A Survey of Phthalates and Parabens in Personal Care Products from the United States and Its Implications for Human Exposure

ARTICLE *in* ENVIRONMENTAL SCIENCE & TECHNOLOGY · NOVEMBER 2013

Impact Factor: 5.33 · DOI: 10.1021/es4042034 · Source: PubMed

2 AUTHORS:

Ying Guo
Wadsworth Center, NYS Department of Health
38 PUBLICATIONS **1,044** CITATIONS
SEE PROFILE

Kurunthachalam Kannan
Wadsworth Center, NYS Department of Health
637 PUBLICATIONS **28,629** CITATIONS
SEE PROFILE

Environmental Science & Technology

Article

pubs.acs.org/est

A Survey of Phthalates and Parabens in Personal Care Products from the United States and Its Implications for Human Exposure

Ying Guo and Kurunthachalam Kannan*

Wadsworth Center, New York State Department of Health and Department of Environmental Health Sciences, School of Public Health, State University of New York at Albany, Empire State Plaza, P.O. Box 509, Albany, New York 12201-0509, United States

Supporting Information

ABSTRACT: Despite the widespread usage of phthalates and parabens in personal care products (PCPs), little is known about concentrations and profiles as well as human exposure to these compounds through the use of PCPs. In this study, nine phthalates and six parabens were determined in 170 PCPs (41 rinse-off and 109 leave-on), including 20 baby care products collected from Albany, New York. Phthalates were less frequently found in rinse-off PCPs but were more frequently found in perfumes (detection frequency of 100% for diethyl phthalate [DEP], 67% for dibutyl phthalate [DBP]), skin toners (90% for DEP), and nail polishes (90% for DBP). Parabens were found in ∼40% of rinse-off products and ∼60% of leave-on products. The highest concentrations of DEP, DBP, methyl- (MeP), ethyl- (EtP), propyl- (PrP), and butyl parabens (BuP) were on the order of 1000 μg per gram of the product. On the basis of amount and frequency of use of PCPs and the measured median concentrations of target analytes, the total dermal intake doses (sum of all phthalates or parabens) were calculated to be 0.37 and 31.0 μg/kg-bw/day for phthalates and parabens, respectively, for adult females. The calculated dermal intake of phthalates from PCPs was lower for infants and toddlers than for adult females. In contrast, dermal intake of parabens from PCPs by infants and toddlers was higher than that for adult females. The calculated maximum daily exposure dose of MeP, EtP, and PrP from PCPs ranged between 58.6 and 766 μg/kg-bw/day for infants and toddlers, which was 3 times higher than that calculated for adult females. PCPs are an important source of human exposure to parabens; the contribution of PCPs to phthalate exposure is low, except for DEP.

INTRODUCTION

The esters of phthalic acid (phthalates) and *p*-hydroxybenzoic acid (parabens) are widely used as additives in personal care products (PCPs), owing to their low acute toxicity and low cost. Phthalates are added as humectants, emollients, or skin penetration enhancers, whereas parabens are used as broad-spectrum microbial preservatives. In addition, these two types of esters are used in several consumer products. Phthalates are used in medical devices, children's toys, food packaging, and building materials,[1] whereas parabens are used in pharmaceuticals and foodstuffs. People are exposed to these chemicals on a daily basis. For instance, the National Health and Nutrition Examination Survey (NHANES) conducted by the Centers for Disease Control and Prevention (CDC) in the United States showed that >90% of the population is exposed to phthalates and parabens.[2−4]

Phthalates and parabens have short half-lives (on the order of hours) in the human body. Phthalates are rapidly metabolized to their respective monoesters, and some of the primary metabolites can be further metabolized.[5−7] For example, approximately 75% of the oral dose of bis(2-ethylhexyl) phthalate (DEHP) is excreted in urine within 48 h of exposure.[5,7] Another study showed that the highest serum concentration of butyl parabens (BuP) was found at 3 h after dermal application of a body lotion that contained this compound.[8] Both phthalates and parabens have been detected in urine,[4] breast milk,[9] breast tissue,[10] and plasma [11] due to humans' constant exposures.

Exposure to phthalates and parabens has been associated with reproductive effects in laboratory animals and humans. Several phthalates are endocrine-disrupting compounds and affect the male reproductive system.[12,13] A negative correlation between semen volume and concentrations of DBP or DEHP and a positive correlation between sperm malformation and concentrations of DEHP have been reported.[14] In addition, phthalate exposure has been shown to increase the risk of allergic diseases, including asthma and eczema.[15] Parabens were shown to possess estrogenic activity[16] and were associated with breast cancer etiology.[10] Parabens affect the metabolism of endogenous estrogens and cause mitochondrial dysfunction.[17] A recent study indicated that concentrations of urinary BuP were positively associated with male sperm DNA damage.[18] Considering that humans are constantly exposed to phthalates

Received: September 20, 2013
Revised: November 15, 2013
Accepted: November 21, 2013
Published: November 21, 2013

and parabens, investigations into the sources and pathways of exposure are important. Consumer products were suggested as important sources of exposure to dimethyl phthalate (DMP), diethyl phthalate (DEP), and butyl benzyl phthalate (BzBP), whereas diet was considered the major source of DEHP exposure.[19] The sources of human exposures can vary depending on the usage pattern of consumer products and dietary habits. For instance, dietary intake was the dominant source of exposure to BzBP and DEHP for the general population in Japan,[20] while dust ingestion accounted for 10−58% of the total intake of DEHP by the United States population.[19]

In our previous studies, we evaluated human exposure to phthalates and parabens in the United States through foodstuffs[21,22] and indoor dust.[19,23] However, human exposure to these compounds though the use of PCPs is not known. It was reported that urinary concentrations of phthalates [24] or plasma concentrations of parabens [11] were significantly associated with self-reported use of PCPs. A 2007−2008 study from Canada showed that PCPs were important sources of exposure to certain phthalates.[25] A few earlier studies have reported the concentrations of phthalates and/or parabens in PCPs from the United States.[26,27] Despite this, a comprehensive analysis of sources of human exposure to phthalates and parabens has not been conducted, and the contribution of PCPs to exposure doses of these compounds in the United States is not known. In this study, 170 PCPs collected from New York State in 2012 were analyzed for nine phthalates and six parabens, with the aim of determining concentrations, profiles, and dermal exposure of these compounds.

