Detailed procedures for estimating dietary and dermal intake of PAHs from exposed clothing are provided in Text S4. Briefly, the dermal intake of gaseous (ED_{dg}) and particulate PAHs (ED_{dp}) were estimated by the following:

$$ED_{dg} = C_g \times k_{p\_g} \times SA \times f \times t \quad (1)$$

$$ED_{dp} = C_p \times k_{p\_d} \times SA \times f \times t \quad (2)$$

where C_g and C_p are the concentrations of gaseous and particulate PAHs, respectively (ng m^{-3}); f is the exposed dermal fraction, assumed to follow uniform distribution with a minimum value of 15% and a maximum value of 30%; k_{p_g} and k_{p_d} are the transdermal permeability coefficients of target PAHs in the gaseous and particulate phases, respectively (m h^{-1}); and t is the exposure time (h). Inhalation intakes of gaseous (ED_{ig}) and particulate PAHs (ED_{ip}) were estimated by the following:

$$ED_{ig} = C_g \times IR \times t \quad (3)$$

$$ED_{ip} = C_{dp} \times IR \times t \quad (4)$$

where C_{dp} is the sum of particulate PAH concentrations deposited in three regions of the respiratory tract (ng m^{-3}), and IR is the participants' breathing rate (m^3 h^{-1}). Dietary intake (ED_{food}) was estimated by the following:

$$ED_{food} = C_{food} \times IN_{food} \quad (5)$$

where C_{food} is the concentration of PAHs in barbecued food (ng g^{-1}), and IN_{food} is the amount of dietary ingestion (g).

Monte Carlo simulation was used to evaluate the uncertainty and variability of intake amounts of PAHs via dermal and inhalation pathways, as well as dermal intake from clothing. Significance analysis between groups B and C was tested by independent-samples *t*-test with SPSS 20.0 at a significance level of $\alpha = 0.05$. Detailed data analysis and results from the confirmatory experiment are presented in Tables S12 and S13 and Figures S2, S3, S6 and S7.

RESULTS AND DISCUSSION

Urinary Excretion of OH-PAHs Ingested via Dermal Absorption and Inhalation. Creatinine-corrected concentrations of OH-PAHs in the participants' urine reached the highest level within 10 h after exposure to BBQ fumes, and mostly declined to the initial levels within 24 h (Figures S4−S6). Although concentrations of urinary OH-PAHs were higher via dietary ingestion than via dermal absorption and inhalation, they clearly increased after exposure to BBQ fumes via dermal absorption and inhalation (Figure 1). The increased concentrations of OH-Nap, OH-Flu, OH-Phe, and OH-Pyr via combined dermal and inhalation exposure were greater than those via dermal absorption only, but the dermal and inhalation pathways for isomers of some PAH metabolites were different. In addition, the increased concentrations of 2-OH-Nap, 2-OH-Phe, and 3-OH-Phe were greater via dermal absorption than via combined dermal and inhalation exposure, whereas opposite was true for 1-OH-Nap, 1+9-OH-Phe, and 4-OH-Phe. We hypothesized that dermal absorption and inhalation exerted different effects on the metabolism of PAHs, and consequently

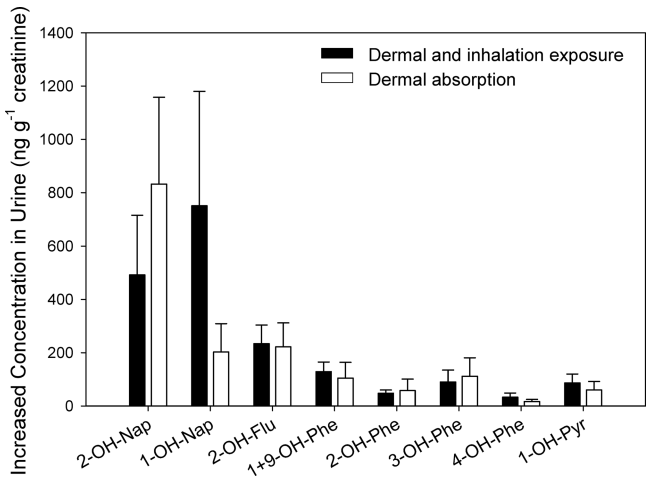

Figure 1. Increased concentrations in urine (ng g^{-1} creatinine) of nine OH-PAHs after exposure to barbecue fumes via combined dermal and inhalation exposure (B) and dermal absorption only (C).

