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ESTIMATED EXPOSURE TO PHTHALATES IN COSMETICS AND RISK ASSESSMENT

Hyun Jung Koo, Byung Mu Lee

Division of Toxicology, College of Pharmacy, Sungkyunkwan University,
Suwon, Kyonggi-do, South Korea

Some phthalates such as di(2-ethylhexyl) phthalate (DEHP) and dibutyl phthalate (DBP) and their metabolites are suspected of producing teratogenic or endocrine-disrupting effects. To predict possible human exposure to phthalates in cosmetics, the levels of DEHP, diethyl phthalate (DEP), DBP, and butylbenzyl phthalate (BBP) were determined by high-performance liquid chromatography (HPLC) in 102 branded hair sprays, perfumes, deodorants, and nail polishes. DBP was detected in 19 of the 21 nail polishes and in 11 of the 42 perfumes, and DEP was detected in 24 of the 42 perfumes and 2 of the 8 deodorants. Median exposure levels to phthalates in cosmetics by dermal absorption were estimated to be 0.0006 µg/kg body weight (bw)/d for DEHP, 0.6 µg/kg bw/d for DEP, and 0.103 µg/kg bw/d for DBP. Furthermore, if phthalates in cosmetics were assumed to be absorbed exclusively via 100% inhalation, the median daily exposure levels to phthalates in cosmetics were estimated to be 0.026 µg/kg bw/d for DEHP, 81.471 µg/kg bw/d for DEP, and 22.917 µg/kg bw/d for DBP, which are far lower than the regulation levels set by the Scientific Committee on Toxicity, Ecotoxicity, and the Environment (CSTEE) (37 µg/kg bw/d, DEHP), Agency for Toxic Substances and Disease Registry (ATSDR) (7000 µg/kg bw/d, DEP), and International Programme on Chemical Safety (IPCS) (66 µg/kg bw/d, DBP), respectively. Based on these data, hazard indices (HI, daily exposure level/regulation level) were calculated to be 0.0007 for DEHP, 0.012 for DEP, and 0.347 for DBP. These data suggest that estimated exposure to phthalates in the cosmetics mentioned are relatively small. However, total exposure levels from several sources may be greater and require further investigation.

Endocrine-disrupting chemicals (EDCs) are well classified and characterized in terms of toxicological manifestations, such as developmental toxicity, carcinogenicity, mutagenicity, immunotoxicity, and neurotoxicity (Choi et al., 2004). The dialkyl or alkylaryl esters of 1,2-benzenedicarboxylic acid are commonly called phthalates, an important class of EDCs. These agents possess excellent plasticizing properties and are incorporated into polymeric materials such as polyvinyl chloride (PVC) to improve their processing properties and increase their flexibility (CMA, 1999). They also have other applications, for example, as (1) humectants (skin moisturizers), emollients (skin softeners) and skin penetration enhancers in cosmetics, (2) agents to prevent brittleness and cracking in nail

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Address correspondence to Dr. Byung Mu Lee, Division of Toxicology, College of Pharmacy, Sungkyunkwan University, Chunchun-dong 300, Changan-ku, Suwon, Kyonggi-do, 440-746, South Korea.
E-mail: bmlee@skku.ac.kr

polishes and sealants, (3) antifoaming agents in aerosols, and (4) solvents in a wide range of applications. People are exposed to phthalates through their daily contact with consumer products, food, and indoor air (ATSDR, 1993, 1999; NTP-CERHR, 2000a, 2000b, 2000c; Houlihan & Wiles, 2000; Api, 2001; CIR, 2002).

In 1995, diethyl phthalate (DEP) was reported to be present in 67 cosmetic formulations at concentrations ranging from 0.1 to 50% (SCCNFP, 2002). In 2000, the U.S. Patent and Trademark Office held 309 patents involving the use of dibutyl phthalate (DBP) in cosmetics, including 120 nail base coats, polishes, and enamels and 27 manicuring preparations (Houlihan & Wiles, 2000; DiGangi et al., 2002). These products are applied to skin, hair, and nails, and may come into contact with mucous membranes and the respiratory tract. In addition, contact may be frequent (several times a day) and prolonged (years).