METHODS AND MATERIALS

Standards. Nine phthalates standards, DMP, DEP, dibutyl phthalate (DBP), di-iso-butyl phthalate (DIBP), BzBP, DEHP, di-n-hexyl phthalate (DNHP), dicyclohexyl phthalate (DCHP), and di-*n*-octyl phthalate (DNOP), and their corresponding deuterated (d_4) internal standards, six paraben standards, methyl paraben (MeP), ethyl paraben (EtP), propyl paraben (PrP), BuP, benzyl paraben (BzP), and heptyl paraben (HepP), were purchased from AccuStandard, Inc. (purity >99%; New Haven, CT, U.S.A.). $^{13}C_6$-MeP (for the quantification of MeP, EtP, and PrP) and $^{13}C_6$−BuP (for the quantification of BuP, BzP, and HepP) were purchased from Cambridge Isotope Laboratories (purity >99%; Andover, MA, U.S.A.).

Sample Collection and Preparation. A total of 170 PCPs comprising 41 rinse-off products (surfactant-based formulations such as shampoos, body washes, and baby wash), 109 leave-on products, and 20 baby care products were purchased in several supermarkets in Albany, New York, in April 2012. The rinse-off PCPs analyzed include 11 body washes, 9 shampoos, 7 hair conditioners, 9 face cleansers, and 5 shaving gels. The leave-on PCPs include 23 skin lotions, 6 hair care products, 12 perfumes, 9 skin toners, 14 deodorants, 33 skin creams, 4 lipsticks, and 8 nail polishes. The baby care products were 4 shampoos, 4 body lotion or oils, 6 sunscreens, 3 diaper creams, and 1 powder. All samples analyzed were popular brands and are distributed in supermarkets throughout the United States. Samples were stored at −20 °C until analysis.

Samples (~0.05 g, wet weight) were extracted in a 12 mL glass tube. After fortification of samples with 500 ng each of d_4-labeled phthalate internal standards and 50 ng each of $^{13}C_6$-parabens, 2 mL of Milli-Q water was added and equilibrated overnight at room temperature. Samples were then extracted twice with 4 mL aliquots of methyl *tert*-butyl ether (MTBE) by shaking in an orbital shaker (250 strokes per minute; Eberbach Corp., Ann Arbor, MI, U.S.A.) for 30 min, followed by centrifugation at 4400*g* for 20 min. The combined extracts were divided into two equal halves and concentrated under a gentle stream of nitrogen; the solvent was reconstituted with hexane for the analysis of phthalates and methanol for the analysis of parabens.

Instrumental Analysis. Analysis of the nine phthalate esters was carried out using gas chromatography (Agilent Technologies 6890N) coupled with mass spectrometry (Agilent Technologies 5973). A fused-silica capillary column (DB-5; 30 m × 0.25 mm i.d.; 0.25 μm film thickness) was used for the separation of phthalates. The oven temperature was programmed from 80 °C (held for 1.0 min) to 180 °C at 12 °C/min (held for 1.0 min), increased to 230 °C at 6 °C/min, then to 270 °C at 8 °C/min (held for 2.0 min) and, finally, increased to 300 °C at 30 °C/min (held for 12.0 min). The limits of quantification (LOQs) for DNOP and eight other phthalates were 10 and 2 ng/g, respectively (calculated based on the sample concentration/enrichment factor and the lowest concentration of the calibration standard). Samples were diluted and reanalyzed when concentrations exceeded the calibration range of the instrument.

An API 2000 electrospray triple quadrupole mass spectrometer (ESI-MS/MS; Applied Biosystems, Foster City, CA, U.S.A.) interfaced with an Agilent 1100 Series HPLC system (Agilent Technologies Inc., Santa Clara, CA, U.S.A.) was used for the determination of the six parabens. Chromatographic separation was achieved using a Betasil C18 column (Thermo Electron, Bellefonte, PA, U.S.A.; 100 mm × 2.1 mm, 5 μm). The mobile phase was 100% methanol (A) and 10% methanol in Milli-Q water (B) at a flow rate of 300 μL/min. The LOQ of parabens was 2 ng/g. Further details on the instrumental analysis have been described in our previous studies.[19,23]

Quality Assurance/Quality Control and Data Analysis. For each batch of samples analyzed, two method blanks, a spiked blank, and a pair of matrix-spiked samples/duplicates were processed. Low concentrations of phthalates (average values for DEP, DBP, DIBP, and DEHP were 3.5, 2.3, 3.0, and 5.6 ng/g, respectively) and parabens (average values for MeP and PrP were 1.0 and 2.5 ng/g, respectively) were found in procedural blanks. Concentrations measured in samples were subtracted from blank values for these compounds. The mean recoveries of deuterated phthalate internal standards, spiked into PCPs prior to extraction, ranged from 79% to 94%. The recoveries of phthalates and parabens in procedural blanks were 91−95% and 70−116%, respectively. Recoveries of internal standards for parabens spiked into samples were not calculated due to the elevated concentrations of MeP and PrP found in most of the samples analyzed, which required significant dilution of the sample extracts. However, selected samples were extracted 3 times, and each extract was analyzed separately. MeP and PrP were found at <5% of the total concentrations, and other parabens were not found in the third extract, which suggested that the first two MTBE extractions of samples recovered >95% of the target chemicals present in samples. Concentrations below the LOQ were assigned a value of zero for data analysis. The concentrations are reported on a nanogram per gram product, unless stated otherwise.