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the formation of PAH metabolites. Subject-to-subject variability would be another possibility.

Net amounts of OH-PAHs excreted from the participants in both groups B and C decreased with increasing molecular weights (Figure 2). Exposure to BBQ fumes through either

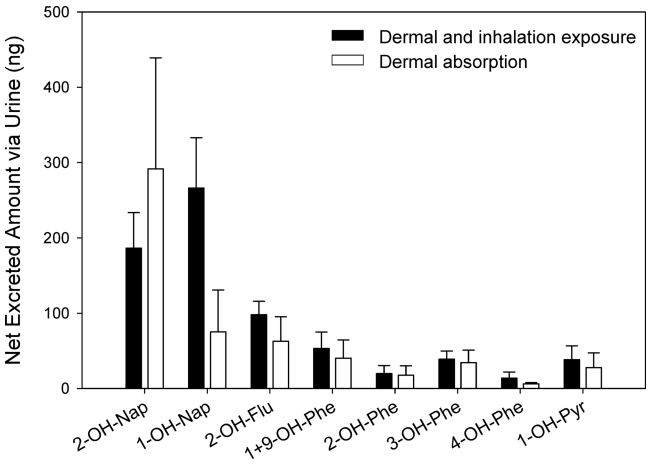

Figure 2. Net excreted amounts of OH-PAHs via urine for combined dermal and inhalation exposure to barbecue fumes (B) and for dermal absorption of the fumes (C). Net excreted amount has been corrected by the urinary initial concentration level in each participant.

dermal absorption or inhalation would result in considerable amounts of OH-PAHs excreted in urine. Although the net excreted amounts of OH-PAHs upon combined dermal and inhalation exposure were generally greater than those upon dermal absorption (except for 2-OH-Nap), they were comparable for OH-Flu, OH-Phe, and OH-Pyr (Figure 2). The net urinary excreted amounts of OH-PAHs were not significantly different between groups B and C, except for 1-OH-Nap ($p < 0.05$), 2-OH-Flu ($p < 0.05$), and 4-OH-Phe ($p < 0.05$), but the difference between groups B and C was smaller than the net excreted amount for group C. Hence, dermal absorption yielded greater excreted amounts of PAHs than inhalation based on the net excreted amounts of OH-PAHs. Gong et al.[30] estimated that dermal absorption from skin lipids found on head, hands, and arms was comparable to inhalation, and would be greater than inhalation if an entire body was counted. In the present study, a real barbecue was conducted, and the fraction of exposed skin areas for each participant was approximately 15−30%. Because dermal absorption of PAHs increases with increasing exposed skin area, the intake amounts of PAHs via dermal absorption would be even greater than those via inhalation in the present study if the fraction of exposed skin area increased.

The net excreted amount of 1-OH-Nap derived from combined dermal and inhalation exposure was significantly ($p < 0.001$) higher than that from dermal absorption only. Besides, urinary 1-OH-Nap in the participants of group B exposed to BBQ fumes via combined dermal absorption and inhalation largely accounted for the increased portion of total OH-PAHs during the period of metabolism, but not for dermal absorption only. Therefore, 1-OH-Nap may be used as a biomarker of inhalation exposure to PAHs. Adetona et al.[21] corroborated that the creatinine-corrected 4-OH-Phe concentration was associated with personal exposure to airborne PAHs and can be used as a biomarker of exposure to wild fire or vegetative biomass smoke. Although 4-OH-Phe concentrations were significantly different between dermal exposure and inhalation, they were low in urine in the present study. Hence 4-OH-Phe is not a suitable biomarker for assessing dermal absorption or inhalation.