It has previously been reported that di(2-ethylhexyl) phthalate (DEHP) is a reproductive toxicant (Davis et al., 1994) and acts as a rodent liver carcinogen via a mechanism involving peroxisome proliferation (Carpenter et al., 1953; Kluwe et al., 1982; Lamb et al., 1987; David et al., 1999; Tickner et al., 2001). In addition, dibutyl phthalate (DBP) produces testicular toxicity in rats through an antiandrogenic mechanism (Heindel & Powell, 1992; Akingbemi et al., 2004; Barlow et al., 2004), and butyl benzyl phthalate (BBP) is weakly estrogenic in vitro (Zacharewski et al., 1998).

In spite of their widespread presence in cosmetics and other common consumer products, little is known about human exposure to phthalates. In 2000, researches at the Centers for Disease Control and Prevention (CDC) reported that they had identified 7 urinary phthalate metabolites in 289 subjects (Blount et al., 2000). Moreover, CDC report demonstrated that levels of some phthalates in women of childbearing age, including DBP and DEHP, exceeded the safety levels set to prevent birth defects (Kohn et al., 2000).

Regulators have responded to some extent to recent research findings. In 2003, an amendment to the European Commission (EC) Cosmetics Directive was approved, banning chemicals classified as carcinogenic, mutagenic, or reprotoxic from being used in cosmetic products (European Commission, 2003). Two of the phthalates (DEHP and DBP) are classified as category 2 reproductive toxicants. However, according to the legislation, manufacturers do not have to state whether phthalates are present in their products.

In this study, 4 phthalate diesters (DEHP, DEP, DBP, and BBP) were quantified in 102 cosmetic products by high-performance liquid chromatography (HPLC), which allowed us to estimate individual exposures to phthalates.

MATERIALS AND METHODS

Chemicals

Di-(2-ethylhexyl) phthalate (DEHP), diethyl phthalate (DEP), dibutyl phthalate (DBP), butylbenzyl phthalate (BBP), and di-*n*-hyptyl phthalate (DNHP) were

purchased from Sigma-Aldrich (Munich, Germany). HPLC-grade acetonitrile and methanol were purchased from J. T. Baker Chemical Co. (Phillipsburg, NJ). The water used to prepare aqueous buffers was deionized and purified using a Milli-Q water purification system (Millipore, Molsheim, France). To minimize contamination with phthalates during samples handling and analysis, all glassware used in the study was washed using a tetrahydrofuran–methanol mixture then rinsed with hexane.

Cosmetics Sampling

One hundred and two cosmetic products including 42 perfumes, 8 deodorants, 21 nail polishes, and 31 hair products (hair gels, hair mousses, and hair sprays) were purchased at retail stores in Seoul, Korea. Cosmetic samples were stored at room temperature.

Standard and Sample Preparations

Phthalate standards were prepared by dissolving the pure chemicals in methanol at 1 mg/ml in previously washed glass tubes and stored at 4°C. The standard samples were then prepared by dilution with the stocking solutions. Calibration graphs were obtained using standard samples prepared with 10–400 µg of DEHP, DEP, DBP, or BBP containing 2500 ng DNHP as internal standard.

For each product sample, 0.1 g was weighed and spiked with 2500 ng/ml of DNHP as an internal standard. This mixture was added to 10 ml methanol, vortexed, and centrifuged (3000 rpm for 15 min).

HPLC Analysis

HPLC was performed using a Hitachi high-performance liquid chromatograph (model L-7100, Tokyo) equipped with a Hitachi model L-7200 autosampler and a Hitachi pump. The output from the detector was connected to a Hitachi model D-7000 interface module, and data were recorded on an HP deskjet printer. Separation was achieved using a 5-µm SUPELCOSIL LC-18 column (250 × 4.6 mm) (Tokyo) operating at 20 ± 2°C. Elution was performed isocratically using a mobile phase consisting of acetonitrile–aqueous buffer (0.08% triethylamine adjusted to pH 2.8 with 1 M phosphoric acid) mixture (88:12, v/v) at a flow rate of 0.7 ml/min. The mobile phase was prefiltered through a 0.45-µm membrane and degassed. The run time was 50 min.

Analytical reproducibility for the individual phthalates at 10, 25, 50, 100, 150, 200, 250, 300, 350, and 400 ppm was assessed using 5 sample replicates. Calibration curves were prepared as peak–area ratios versus the DNHP internal standard. The correlation coefficients obtained for the 5 replicate samples were 0.9999 for DEHP, 0.9921 for DEP, 0.9946 for DBP, and 0.9926 for BBP (Figure 1).