RESULTS AND DISCUSSION

Occurrence. Concentrations and profiles of phthalates and parabens in PCPs of all three categories, rinse-off, leave-on, and baby care products, are shown in Figure 1 and Table 1 (further

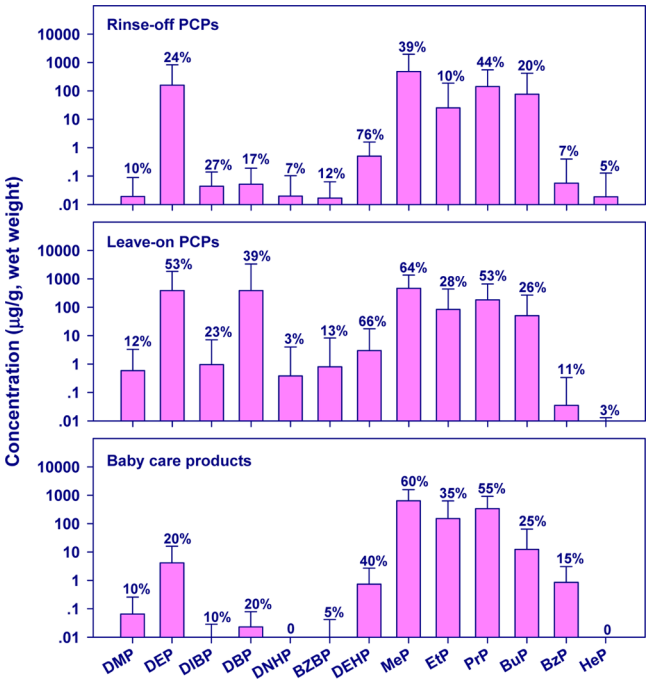

Figure 1. Concentrations (μg/g, mean and standard deviation) of phthalates and parabens in personal care products from New York state, United States (n = 170) (values above the bar are the detection frequencies of the analytes).

details are provided in Table S1, Supporting Information). DNOP and DCHP were rarely detected in samples (<1% detection frequency), and therefore, these two compounds were not discussed further.

Rinse-Off PCPs. DEHP was the most frequently detected phthalate ester (76%), followed by DIBP and DEP (~25%) in rinse-off PCPs. Other phthalates were seldom found in PCPs (~10%). The high detection frequency of DEHP in PCPs can be partly explained by the migration of this compound from plastic packaging materials, as DEHP is the major plasticizer used in polyvinyl chloride (PVC) plastics (at 1% to 40% by weight). Among the five categories of rinse-off PCPs analyzed, DEP was found in body washes (5 of 11); and DIBP was found in body washes (5 of 11) and face cleansers (4 of 9). The concentrations of phthalate esters in rinse-off PCPs varied from below the limit of quantitation to 3530 μg/g DEP (in shampoos). Despite the frequent detection of DEHP, the highest concentration of this compound (6.15 μg/g) was below 0.001% of the sample weight, which indicates that migration from packaging material is the source of contamination of these products. A recent study showed that DEHP levels in urine were substantially reduced by avoiding consumption of foods that were packaged in plastic products,[28] which further suggests that DEHP can migrate from plastic packaging materials. The median concentrations of other phthalates were all below the LOQ, which indicates that they are not common ingredients in rinse-off PCPs.

Among parabens, MeP and PrP were detected in ~40% of the samples analyzed, followed by BuP (~ 20%); other parabens were seldom found. This pattern was similar to that seen in a recent study from Sweden that reported parabens in 44% of the rinse-off PCPs analyzed.[29] The highest concentrations of MeP, EtP, PrP, and BuP ranged from 1040 to 8200 μg/g, accounting for approximately 0.1−0.8% by product weight. The concentrations of BzP and HepP in rinse-off PCPs were below 2.19 μg/g;

Leave-On PCPs. DEHP was the most commonly detected phthalate ester in leave-on PCPs (66%); the detection frequencies of DEP, DBP, and DIBP in leave-on PCPs were ~50%, ~40%, and ~25%, respectively. Among the seven categories of leave-on PCPs analyzed, phthalates were frequently found in perfumes, skin toners, nail polishes, and lipsticks. DEHP was found in all perfume and nail polish samples; DEP was found in all perfumes and 8 of 9 skin toner samples; DBP was found in 8 of 12 perfumes and 7 of 8 nail polish samples; and BzBP was found in 4 of 8 nail polish samples analyzed. However, phthalates were seldom found in skin cream, especially in sunscreen products. The highest concentration of DMP was found in deodorants (20.6 μg/g), DEP and BzBP in perfumes (7980 and 78.3 μg/g, respectively), and DIBP, DBP, and DEHP in nail polishes (58.9, 27400, and 135 μg/g, respectively). It should be noted that the median concentration of DEP in perfumes was 3930 μg/g (approximately 0.4% of the product weight).

Among parabens, MeP was the most frequently detected compound in leave-on PCPs (~65% of detection frequency), followed by PrP (~50%), EtP, and BuP (~25% each). The detection frequencies of BzP and HepP in leave-on PCPs were low. Parabens were commonly found in body lotions, skin care products, and lipsticks. Among 23 body lotion and 33 cream samples analyzed, one body lotion, one eyeliner, and three face cream samples were found to be free of parabens. The concentrations of parabens ranged from the LOQ to 3540 μg/g in all leave-on PCPs. The concentrations of BzP and HepP were <3.12 μg/g, whereas the highest concentrations of other four parabens ranged from 1500 to 3540 μg/g.

Baby Care Products. Both detection frequencies and concentrations of phthalates in baby care products were low. However, MeP and PrP were detected in more than half of the samples analyzed. Parabens were found in all six sunscreen samples, with median MeP, EtP, and PrP concentrations of 1260, 1.71, and 887 μg/g, respectively.