Characteristics and Distribution of PAHs in BBQ Fumes. Because the concentrations of gaseous Nap in field blanks were greater than those in field samples and only trace levels of Nap were detected in several size fractions of particle samples, Nap was not included for analysis of airborne PAHs and assessment of dermal and inhalation intakes. The concentrations of gaseous and particulate PAHs were 1160 and 52 ng m^{-3} at 2-m site, and 685 and 18 ng m^{-3} at 10-m site, respectively (Table 1). Obviously, concentrations of PAHs in

Table 1. Measured Gaseous (C_g; ng m^{-3}) and Particulate Concentrations (C_p; ng m^{-3}) of Polycyclic Aromatic Hydrocarbons (PAHs) around Barbecue Stoves

	2 m			10 m		
	C_g	C_p	total	C_g	C_p	total
Acy[a]	94	0.78	95	17	0.54	18
Ace	30	3.8	34	3.3	2.9	6.3
Flu	95	3.3	98	35	1.6	37
Phe	480	6.8	490	270	3.0	270
Ant	31	2.5	34	19	0.88	20
Fla	170	3.7	170	160	1.5	160
Pyr	110	3.5	110	87	1.9	89
BaA	29	2.5	32	17	1.7	19
Chr	110	3.4	110	73	2.4	75
B[b+k]F	15	13	28	3.8	1.2	5.0
BaP	<RL[b]	6.3	6.0	<RL	0.16	0.16
IcdP	<RL	1.1	1.1	<RL	<RL	<RL
DahA	<RL	RL	RL	<RL	<RL	<RL
BghiP	<RL	1.4	1.4	<RL	<RL	<RL
$\sum_{15}$PAH	1160	52	1200	685	18	700

[a]All acronyms of polycyclic aromatic hydrocarbons are defined in Table S1. [b]RL is the acronym of the reporting limit at 56 pg m^{-3} with an air volume of 4.5 m^3.

both gaseous and particulate phases decreased with increasing distance from the BBQ stoves, consistent with our previous results obtained in Urumqi, China.[2] The concentrations of gaseous PAHs were comparable at two different distances, with 3−4 ring PAHs as the dominant constituents accounting for 81% and 92% of $\sum_{15}$PAH at 2-m and 10-m sites, respectively. However, 4−6 ring PAHs dominated the particle phase, particularly in fine particles ranging from 0.18 to 1.8 μm, also consistent with our previous study conducted in urban Guangzhou, China.[3]

Dermal versus Inhalation Intakes of PAHs. Transdermal permeability coefficient (k_{p_g}) is a mass-transfer parameter that describes the ability of organic compounds to transfer from air to dermal capillaries.[24] The values of k_{p_g} estimated in the present study (Text S2) were in the range of 3.3−6.0 m h^{-1} for selected PAHs (Table S3), all greater than 3.0 m h^{-1}, implicating direct dermal absorption of PAHs as an important pathway.[24] The values of k_{p_g} decrease with increasing molecular weight of PAHs (Table S3), i.e., higher molecular-weight PAHs possess less likely to transfer from air to dermal capillaries. Weschler et al.[31] also argued that dermal absorption is presumably less important with higher molecular-weight phthalates. Conversely, high molecular-weight PAHs tend to affiliate with particles. Because coarse particles settle rapidly by

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gravitation whereas ultrafine particles diffuse efficiently, they both can deposit quickly onto human surfaces and contribute to dermal absorption.[32] Thus, particle sizes have great influence on dermal absorption of particle-bound PAHs. In the present study, the transdermal permeability coefficients (k_{p_d}) of particle-bound PAHs were estimated from the same equation used for those of gaseous PAHs but based on deposition velocities for different particle sizes (Text S2), which were subsequently used to assess dermal absorption of particle-bound PAHs.