The limits of detection (LOD), defined as a 3 × signal-to-noise ratio, were estimated to be 0.0005–0.004 µg/ml (DEHP 0.004, DEP 0.0005, DBP 0.0005, BBP 0.0005 µg/ml).

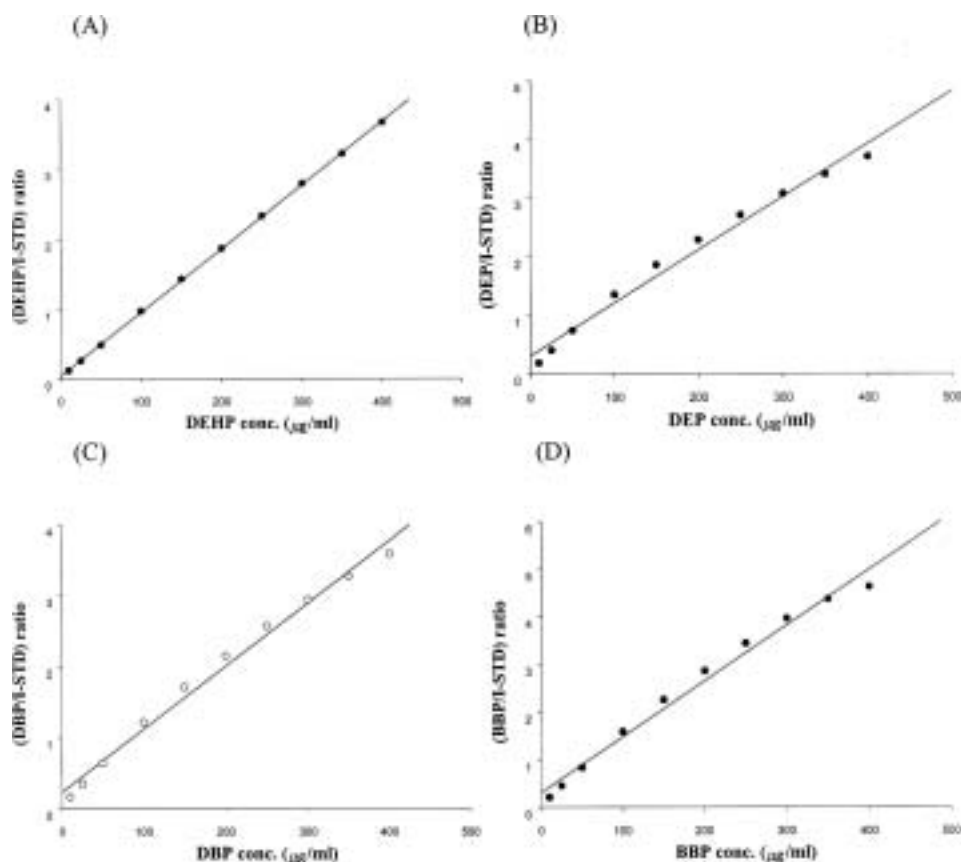


FIGURE 1. Calibration curves of phthalates: (A) DEHP ($r^2 = .9999$); (B) DEP ($r^2 = .9921$); (C) DBP ($r^2 = .9946$); (D) BBP ($r^2 = .9926$). The calibration curves were derived by calculating the peak-area ratio (each phthalate/internal standard [DNHP], I-STD) versus each phthalate concentration.

RESULTS

DEHP, DEP, DBP, and BBP were monitored to cosmetics (e.g., hair sprays, perfumes, deodorants and nail polishes) by HPLC to estimate possible human exposure to phthalates for risk assessment (Table 1).

HPLC analysis showed that 57% of the perfumes surveyed (24 of 42) and 25% the deodorants (2 of 8) contained DEP, whereas 26% of the perfumes (11 of 42) and 90% of the nail polishes (19 of 21) contained DBP (Table 1). Concentrations of the phthalate in perfumes were 0.678 ± 2.788 µg/ml for DEHP, 3044.236 ± 3197.380 µg/ml for DEP, 444.567 ± 1053.317 µg/ml for DBP, and 1.640 ± 9.665 µg/ml for BBP. In the case of nail polishes, the detection levels of phthalates were 1.615 ± 5.426 µg/ml for DEHP, 1.585 ± 6.743 µg/ml for DEP, 1671.139 ± 1039.140 µg/ml for DBP, and < LOD for BBP, respectively. Concentrations of the phthalate in hair

TABLE 1. Summary of Phthalates Detected in Cosmetic Products

Type (number of samples)	Percent of products detected (number)			
	DEHP	DEP	DBP	BBP
Perfume (42)	4.8% (2) ^a	57.1% (24)	26.2% (11)	4.8% (2)
Nail polish (21)	9.5% (2)	9.5% (2)	90.5% (19)	0% (0)
Hair product (31)	0% (0)	3.2% (1)	0% (0)	0% (0)
Deodorant (8)	0% (0)	25% (2)	0% (0)	0% (0)

^a Number of samples detected.