Several earlier studies have reported the occurrence of phthalates and parabens in PCPs from the United States,[26] Canada,[25] Korea,[30] and European countries.[31] The high detection frequencies of DEP in perfumes and DBP in nail polishes have been reported.[25,26,30] The reported concentrations of DEP and DBP in perfumes and nail polishes were generally on the order of 1000 μg/g, which was similar to that found in our study. The median concentration of DEP in perfumes (3930 μg/g) analyzed in our study was 2 times higher than that reported in a Canadian study (1680 μg/g).[25] DEP and DBP are used in nail polishes as a solvent for nitrocellulose and cellulose acetate, in perfumes as a fixative and a solvent, and in fingernail elongators as a plasticizer.[32,33] The detection frequency of DEHP in PCPs analyzed in previous studies was lower than that found in our study (65%); DEHP was found in 8/252 PCPs from Canada,[25] 4/72 samples from the United States,[26] and 4/102 samples from Korea.[30] The high detection frequency of DEHP found in our study was due to the sensitive analytical method employed in our study (LOQ of 2 ng/g). Considering the low detection frequency and low concen-

Table 1. Concentrations (μg/g, wet weight) of Phthalates and Parabens in Personal Care Products from New York State, United States (n = 170)

		DMP	DEP	DIBP	DBP	DNHP	BzBP	DEHP	MeP	EtP	PrP	BuP	BzP	HepP
Rinse-off products (n = 41)														
body wash (n = 11)	mean	0.01	270	0.07	0.07	0.07	0.01	0.48	757	94.5	47.2	65.0	0.01	0.01
	max	0.09	2420	0.39	0.36	0.49	0.13	1.92	8200	1040	488	714	0.11	0.07
shampoo (n = 9)	mean	0.07	393	0.02	0.02	–	0.03	0.35	133	0.24	1.77	0.41	–	0.08
	max	0.32	3530	0.21	0.14	–	0.18	1.87	1180	2.14	14.0	1.88	–	0.69
hair conditioner (n = 7)	mean	–	0.16	0.03	0.05	–	0.02	0.18	603	–	194	3.40	0.31	–
	max	–	1.09	0.19	0.34	–	0.14	0.39	2610	–	1350	23.8	2.19	–
face cleanser (n = 9)	mean	0.01	0.05	0.07	0.10	–	0.01	0.82	668	–	440	267	–	–
	max	0.06	0.43	0.33	0.69	–	0.10	6.15	3730	–	1670	2090	–	–
shaving gel (n = 5)	mean	–	–	–	–	–	–	0.69	2.12	0.02	0.45	0.05	–	–
	max	–	–	–	–	–	–	2.70	10.5	0.11	2.26	0.26	0.01	–
Total	*mean*	*0.02*	*159*	*0.04*	*0.05*	*0.02*	*0.02*	*0.50*	*482*	*25.4*	*143*	*76.7*	*0.06*	*0.02*
	max	*0.32*	*3530*	*0.39*	*0.69*	*0.49*	*0.18*	*6.15*	*8200*	*1040*	*1670*	*2090*	*2.19*	*0.69*
Leave-on products (n = 109)														
skin lotion (n = 23)	mean	0.39	2.47	0.17	0.29	0.13	0.03	0.96	912	81.3	489	109	–	–
	max	5.68	52.3	1.45	2.40	2.96	0.56	11.3	2880	620	2030	845	0.06	–
hair care (n = 6)	mean	3.71	179	–	–	0.14	–	0.12	561	1.61	0.16	0.01	–	–
	max	12.1	897	–	0.01	0.86	–	0.56	3370	9.65	0.98	0.07	–	–
perfume (n = 12)	mean	–	3420	0.72	0.21	–	6.70	2.71	1.57	0.32	0.23	0.47	0.05	0.01
	max	–	7980	8.61	0.97	–	78.3	12.2	17.3	3.88	2.79	5.63	0.46	0.11
skin toner (n = 9)	mean	0.03	2.14	–	–	–	0.01	0.18	159	1.34	41.0	0.76	–	–
	max	0.28	13.1	–	–	–	0.06	0.60	1230	9.60	367	5.57	–	–
deodorant (n = 14)	mean	1.51	0.20	0.02	0,03	2.69	0.01	4.98	0.08	0.04	0.13	0.02	–	–
	max	20.6	1.15	0.14	0.26	37.7	0.14	65.3	0.92	0.61	1.45	0.27	–	–
creams (n = 33)														
face cream	mean	0.52	0.01	0.08	0,03	–	–	0.40	885	246	221	81.6	–	–
(n = 21)	max	10.7	1.64	1.48	0.31	–	–	2.45	3540	2270	2720	1500	–	–
eyeliner cream	mean	–	0.12	–	–	–	–	0.64	5.83	1.11	1.01	–	–	–
(n = 4)	max	–	0.30	–	–	–	–	1.46	20.0	3.69	3.81	–	–	–
hand cream	mean	–	36.1	0.15	0.11	–	0.03	0.45	622	–	39.5	–	–	–
(n = 3)	max	–	108	0.45	0.34	–	0.09	0.53	1420	–	119	–	–	–
sunscreen	mean	–	0.02	–	0.02	–	–	–	908	419	607	0.05	0.62	–
(n = 5)	max	–	0.08	–	0.98	–	–	–	2930	2100	2120	0.17	3.12	–
lipstick (n = 4)	mean	0.04	1.95	0.30	0.55	–	0.05	1.79	3.92	0.12	98.7	318	0.01	–
	max	0.18	6.92	0.80	1.22	–	0.20	6.45	11.0	0.37	307	1270	0.02	–
nail polish (n = 8)	mean	0.03	1.28	11.0	5280	–	0.70	22.5	0.04	0.04	0.15	0.01	–	–
	max	0.22	9.22	58.9	27400	–	2.20	135	0.26	0.33	1.16	0.11	–	–
Total	*mean*	*0.59*	*389*	*0.95*	*388*	*0.38*	*0.80*	*2.99*	*466*	*84.2*	*182*	*50.6*	*0.03*	–
	max	*20.6*	*7980*	*58.9*	*27400*	*37.7*	*78.3*	*135*	*3540*	*2770*	*2720*	*1500*	*3.12*	*0.11*
Baby care products (n = 20)														
shampoo (n = 4)	mean	0.17	0.02	0.03	0.02	–	0.04	0.09	0.01	–	–	–	–	–
	max	0.68	0.08	0.09	0.05	–	0.14	0.26	0.05	–	–	–	–	–
lotion and oil (n = 4)	mean	–	–	–	–	–	–	0.33	392	113	89.2	0.03	–	–
	max	–	–	–	–	–	–	1.22	1570	453	356	0.07	–	–
sunscreen (n = 6)	mean	–	12.1	–	0.02	–	–	0.02	1360	376	849	36.9	2.56	–
	max	–	42.4	0	0.11	–	–	0.10	2800	2020	2020	221	8.18	–
diaper cream (n = 3)	mean	0.17	–	–	0.07	–	–	3.87	591	0.11	211	–	–	–
	max	0.51	–	–	0.22	–	–	8.22	1770	0.32	632	–	–	–
powder (n = 1)		–	1.57	–	–	–	–	–	–	–	–	–	0.03	–
Total	*mean*	*0.06*	*4.12*	*0.01*	*0.02*	–	*0.01*	*0.74*	*640*	*151*	*338*	*12.3*	*0.86*	–
	max	*0.68*	*42.4*	*0.09*	*0.22*	–	*0.14*	*8.22*	*2800*	*2020*	*2020*	*221*	*8.18*	–