The concentrations of airborne PAHs at the 2-m site were used to estimate dermal and inhalation intakes of PAHs. The estimated intake amounts of gaseous Flu, Phe, and Pyr were 560, 2750, and 650 ng via dermal absorption, greater than inhalation intakes of 360, 1790, and 430 ng, whereas opposite was true for particulate PAHs (Table 2). These results are consistent with a previous study by Wu et al.[2] and a modeled assessment of dermal and inhalation exposures to PAHs by Shi and Zhao.[20] Inhalation exposure to particle-bound PAHs is highly particle-size dependent, which influences the efficiency of PAHs to enter into human body and deposit in the respiratory tract.[3] The proportion of particle-bound PAHs deposited in the head airway, tracheobronchial region, and alveolar region ranged from 60−87%, 3.7−6.9%, and 8.6−33%, respectively (Table S4). Calculated concentrations of particulate Flu, Phe, and Pyr deposited in the human respiratory tract were 1.68, 3.08, and 2.00 ng m^{-3} respectively (Table S4), the fractions of which deposited in the respiratory tract were 50%, 46%, and 57%, i.e., not all particle-bound PAHs are available for inhalation intake. Low molecular-weight particle-bound PAHs tend to deposit in the head airway not the alveolar region (Tables S4). High molecular-weight particle-bound PAHs prefer to occur in fine particles, which tend to deposit in the alveolar region but much of it can also be easily exhaled. Therefore, the amounts of particle-bound PAHs ingested via inhalation may be overestimated.

As Flu, Phe, and Pyr mainly exist in the gaseous phase, dermal and inhalation exposures to gaseous Flu, Phe, and Pyr dominated the total intakes from the combined gaseous and particulate phase based on model estimation. Moreover, dermal absorption of these target compounds in the gaseous phase was calculated to contribute to 61%, 60%, and 60% of the dermal plus inhalation intake, higher than inhalation with 39%, 39%, and 39%, respectively (Table 2). These estimated results were consistent with previous findings that the contributions to both dermal and inhalation intake from gaseous Phe and Pyr were 49% and 65% via dermal absorption and 46% and 30% via inhalation.[20] Overall, the dermal intake of selected PAHs was greater than inhalation intake for the gaseous plus particle phases.

Comparison of Exposure Pathways for Metabolism of PAHs. The urinary net excreted amounts of OH-Nap, OH-Flu, OH-Phe, and OH-Pyr ingested via dietary exposure, estimated from the difference between groups A and B, were 2850 ± 1080, 826 ± 499, 2010 ± 1240, and 183 ± 181 ng, while the intake amounts of Nap, Flu, Phe, and Pyr estimated by eq 5 were 5380 ± 440, 2150 ± 282, 14 900 ± 2020, and 3050 ± 788 ng (Tables S6−S8). On the basis of the intake amounts of PAHs and net excreted amounts of OH-PAHs via diet (Figure 3a), dermal absorption (Figure 3b), combined dermal absorption and inhalation (Figure 3c), and inhalation (Figure 3d), diet contributed to the largest intake amounts of PAHs and excreted amounts of OH-PAHs, varying with the

Table 2. Amount of PAH Intake (ng) by Dermal and Inhalation Exposure to Barbecue Fumes during 2.5-h Period

		ED_d[a]			ED_i[b]			ED_{d+i}[c]		
		Flu[d]	Phe[e]	Pyr[f]	Flu	Phe	Pyr	Flu	Phe	Pyr
gas phase	mean	560	2750	650	360	1790	430	910	4540	1080
	95% CI[g]	380−740	1900−3650	450−860	340−380	1690−1890	410−450	740−1100	3700−5400	880−1300
particle phase	mean	1.9	3.4	2.7	6.3	12	7.5	8.2	15	10
	95% CI	1.2−2.7	2.1−5.0	1.7−4.0	6.0−6.7	11−12	7.1−7.9	7.4−9.1	14−17	9.1−12
Sum	mean	560	2750	650	360	1800	440	920	4560	1090

[a]Intake amount of PAHs via dermal absorption. [b]Intake amount of PAHs via inhalation. [c]Intake amount of PAHs via combined dermal and inhalation exposure. [d]Flu = fluorene. [e]Phe = phenanthrene. [f]Pyr = pyrene. [g]CI = confidence interval.