TABLE 2. Levels of Phthalates in Cosmetic Products Determined by HPLC

Type of products	Phthalate	Mean (ppm, µg/ml)	Max (ppm, µg/ml)	Min (ppm, µg/ml)
Perfume	DEHP	0.678	18.315	< LOD
	DEP	3044.236	12,401.989	< LOD
	DBP	444.567	5050.760	< LOD
	BBP	1.640	62.785	< LOD
Nail polish	DEHP	1.615	25.077	< LOD
	DEP	1.585	31.011	< LOD
	DBP	1671.139	3901.869	< LOD
	BBP	< LOD	< LOD	< LOD
Hair product	DEHP	< LOD	< LOD	< LOD
	DEP	3.280	98.622	< LOD
	DBP	< LOD	< LOD	< LOD
	BBP	< LOD	< LOD	< LOD
Deodorant	DEHP	< LOD	< LOD	< LOD
	DEP	1473.154	6906.459	< LOD
	DBP	< LOD	< LOD	< LOD
	BBP	< LOD	< LOD	< LOD

Note. LOD, limit of detection (DEHP, 0.004; DEP, 0.0005; DBP, 0.0005; BBP, 0.0005; MEHP, 0.012 µg/ml). For estimation, <LOD was considered to be halfway between 0 and the LOD values of each phthalate.

products were 3.280 ± 17.695 for BBP, but <LOD for DEHP, DEP, and DBP. Concentrations of the phthalate in deodorants were 1473.154 ± 2780.874 µg/ml for DEP, but <LOD for DEHP, DBP, and BBP (Table 2).

Frequency and Volume of Cosmetics Use

A questionnaire was designed to obtain information about the frequency and volume of cosmetics use from 150 women (aged 20–73 yr) living in Suwon, Korea. Demographic information of female consumers was also determined: mean body weight 55.86 ± 7.99 kg, height 156.51 ± 5.51 cm, and body mass index (BMI) 22.84 ± 3.3 kg/m².

The frequency of cosmetics use is summarized in Table 3, and the frequency of use by the 90th percentile of users was determined to identify the highly exposed subgroup (Figure 2).

TABLE 3. Frequency and Volume of Cosmetics Use Based on Questionnaire for 150 Users (Women, Aged 20–73 yr)

Type of products	Frequency (times/d)/volume (ml/time)			
	Perfume	Hair product	Nail polish	Deodorant
Mean \pm SD	0.62/0.5	0.59/5	0.16/0.3	0.59/0.5
Maximum	5/5	3/20	2/2	2/3
Minimum	0/0	0/0	0/0	0/0
Median	1/1	1/10	1/0.5	1/1
90th Percentile	3/1.5	2/18	1/0.5	1/1

Human Exposure Estimates to Phthalates in Cosmetics

In this study, phthalate content of 102 cosmetic products were determined. Daily human exposure levels to phthalates were estimated from cosmetics by using the following formula:

$$\text{Daily human exposure } (\mu\text{g/kg bw/d}) = \frac{C(\mu\text{g/g}) \times V(\text{ml/time}) \times F(\text{times/d})}{\text{Body weight (kg)}} \times \text{abs.} \quad (1)$$

where C is the concentration of phthalates in the products ($\mu\text{g/ml}$, ppm), V the volume of cosmetics consumed per time (ml/time), F the frequency of use (times/d), and abs. the absorption rate.

Model 1 Since no human data were reported on actual dermal absorption or inhalation at given exposure scenarios, we extrapolated using animal data. Elsisi et al. (1989) reported that the dermal absorption rates of certain phthalates (DEHP, DEP, DBP, and BBP) ranged from 5 to 27% (5% for DEHP, 24% for DEP, 60% for DBP, and 27% for BBP) in F-344 rats.