- is not detected or concentrations below 0.01 μg/g.

trations of DEHP in PCPs (<10 μg/g, except for nail polishes, perfumes, deodorants, and skin lotions), we propose that DEHP contamination in PCPs arises from the plastic packaging materials. Parabens were detected in 77% of PCP samples analyzed from several European countries, with 99% of 158 leave-on PCPs containing parabens, at concentrations ranging from 0.01% to 0.87%;[31] the reported concentrations of parabens in PCPs from some European countries are similar to those found in our study. The European Union permits the use of parabens in cosmetic products in concentrations of up to 0.4% for each paraben, with a total maximum concentration of 0.8% (EU Cosmetics Directive 76/768/EEC). In this study, the

Table 2. Dermal Absorption Dose for Phthalates and Parabens from Use of Personal Care Products by Adult Females, Infants, and Toddlers in the United States (μg/kg-bw/day)

	DMP	DEP	DIBP	DBP	BzBP	DEHP	Total	MeP	EtP	PrP	BuP	BzP	HepP	Total
Exposure dose calculated from mean concentration of PCPs														
adult females														
rinse-off	–[a]	0.017	–	–	–	–	0.013	0.59	0.0066	0.19	0.054	0.0002	–	0.84
leave-on	0.0006	0.33	0.0005	0.16	0.0003	0.0002	0.49	44.8	5.33	21.8	0.54	0.0020	–	77.1
infants	0.0010	0.0050	–	0.0007	–	0.0028	0.0095	228	23.7	70.7	0.0054	0.0021	–	322
toddlers	0.0006	0.0041	–	0.0004	–	0.0017	0.0059	141	14.7	43.7	0.0033	0.0013	–	200
Exposure dose calculated from median concentration of PCPs														
adult females														
rinse-off	–	–	–	–	–	–	–	–	–	0.0004	–	–	–	0.0004
leave-on	–	0.37	–	0.0003	–	–	0.37	22.5	–	8.41	–	–	–	31.0
infants	–	0.0050	–	–	–	0.0017	0.0067	0.083	–	0.11	0.0042	0.0018	–	0.20
toddlers	–	0.0031	–	–	–	0.0010	0.0041	0.051	–	0.068	0.0026	0.0011	–	0.12
Exposure dose calculated from the highest concentration of PCPs														
adult females														
rinse-off	–	0.11	–	–	–	–	0.11	3.38	0.073	1.10	0.44	0.0012	0.0004	5.00
leave-on	0.0090	0.87	0.0040	0.85	0.0030	0.0020	1.74	150	43.8	105	46.7	0.0031	0.0002	346
infants	0.0030	0.0050	–	0.0021	–	0.0063	0.016	766	94.9	231	0.015	0.0018	–	1090
toddlers	0.0019	0.0031	–	0.0013	–	0.0039	0.010	474	58.6	143	0.0091	0.0011	–	676

[a]Exposure dose was below 0.0001 μg/kg-bw/day.

mean concentration of the sum of six parabens was <700 μg/g in all rinse-off and leave-on PCPs and was ~1000 μg/g in baby care products. However, the sum concentrations of parabens were above 0.8% in one body wash (10,400 μg/g) and one face cream sample (8530 μg/g) analyzed in this study.

Exposure through Dermal Absorption. On the basis of the mean, median, and maximum concentrations of phthalates and parabens measured in PCPs in this study, we estimated the daily exposure dose of these chemicals through dermal absorption for adult females (21–60 years), infants (0–1 year), and toddlers (2–3 years) in the United States, as shown in eq 1:

$$\mathrm{DED} = \frac{C_{\mathrm{PCPs}} M}{\mathrm{BW}} f1 f2 \quad (1)$$

where DED is daily exposure dose of phthalate or paraben from PCPs (μg/kg-bw/day), C_{PCPs} is measured concentration in PCPs (μg/g), M is amount of daily use of PCPs (g), BW is average body weight (kg), f_1 is retention factor (products retained by skin after use), and f_2 is dermal absorption factor. For M, the average values were obtained from the United States and European studies;[34,35] for BW, average values of 75 kg for adult females (adults, 21–60 years), 7.8 kg for infants, and 12.6 kg for toddlers were used;[35] for f_1, values were obtained from an earlier investigation,[36] and for f_2 (based on the information from a study that reported DEP absorption factor for human skin was 7 times lower than that found for rats), dermal absorption factor reported for rats divided by a factor of 7 for phthalates [34] was used. For parabens, a factor of 0.4 was used, based on laboratory studies that reported the factors of between 0.15 and 0.75.[37] The f_2 values used for infants and toddlers were twice that for adults. For adult females, we estimated phthalate and paraben exposure through rinse-off and leave-on PCPs, including body washes, shampoos, hair conditioners, facial cleansers, skin and hair care products, perfumes, deodorants, and lipsticks. For infants and toddlers, sunscreen products were not included. Further details of dermal exposure analysis are shown in Table S2 of the Supporting Information.