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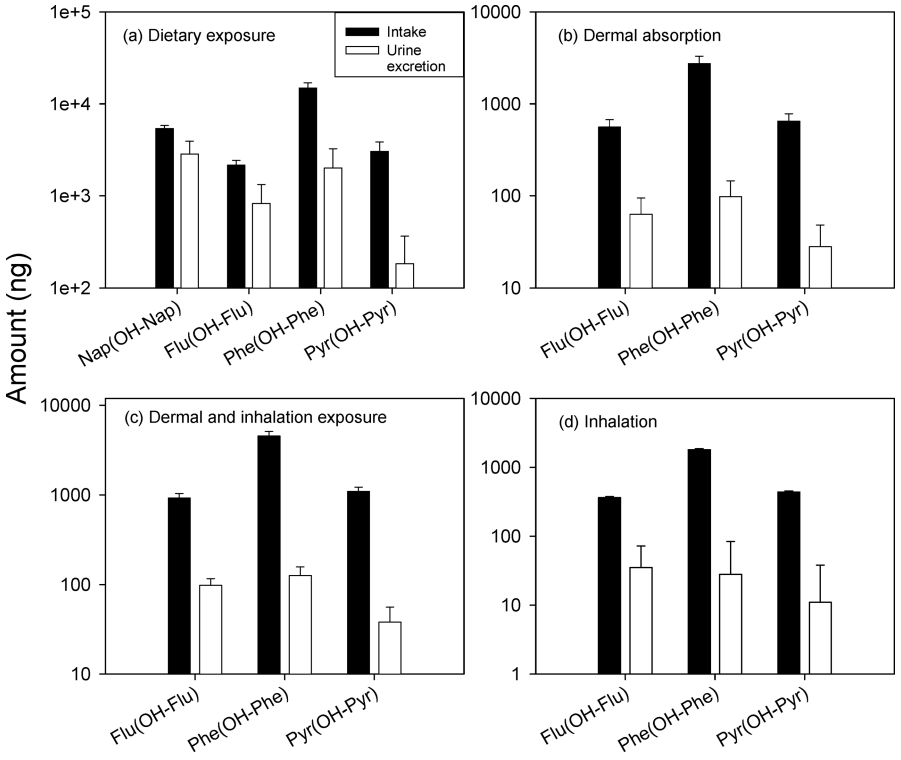

Figure 3. Amounts of PAHs intake and OH-PAHs urinary excretion for (a) dietary exposure, (b) dermal absorption, and (c) combined dermal and inhalation exposure. The difference between exposure wearing a hood (dermal absorption) and exposure without wearing a hood (dermal and inhalation exposure) represents (d) inhalation. The black and white bars represent the amounts of PAHs intake and OH-PAHs excretion, respectively.

concentrations of PAHs in BBQ foods and the intake rates within the gastrointestinal tract, for which the intake rate was at least 30%.[33] Moreover, the ratios of excretion to intake for Nap, Flu, Phe, and Pyr were 0.53, 0.38, 0.14, and 0.060 via diet, respectively (Table S9), indicating that the urinary excretion amounts of PAH metabolites decreased with increasing molecular weights, as gastrointestinal fluids and transport process across the intestine can affect the bioavailability of PAHs.[34] High molecular-weight PAHs were detected in BBQ foods, but metabolites of 4−5 ring PAHs were not detected in urine samples, which were strongly dependent upon the presence of bile in the intestinal lumen,[35] and preferred to be excreted in feces.[34]