When only rat in vivo dermal absorption studies are available, the most conservative approach is to assume that human skin absorption is similar to that of rat in terms of in vivo dermal absorption (European Commission, 2002). Based on rat in vivo dermal absorption data (Elsisi et al., 1989), the expected exposure levels were calculated by using model 1 (Table 4). The estimated exposure levels of phthalates, assuming that cosmetics users were exposed to phthalates through 100% dermal application, from the concurrent use of multiple cosmetic products came to 5.971 $\mu\text{g/kg/d}$ for DEP, 2.361 $\mu\text{g/kg/d}$ for DBP, 0.002 $\mu\text{g/kg/d}$ for BBP, and 0.0003 $\mu\text{g/kg/d}$ for DEHP.

In the highly exposed subgroup (90th percentile of users), the estimated exposure levels of phthalates from the concurrent use of multiple cosmetic products was 65.696 $\mu\text{g/kg/d}$ for DEP, 30.463 $\mu\text{g/kg/d}$ for DBP, 0.036 $\mu\text{g/kg/d}$ for BBP, and 0.004 $\mu\text{g/kg/d}$ for DEHP (Table 5).

Model 2 If appropriate dermal penetration data are available for the rat in vivo and for the rat and human skin in vitro, the in vivo dermal absorption in rats may be adjusted to provide the in vivo dermal absorption in humans by

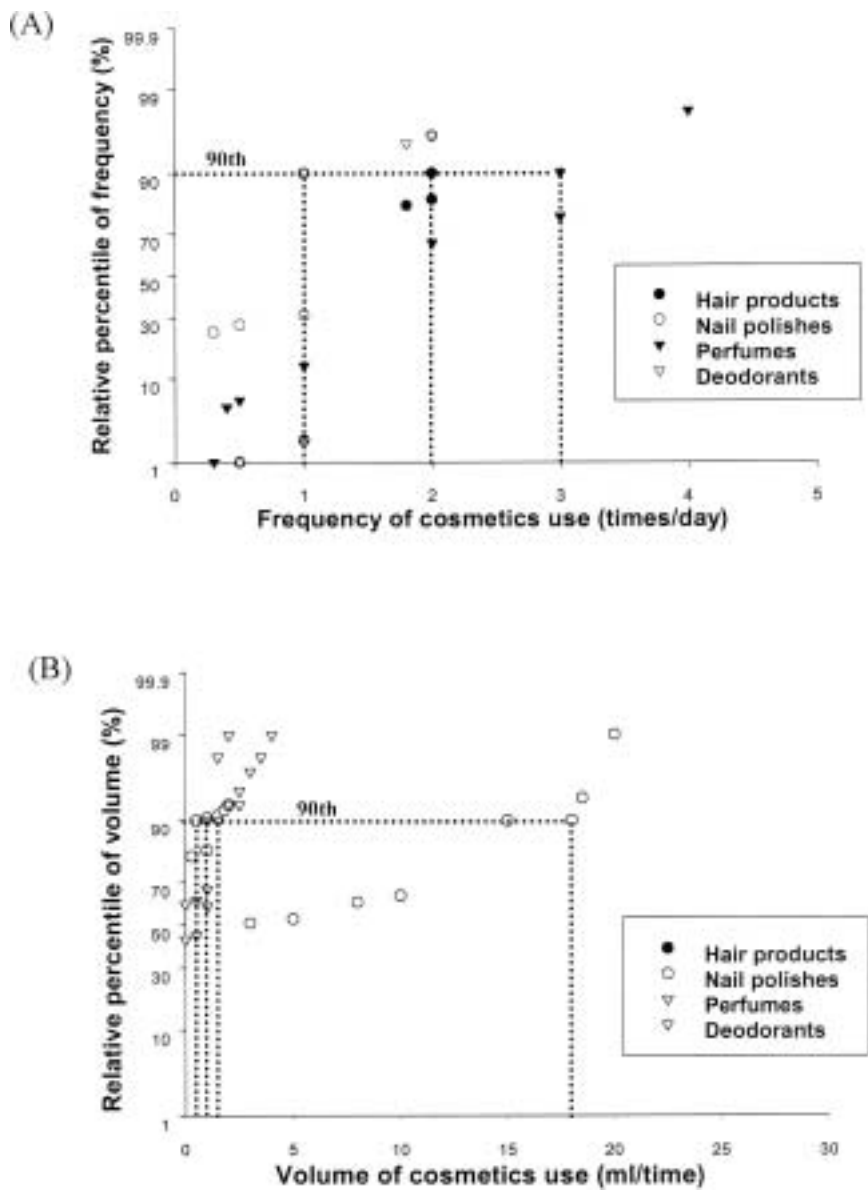


FIGURE 2. (A) Frequency and (B) volume distribution of cosmetics used by women ($n = 150$).