As shown in Table 2, for adult females, the calculated dermal exposure doses for the sum of phthalates and parabens from PCPs were 0.37 and 31.0 μg/kg-bw/day, respectively (calculated based on median concentrations). Leave-on PCPs contributed to >99% of exposure to DEP (perfumes) and MeP and PrP (skin lotion). A previous study also reported high concentrations of DEP metabolite in urine of women who frequently applied perfumes.[24] The exposure doses of phthalates and parabens calculated based on the highest concentrations in PCPs were 5 to 10 times greater than those estimated based on median concentrations and were 1.85 and 350 μg/kg-bw/day, respectively. A recent study from Canada reported the highest exposure doses for DMP, DEP, DBP, and DEHP to be 0.03, 78, 0.36, and 0.82 μg/kg-bw/day, respectively;[25] the DBP exposure dose calculated in our study (0.85 μg/kg-bw/day) was similar to that reported for Canada. Nevertheless, our values for DEHP (0.002 μg/kg-bw/day) and DEP (0.99 μg/kg-bw/day) were lower than those reported from Canada but similar to those reported from Korea (0.00013 and 0.183 μg/kg-bw/day, respectively).[30] The discrepancies among the three studies were partly explained by the use of different exposure models, especially the dermal absorption factors. For example, the dermal absorption factor of 5% was applied for all phthalates in the Canadian study,[25] whereas we applied a factor of 0.1–4% in our study (Table S2, Supporting Information).

The calculated exposure doses of phthalates by infants and toddlers were lower than those calculated for adult females. The highest dermal exposure dose of phthalates for infants and toddlers was 0.010–0.016 μg/kg-bw/day. The calculated exposure dose for parabens by infants and toddlers was greater than those found for adults. The maximum daily exposure dose calculated for MeP, EtP, and PrP for infants and toddlers was between 58.6 and 766 μg/kg-bw, which was 2 to 3 times higher than that found for adult females. It should be noted that sunscreen products, which contain very high concentrations of parabens (Table S1, Supporting Information), were not included in the exposure calculation for infants and toddlers. Our estimates of paraben exposure in infants and toddlers can be an underestimation of actual doses of exposure.

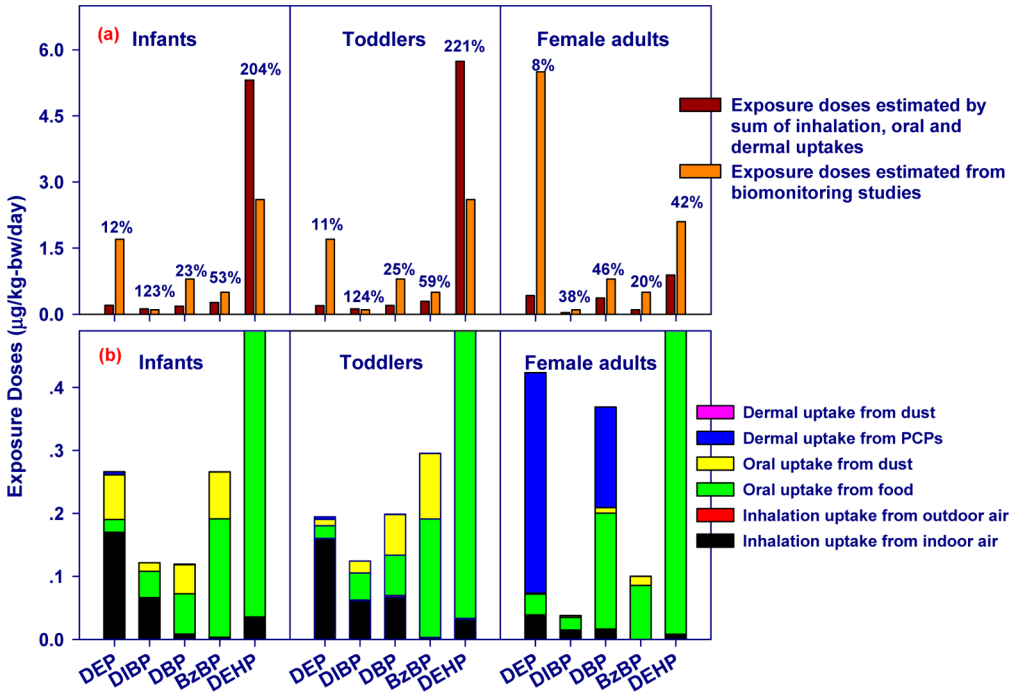

Figure 2. Cumulative exposure doses of phthalates through various pathways for the United States populations (μg/kg-bw/day). Values on the column indicate the ratios of exposure doses calculated using an environmental monitoring approach to exposure doses estimated using a biominitoring approach (see details in Table S5, Supporting Information).

Comparison of Various Exposure Pathways of Phthalates and Parabens. We have reported the occurrence of phthalates and parabens in foodstuffs[,22] and indoor dust[19,23] and estimated the exposure of these compounds through dietary and dust ingestion pathways in the United States in our previous studies. Along with the dietary and dust ingestion exposures, dermal exposure doses through the use of PCPs calculated in the present study enabled evaluation of relative significance of each of the pathways to phthalate and paraben exposures.

For phthalates, cumulative exposure doses were estimated using two approaches. The first is based on the sum of exposures calculated through inhalation (air), ingestion (food and dust), and dermal absorption (PCPs) pathways (i.e., environmental monitoring approach or forward approach), and the second is based on the data obtained from urinary biomonitoring studies (backward approach).[19] For the estimation of exposures through inhalation, reported median concentrations of phthalates in air from California were used.[38] Other sources of data for exposure assessment include indoor dust (median value[19]), foodstuffs (mean value[21]), and PCPs (mean value; present study) (Table S3−S4, Supporting Information). Ratios of exposure doses calculated using an environmental monitoring approach to exposure doses estimated using a biomonitoring approach were calculated (Figure 2; Table S5, Supporting Information). A ratio of 100% indicates the consistency between the two approaches of the exposure assessment. A ratio below 100% would suggest existence of other sources of exposures, and a ratio above 100% would suggest overestimation or unreliability of one of the approaches. Estimation of exposure doses based on biomonitoring involves several assumptions, and therefore, this method is expected to overestimate or underestimate actual exposures.