Although dietary ingestion was a predominant exposure route for PAHs, dermal absorption and inhalation should not be overlooked. The ratios of excretion to intake for Flu, Phe, and Pyr were 0.11, 0.036, and 0.043 via dermal absorption, 0.11, 0.028, and 0.035 via combined dermal absorption and inhalation, and 0.097, 0.016, and 0.025 via inhalation, respectively (Table S9). Dermal absorption had the second highest excretion rate of OH-PAHs after dietary ingestion (Figure 3a, b). The mean ratio of excretion to intake of PAHs by dermal absorption was more than a quarter of that by dietary exposure; particularly, the excretion to intake ratio for Pyr via dermal absorption was comparable to that via dietary ingestion. For Flu, Phe, and Pyr, the ratios of excretion to intake via dermal absorption were higher than those via inhalation, possibly attributed to greater bioavailability of PAHs through dermal absorption than through inhalation. Previous studies suggested that the lipophilicity of PAHs affects the reactivity and accessibility of metabolism.[34,36] Stratum corneum, which is not only hydrophilic but also hydrophobic, is the main barrier for molecular diffusion in dermal absorption.[37,38] Thus, oils in BBQ fumes can probably enhance the dermal absorption of PAHs. The activity of enzymes can also influence dermal absorption, and skin contained many of the same enzymes as the liver for PAHs metabolism.[38] Furthermore, gas exchange in the alveoli of the lung would decrease the amount of PAHs via inhalation.[39] All these factors favored dermal absorption over inhalation as the exposure pathway of light molecular-weight PAHs from BBQ fumes.

In particular, urinary excretion of Nap metabolites was correlated to exposed skin area (Figure 4), suggesting more efficient intake of low molecular-weight PAHs by dermal absorption than inhalation. Weschler et al.[31] also demonstrated that dermal absorption of polluted air contributed great amounts of low-molecular-weight phthalates to the total intake. However, a large proportion of PAH metabolites may remain in the body and are not excreted, resulting in tissue accumulation.[34] Residual PAH metabolites may be transferred to other tissues and become protein- or DNA-adducts, which can damage DNA or cause tumors.[34] Yet little is known about the effects on the tumorigenicity of PAH mixtures, including light molecular-weight components, which still needs further examination.[34]

Effects of Clothing on Dermal Absorption. Given the importance of dermal absorption in intake of PAHs from BBQ fumes, it is natural to further look into the impacts of clothing on dermal absorption of BBQ fumes. No such effort has been reported in the literature. In the present study, cotton cloth samples exposed to barbecue fumes contained detectable 2−4 ring PAHs (Table S10), and the concentration distribution of PAHs in clothes was similar to that in gaseous samples, suggesting that clothes are able to sorb PAHs and may facilitate

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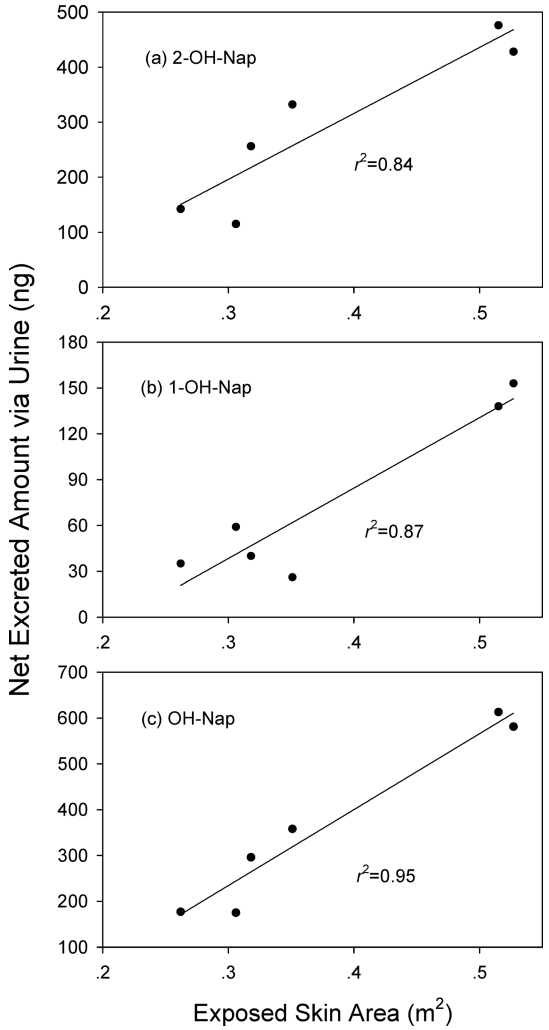