using the relative absorptions of rat and human skin in vitro (European Commission, 2002). Consequently, based on rat in vivo and rat and human skin in vitro data (Table 6), in vivo human absorption was estimated by model 2 [Eq. (2)], and results were summarized in Table 7.

TABLE 4. Mean Expected Daily Human Exposure Levels to Phthalates from Cosmetics Estimated Using Model 1

Type	Expected daily exposure ($\mu\text{g/kg/d}$) ^a			
	DEHP	DEP	DBP	BBP
Perfume	0.0002	4.058	1.481	0.002
Deodorant	< LOD ^b	1.871	< LOD	< LOD
Nail polish	0.0001	0.0003	0.880	< LOD
Hair product	< LOD	0.042	< LOD	< LOD
Total	0.0003	5.971	2.361	0.002

^a Mean.^b LOD, limit of detection. For estimation, <LOD was considered to be halfway between 0 and the LOD values of each phthalate.**TABLE 5.** Expected Daily Human Exposure Levels for Phthalates in Highly Frequent Cosmetic Users, as Estimated Using by Model 1

			Expected daily exposure ($\mu\text{g/kg/d}$)			
			DEHP	DEP	DBP	BBP
Median	Perfume	1	0.0006	13.079	4.775	0.008
	Deodorant	1	< LOD	6.329	< LOD	< LOD
	Nail polish	1	0.001	0.003	8.975	< LOD
	Hair product	1	< LOD	0.141	< LOD	< LOD
	Total		0.0016	19.552	13.75	0.008
90th Percentile	Perfume	3	0.003	58.857	21.488	0.036
	Deodorant	1	< LOD	6.329	< LOD	< LOD
	Nail polish	1	0.001	0.003	8.975	< LOD
	Hair product	2	< LOD	0.507	< LOD	< LOD
	Total		0.004	65.696	30.463	0.036

Note. LOD, limit of detection.

$$\text{In vivo human abs.} = \text{In vivo animal abs.} \times \frac{\text{In vitro human abs.}}{\text{In vitro animal abs.}} \quad (2)$$

The estimated exposure levels of phthalates from the concurrent use of multiple cosmetic products came to 0.183 $\mu\text{g/kg/d}$ for DEP, 0.018 $\mu\text{g/kg/d}$ for DBP, and 0.00013 $\mu\text{g/kg/d}$ for DEHP. For the highly exposed subgroup, the estimated exposure levels of phthalates from the concurrent use of multiple cosmetic products came to 2.017 $\mu\text{g/kg/d}$ for DEP, 0.228 $\mu\text{g/kg/d}$ for DBP, and 0.0013 $\mu\text{g/kg/d}$ for DEHP (Table 8).

Model 3 Fragrance chemicals can enter the body by inhalation as well as dermal absorption. Radiolabeled DEHP was found to be rapidly absorbed in rats when exposed (singly or repeatedly) by inhalation to 100 mg/m^3 DEHP for

TABLE 6. Dermal Absorption Rate of Phthalates In Vitro and In Vivo

	Study	Species	Absorption rate (%)
DEHP	In vivo	F-344 rat	5%
	In vitro	Human	1.06µg/cm ² /h
		AL/pk rat	2.24µg/cm ² /h
DEP	In vivo	F-344 rat	24%
	In vitro	Human	1.27µg/cm ² /h
		AL/pk rat	41.37µg/cm ² /h
DBP	In vivo	F-344 rat	60%
	In vitro	Human	0.07µg/cm ² /h
		AL/pk rat	9.33µg/cm ² /h

Note. From Scott et al. (1987) and Elsisi et al. (1989).

TABLE 7. Mean Expected Daily Human Exposure Levels to Phthalates from Cosmetics, Estimated by Using Model 2

Type	Expected daily exposure (µg/kg/d) ^a		
	DEHP	DEP	DBP
Perfume	0.0001	0.125	0.011
Deodorant	< LOD ^b	0.057	< LOD
Nail polish	0.00003	0.00001	0.007
Hair product	< LOD	0.001	< LOD
Total	0.00013	0.183	0.018

^a Mean.