As shown in Figure 2, for infants and toddlers, ratios of exposures calculated by environmental and biomonitoring approaches for DIBP and DEHP were over 100% (Figure 2a), which suggested that DEHP exposure arises mainly from dietary intake and dust ingestion; DIBP exposure was mainly through indoor air inhalation and dietary intake (Figure 2b). For adults, the ratios of exposures calculated based on environmental and biomonitoring approaches were between 8% and 50% (Figure 2a). The contribution of PCPs to DEP and DIBP exposures cannot be neglected (Figure 2b). Wormuth et al. performed a similar analysis for populations in Europe [34] and found significant discrepancies in phthalate exposures estimated by the two approaches. The variability in the concentrations of urinary phthalate metabolites [39] that were used in the calculation of human exposure doses introduced some discrepancies. Despite these ratios of exposure, doses between the two approaches varied within 2-fold, which suggests that a biomonitoring approach also can be used in the estimation of exposure doses with a reasonable level of uncertainty.

For parabens, our dietary exposure assessment indicated that only 0.6−0.8% of total exposures were from food.[22] Infants had the highest exposures, with the respective daily exposure doses of MeP, BtP, PrP, and BuP at 1.38, 1.74, 0.387, and 0.0046 μg/kg-bw/day (95th percentile), respectively, which were slightly higher than that found for toddlers but 3 times higher than for adults. In addition, the daily intake of parabens by the United States population through the ingestion of indoor dust was lower than that calculated through dietary sources.[23] Thus, diet and indoor dust are not the major sources of paraben exposure in the United States population. In addition, parabens were seldom detected in the outdoor and indoor air in the United States.[38] However, the daily exposure doses of MeP, EtP, and PrP through the use of PCPs were 5−50 μg/kg-bw/day (based on mean concentrations of chemicals in PCPs) for adults and 15−230 μg/kg-bw/day for infants and toddlers, which indicates

that PCPs are the major sources of paraben exposure in the United States.

■ ASSOCIATED CONTENT

Supporting Information

Concentrations and profiles of phthalates and parabens in each category of PCPs, parameters used to estimate human exposure to phthalates and parabens, and methods to estimate human exposure to phthalates from inhalation. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Tel: 1-518-474-0015. Fax: 1-518-473-2895. E-mail: kkannan@wadsworth.org.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This study was supported by a biomonitoring grant (1U38EH000464-01) from the Centers for Disease Control and Prevention (CDC), Atlanta, GA. Its contents are the sole responsibility of the authors and do not necessarily represent the official views of the CDC.

■ REFERENCES

(1) Antian, J. Toxicity and health threats of phthalate esters: Review of the literature. *Environ. Health Perspect.* **1973**, 1−26.

(2) Calafat, A. M.; Ye, X.; Wong, L. Y.; Bishop, A. M.; Needham, L. L. Urinary concentrations of four parabens in the U.S. population: NHANES 2005−2006. *Environ. Health Perspect.* **2010**, *118*, 679−685.

(3) Silva, M. J.; Barr, D. B.; Reidy, J. A.; Malek, N. A.; Hodge, C. C.; Caudill, S. P.; Brock, J. W.; Needham, L. L.; Calafat, A. M. Urinary levels of seven phthalate metabolites in the US population from the National Health and Nutrition Examination Survey (NHANES) 1999−2000. *Environ. Health Perspect.* **2004**, *112*, 331−338.

(4) Ye, X.; Bishop, A. M.; Reidy, J. A.; Needham, L. L.; Calafat, A. M. Parabens as urinary biomarkers of exposure in humans. *Environ. Health Perspect.* **2006**, *114*, 1843−1846.

(5) Koch, H. M.; Bolt, H. M.; Preuss, R.; Angerer, J. New metabolites of di(2-ethylhexyl)phthalate (DEHP) in human urine and serum after single oral doses of deuterium-labelled DEHP. *Arch. Toxicol.* **2005**, *79*, 367−376.

(6) Koch, H. M.; Rossbach, B.; Drexler, H.; Angerer, J. Internal exposure of the general population to DEHP and other phthalates: Determination of secondary and primary phthalate monoester metabolites in urine. *Environ. Res.* **2003**, *93*, 177−185.

(7) Koch, H. M.; Bolt, H. M.; Angerer, J. Di(2-ethylhexyl)phthalate (DEHP) metabolites in human urine and serum after a single oral dose of deuterium-labelled DEHP. *Arch. Toxicol.* **2004**, *78*, 123−130.

(8) Janjua, N. R.; Mortensen, G. K.; Andersson, A. M.; Kongshoj, B.; Skakkebaek, N. E.; Wulf, H. C. Systemic uptake of diethyl phthalate, dibutyl phthalate, and butyl paraben following whole-body topical application and reproductive and thyroid hormone levels in humans. *Environ. Sci. Technol.* **2007**, *41*, 5564−5570.

(9) Ye, X.; Bishop, A. M.; Needham, L. L.; Calafat, A. M. Automated on-line column-switching HPLC-MS/MS method with peak focusing for measuring parabens, triclosan, and other environmental phenols in human milk. *Anal. Chim. Acta* **2008**, *622*, 150−156.

(10) Darbre, P. D.; Aljarrah, A.; Miller, W. R.; Coldham, N. G.; Sauer, M. J.; Pope, G. S. Concentrations of parabens in human breast tumours. *J. Appl. Toxicol.* **2004**, *24*, 5−13.

(11) Sandanger, T. M.; Huber, S.; Moe, M. K.; Braathen, T.; Leknes, H.; Lund, E. Plasma concentrations of parabens in postmenopausal women and self-reported use of personal care products: The NOWAC postgenome study. *J. Exposure Sci. Environ. Epidemiol.* **2011**, *21*, 595−600.

(12) Martino-Andrade, A. J.; Chahoud, I. Reproductive toxicity of phthalate esters. *Mol. Nutr. Food Res.* **2010**, *54*, 148−157.

(13) Matsumoto, M.; Hirata-Koizumi, M.; Ema, M. Potential adverse effects of phthalic acid esters on human health: A review of recent studies on reproduction. *Regul. Toxicol. Pharmacol.* **2008**, *50*, 37−49.

(14) Zhang, Y. H.; Zheng, L. X.; Chen, B. H. Phthalate exposure and human semen quality in Shanghai: A cross-sectional study. *Biomed. Environ. Sci.* **2006**, *19*, 205−209.

(15) Braun, J. M.; Sathyanarayana, S.; Hauser, R. Phthalate exposure and children's health. *Curr. Opin. Pediatr.* **2013**, *25*, 247−254.