Figure 4. Relationship between the net excreted amounts of (a) 2-OH-Nap, (b) 1-OH-Nap, and (c) OH-Nap (sum of 2-OH-Nap and 1-OH-Nap) via urine by dermal absorption of barbecue fumes and exposed area of skin in group C.

dermal intake of PAHs. Morrison et al.[40] confirmed that clothes previously exposed to pollutants could increase the amounts of dermal intake, whereas clean clothes could impede skin absorption. On the basis of the correlation between net excreted amount of OH-Nap and exposed skin area (Figure 4), clothes may reduce dermal intake of PAHs in short-term exposure to BBQ fumes.

However, clothes could not protect skin completely from pollutant exposure.[41] The mass-transfer barrier of clothes to dermal intake would substantially be lowered once the absorption capacity of clothes is partially breached.[42] Estimation of dermal absorption from exposed clothes was based on the PAH concentrations in cotton cloth samples, assuming clothes with the same concentrations of PAHs were worn for 1 day. As clothing samples fully sorbed PAHs from BBQ fumes, human skin may sorb considerable amounts of PAHs from polluted clothes (Table S11), especially for 4−5 ring PAHs. The amount of Phe intake is the greatest, followed by those of Chr, Pyr, and Fla, thanks to their high concentrations in the clothes and BBQ fumes. The estimated amounts of Flu, Phe, and Pyr intake from bare-skin absorption of polluted clothes were equal to 18%, 22%, and 18% of those from bare-skin absorption of BBQ fumes. This implies that dermal absorption to polluted clothes is also an important source of PAHs as compared to direct dermal absorption of BBQ fumes. Polluted clothes may become a persistent exposure source under certain circumstances and should be treated properly to reduce dermal absorption of contaminants.

Implications and Limitations. Three pieces of evidence from the present study implicate dermal absorption as a greater contributor than inhalation to human uptake of low molecular-weight PAHs from BBQ fumes. First, modeling results suggested that intakes of low molecular-weight PAHs intakes were greater via dermal absorption than via inhalation. Second, dermal absorption was more significant than inhalation in excreting OH-PAHs through urine. Third, dermal pathway may be more effective than inhalation for metabolism of PAHs. Sensitivity analysis (Table S5) indicated that dermal and inhalation intake amounts of particle-bound PAHs were dominated by exposed skin area/deposition velocity and breathing rate, respectively, the relative importance of dermal and inhalation intakes of particle-bound PAHs may vary with exposure scenarios.

Despite the progress made in the present study, areas of improvements remain. To better examine dermal and inhalation exposures to PAHs, as many participants as feasible in each group should be recruited. Air samples collected by personal samplers need to be separated to gaseous and particulate phases so that dermal and inhalation intakes of PAHs can be accurately determined. Blood samples should also be collected and analyzed to identify the distribution patterns of PAHs and their metabolites in blood, which can better estimate the intake and metabolism rates of PAHs via dermal absorption and inhalation. As clothes may not be able to completely protect human skin from exposing to fumes, wipe skin samples from bare and cloth-covered skins should be collected to more clearly identify the protective role of clothes and calculate the transdermal permeability coefficients. Previous studies also suggested that older people have thinner epidermis with fewer lipids than younger people,[43] resulting in larger intake of diethyl phthalate via dermal absorption.[31] Moreover, effects of gender and usage of personal care products on dermal absorption of PAHs should be further examined in future studies.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.est.8b01689.

Additional tables and figures (PDF)

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