^b LOD, limit of detection. For estimation, < LOD was considered to be halfway between 0 and the LOD values of each phthalate.

TABLE 8. Expected Daily Human Exposure Levels of Phthalates in Highly Frequent Cosmetic Users, as Estimated by Using Model 2

			Expected daily exposure (µg/kg/d)		
			DEHP	DEP	DBP
Median	Perfume	1	0.0003	0.402	0.036
	Deodorant	1	< LOD	0.194	< LOD
	Nail polish	1	0.0003	0.0001	0.067
	Hair product	1	< LOD	0.004	< LOD
	Total		0.0006	0.6	0.103
90th Percentile	Perfume	3	0.001	1.807	0.161
	Deodorant	1	< LOD	0.194	< LOD
	Nail polish	1	0.0003	0.0001	0.067
	Hair product	2	< LOD	0.016	< LOD
	Total		0.0013	2.017	0.228

Note. LOD, limit of detection.

TABLE 9. Mean Expected Daily Exposure Levels to Phthalates from Cosmetics, Estimated by Using Model 3

Type	Expected daily exposure ($\mu\text{g/kg/d}$) ^a		
	DEHP	DEP	DBP
Perfume	0.004	16.907	2.469
Deodorant	< LOD ^b	7.797	< LOD
Nail polish	0.001	0.001	1.466
Hair product	< LOD	0.174	< LOD
Total	0.005	24.879	3.935

^a Mean.^b LOD, limit of detection. For estimation, < LOD was considered to be halfway between 0 and the LOD values of each phthalate.**TABLE 10.** Expected Daily Exposure Levels to Phthalates in Highly Frequent Cosmetic Users Estimated by Using Model 3

		Frequency of cosmetic use (times/day)	Expected daily exposure ($\mu\text{g/kg/d}$)		
			DEHP	DEP	DBP
Median	Perfume	1	0.012	54.498	7.959
	Deodorant	1	< LOD	26.372	< LOD
	Nail polish	1	0.014	0.014	14.958
	Hair product	1	< LOD	0.587	< LOD
	Total		0.026	81.471	22.917
90th Percentile	Perfume	3	0.055	245.239	35.814
	Deodorant	1	< LOD	26.372	< LOD
	Nail polish	1	0.014	0.014	14.958
	Hair product	2	< LOD	2.114	< LOD
	Total		0.069	273.739	50.772

Note. LOD, limit of detection.

6 h (General Motors, 1982). If phthalates in cosmetics were assumed to be absorbed exclusively via 100% inhalation, the estimated exposure levels to phthalates resulting from the concurrent use of multiple cosmetic products would approximate 24.879 $\mu\text{g/kg/d}$ for DEP, 3.935 $\mu\text{g/kg/d}$ for DBP, and 0.005 $\mu\text{g/kg/d}$ for DEHP (U.S. EPA, 2001) (Table 9).

For the highly exposed subgroup, the estimated exposure levels to phthalates from the concurrent use of multiple cosmetic products came to 273.739 $\mu\text{g/kg/d}$ for DEP, 50.772 $\mu\text{g/kg/d}$ for DBP, and 0.069 $\mu\text{g/kg/d}$ for DEHP (Table 10).

Risk Assessment

Risk assessment was performed to estimate daily human exposure levels for phthalates (DEHP, DEP, and DBP) due to cosmetics use.

TABLE 11. Estimated Daily Human Exposure Due to Perfume, Nail Polish, and Hair Product Use, and Risk Assessment

	DEHP		DEP		DBP	
	Median group	90th Percentile group	Median group	90th Percentile group	Median group	90th Percentile group
Daily exposure level (µg/kg bw/d)	0.026	0.069	81.471	273.739	22.917	50.772
NOAEL (mg/kg bw/d)	3.7 (Poon et al., 1997)		2000 (Jones et al., 1993)		66 (Wine et al., 1997)	
UF ^a	100		300		1000	
Regulation level (µg/kg bw/d), adverse effects	TDI = 37 ^c (rat/reproductive toxicity)		MRL = 7000 ^d (rat/Leydig cell conformational change)		ADI = 66 ^e (rat/testis lesion)	
HI ^b	0.0007	0.002	0.012	0.039	0.347	0.769

^a UF, uncertainty factor: interspecies extrapolation (10), interindividual variability in the human population (10), and modifying factor (MF) (3–10).