(16) Darbre, P. D.; Harvey, P. W. Paraben esters: Review of recent studies of endocrine toxicity, absorption, esterase and human exposure, and discussion of potential human health risks. *J. Appl. Toxicol.* **2008**, *28*, 561−578.

(17) Crinnion, W. J. Toxic effects of the easily avoidable phthalates and parabens. *Altern. Med. Rev.* **2010**, *15*, 190−196.

(18) Meeker, J. D.; Yang, T.; Ye, X.; Calafat, A. M.; Hauser, R. Urinary concentrations of parabens and serum hormone levels, semen quality parameters, and sperm DNA damage. *Environ. Health Perspect.* **2011**, *119*, 252−257.

(19) Guo, Y.; Kannan, K. Comparative assessment of human exposure to phthalate ethers from house dust in China and the United States. *Environ. Sci. Technol.* **2011**, *45*, 3788−3794.

(20) Itoh, H.; Yoshida, K.; Masunaga, S. Quantitative identification of unknown exposure pathways of phthalates based on measuring their metabolites in human urine. *Environ. Sci. Technol.* **2007**, *41*, 4542−4547.

(21) Schecter, A.; Lorber, M.; Guo, Y.; Wu, Q.; Yun, S.; Kannan, K.; Miller, J.; Hynan, L. S.; Cheng, D.; Colacino, J.; Birnbaum, L. Phthalate concentrations and dietary exposure from food purchased in New York State. *Environ. Health Perspect.* **2013**, *121*, 473−479.

(22) Liao, C. Y.; Liu, F.; Kannan, K. Occurrence of and dietary exposure to parabens in foodstuffs from the United States. *Environ. Sci. Technol.* **2013**, *47*, 3918−3925.

(23) Wang, L.; Liao, C.; Liu, F.; Wu, Q.; Guo, Y.; Moon, H. B.; Nakata, H.; Kannan, K. Occurrence and human exposure of p-hydroxybenzoic acid esters (parabens), bisphenol a diglycidyl ether (BADGE), and their hydrolysis products in indoor dust from the United States and three East Asian countries. *Environ. Sci. Technol.* **2012**, *46*, 11584−11593.

(24) Parlett, L. E.; Calafat, A. M.; Swan, S. H. Women's exposure to phthalates in relation to use of personal care products. *J. Exposure Sci. Environ. Epidemiol.* **2012**, 1−10.

(25) Koniecki, D.; Wang, R.; Moody, R. P.; Zhu, J. Phthalates in cosmetic and personal care products: Concentrations and possible dermal exposure. *Environ. Res.* **2011**, 329−336.

(26) Houlihan, J.; Brody, C.; Schwan, B. *Not Too Pretty: Phthalates, Beauty Products and the FDA*. http://www.safecosmetics.org/downloads/NotTooPretty_report.pdf (accessed December 2010).

(27) Hubinger, J. C.; Havery, D. C. Analysis of consumer cosmetic products for phthalate esters. *J. Cosmet. Sci.* **2006**, *57*, 127−137.

(28) Rudel, R. A.; Gray, J. M.; Engel, C. L.; Rawsthorne, T. W.; Dodson, R. E.; Ackerman, J. M.; Rizzo, J.; Nudelman, J. L.; Brody, J. G. Food packaging and bisphenol A and bis(2-ethyhexyl) phthalate exposure: Findings from a dietary intervention. *Environ. Health Perspect.* **2011**, *119*, 914−920.

(29) Yazar, K.; Johnsson, S.; Lind, M. L.; Boman, A.; Liden, C. Preservatives and fragrancies in selected consumer-available cosmetics and detergents. *Contact Dermatitis* **2010**, *64*, 265−272.

(30) Koo, H. J.; Lee, B. M. Estimated exposure to phthalates in cosmetics and risk assessment. *J. Toxicol. Environ. Health, Part A* **2004**, *67*, 1901−1914.

(31) Rastogi, S. C.; Schouten, A.; Kruuf, N. d. K.; Weijland, J. W. Contents of methyl-, ethyl-, propyl-, butyl- and benzylparaben in cosmetic products. *Contact Dermatitis* **1995**, *32*, 28−30.

(32) *Toxicological Profile for Diethyl Phthalate*. U.S. Agency for Toxic Substances and Disease Registry. http://www.atsdr.cdc.gov/toxprofiles/tp73.html (accessed November, 2013).
(33) U.S. *Toxicological Profile for Di-n-Butyl Phthalate*. Agency for Toxic Substances and Disease Registry. http://www.atsdr.cdc.gov/toxprofiles/tp135.html (accessed November 2013).
(34) Wormuth, M.; Scheringer, M.; Vollenweider, M.; Hungerbuhler, K. What are the sources of exposure to eight frequently used phthalic acid esters in Europeans? *Risk Anal.* **2006**, *26*, 803−824.
(35) *Exposure Factors Handbook*. U.S. Environmental Protection Agency. http://www.epa.gov/ncea/efh/pdfs/efh-chapter17.pdf (accessed March 2013).
(36) Wormuth, M.; Scheringer, M.; Hungerbuhler, K. Linking the use of scented consumer products to consumer exposure to polycyclic musk fragrances. *J. Ind. Ecol.* **2005**, *9*, 237−258.
(37) Cowan-Ellsberry, C. E.; Robison, S. H. Refining aggregate exposure: Example using parabens. *Regul. Toxicol. Pharmacol.* **2009**, *55*, 321−329.
(38) Rudel, R. A.; Dodson, R. E.; Perovich, R. M. F.; Camann, D. E.; Zuniga, M. M.; Yau, A. Y.; JustII, A. C.; Brody, J. G. Semivolatile endocrine-disrupting compounds in paired indoor and out door air in two northern California communities. *Environ. Sci. Technol.* **2010**, *44*, 6583−6590.
(39) Preau, J. L.; Wang, L.; Silva, M.; Needham, L.; Calafat, A. Variability over 1 week in the urinary concentrations of metabolites of diethyl phthalate and di(2-ethyhexyl) phthalate among eight adults: An observation study. *Environ. Health Perspect.* **2010**, *118*, 1748−1754.