^b Daily exposure level/TDI.

^c Tolerable daily intake (CSTEE).

^d Minimal risk level (ATSDR).

^e Acceptable daily intake (IPSC).

The Scientific Committee on Toxicity, Ecotoxicity, and the Environment CSTEE (1998) set a tolerable daily intake (TDI) of DEHP at 37 µg/kg/d, The Agency for Toxic Substances and Disease Registry (ATSDR) (1995) set a minimal risk level (MRL) of 7000 µg DBP/kg/d, and the International Programme on Chemical Safety (IPCS) (1997) set an acceptable daily intake (ADI) level of 66 µg DBP/kg/d. Table 11 shows the actual TDI, MRL, and ADI for each phthalate, and the no-observed-adverse-effect level (NOAEL) for reproductive toxicity in the rat, and the critical human exposure levels. Based on the U.S. Environmental Protection Agency (EPA) guideline (1981), the hazard indices (HIs = daily exposure level/regulation level [e.g., TDI, MRL, ADI]) were estimated to be 0.0007 for DEHP, 0.012 for DEP, and 0.347 for DBP. The HIs for phthalates were all far below 1, which implies that the daily exposure level and regulation level are equal.

DISCUSSION

In this study, data showed that four individual phthalates (DEHP, DEP, DBP, and BBP) were present in cosmetics. Of these phthalates, DEP was found to be present in highest concentrations in perfumes and deodorants, whereas DBP was the highest in nail polishes.

The Centers for Disease Control (CDC) tested for the presence of seven phthalates in human urine and found all seven corresponding monomeric phthalates (Blount et al., 2000). In particular, women of reproductive age (20–40 yr) were

found to have significantly higher levels of DBP, a reproductive and developmental toxicant in rodents, than other age/gender groups.

Cosmetics are a possible source of exposure to phthalates, and may be the source that leads to high exposures for some women tested by the CDC. People are routinely exposed to many phthalates, sometimes at high levels, as they are present in a wide array of everyday products: food wrap, shower curtains, automobile interiors, grout, paint, pesticides, hospital supplies, and cosmetics (Chan & Meek, 1994; Latini, 2000; Bouma & Schakel, 2002; Earls et al., 2003; Hill et al., 2003; Latini et al., 2003; Tara & Barbara, 2003). The general belief that the ingestion of contaminated food products is the most significant exposure pathway suggests that inhalation and possibly dermal absorption may also contribute to female exposure (NTP-CERHR, 2000a, 2000b, 2000c; Adibi et al., 2003).

In 2002, the expert panel of the Cosmetics Industry Review (CIR) updated the previous safety assessment review that "phthalates are safe for topical application given their present methods of use and their concentration in cosmetics," concluded by the largely self-policing safety review board of the cosmetics industry (CIR, 2002). The CIR Expert Panel assessed the risk of DBP exposure to human users of cosmetics based on the ingredient concentrations of used in cosmetic products (CTFA, unpublished data, 2001; Houlihan et al., 2002), the extent of cosmetic use survey data (Environ Corporation, 1984; CTFA, unpublished data, 2002), and dermal (Mint et al., 1994) and subungual penetration data (Jackson Research Association, 2002). Consequently, the estimated exposure level of DBP resulting from the concurrent use of multiple cosmetic products was 9.13 $\mu\text{g/kg}$ body weight (bw)/d, which is 2.5 times lower than the daily exposure estimated in the present study.

However, health and environmental activists have argued that phthalates have not been proven to be safe for any use, including cosmetics. It should be also noted that the estimation of daily human exposure to phthalates and the risk assessment were performed in our study based on the assumption that either skin absorption or inhalation occurred, which does not reflect the actual exposure scenarios. In addition, there are more uncertainties such as variations in the method of using brand cosmetics (e.g., perfume application to skin or to clothes).

Phthalates are widespread in plastics and cosmetic products, and people are exposed to more than one phthalate from various routes of exposure. However, little is known about the sources and patterns of human exposure. Many exposures from all different sources may be additive and a cause of concern. Therefore, to facilitate the risk assessment of exposure to phthalates, the actual intake of the individual phthalates should be reconsidered and determined more accurately using validated methodologies.

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