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Exposure to di-2-ethylhexyl terephthalate in the U.S. general population from the 2015–2016 National Health and Nutrition Examination Survey

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Abstract

Background—Di-2-ethylhexyl terephthalate (DEHTP) is used as a replacement plasticizer for other phthalates, including di-2-ethylhexyl phthalate (DEHP). Use of consumer products containing DEHTP may result in human exposure to DEHTP.

Objective—To assess exposure to DEHTP in a nationally representative sample of the U.S. general population 3 years and older from the 2015–2016 National Health and Nutrition Examination Survey (NHANES).

Method—We quantified two DEHTP metabolites, mono-2-ethyl-5-hydroxyhexyl terephthalate (MEHHTP) and mono-2-ethyl-5-carboxypentyl terephthalate (MECPTP) in 2,970 urine samples by using online solid-phase extraction coupled with isotope dilution-high-performance liquid chromatography-tandem mass spectrometry. We used linear regression to examine associations between MEHHTP and MECTPP and several parameters including age, sex, race/ethnicity, and household income. We also compared the MEHHTP and MECPTP results to those of their corresponding DEHP metabolite analogs, namely mono-2-ethyl-5-hydroxyhexyl phthalate (MEHHP) and mono-2-ethyl-5-carboxypentyl phthalate (MECPP).

Results—The weighted detection frequencies were 96% (MEHHTP) and 99.9% (MECPTP); urinary concentrations of the two metabolites correlated significantly (Pearson correlation coefficient=0.89, $p < 0.0001$). MECPTP concentrations were higher than MEHHTP in all age, sex, race/ethnicity groups examined. Furthermore, MECPTP adjusted GM concentrations were significantly higher in samples collected in the evening than in the morning or afternoon. Females had significantly higher adjusted GM concentrations of MEHHTP and MECPTP than males. We

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Study approval

The Research Ethics Review Board of the National Centers for Health Statistics of the Centers for Disease Control and Prevention reviewed and approved the study protocol.

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Conflict of interest

The authors declare they have no competing financial interests.

observed no significant associations between the adjusted GM concentrations of the metabolites and race/ethnicity. Both metabolite adjusted GM concentrations increased significantly with household income, and decreased significantly with age. Only household income was significantly associated with the concentrations of MECPP, but not of MEHHP, the two DEHP metabolites. The adjusted GM of the [MEHHTP]:[MECPTP] molar concentrations ratio increased with age, and was significantly higher in samples collected in the morning than in those collected in the afternoon or evening.

Conclusions—Exposure to DEHTP is widespread in the U.S. general population 3 years and older. These data represent the first U.S. population-based representative background exposure to DEHTP.

Keywords

Biomonitoring; Exposure assessment; DEHTP; NHANES

1. Introduction

Di(2-ethylhexyl) terephthalate (DEHTP) is a general purpose plasticizer, and a high production volume chemical (PubChem 2018). DEHTP is used in polymers, coating products, adhesives and sealants, and in a variety of applications such as flooring, cable insulations, toys, medical devices, and food contact materials (Eastman Chemical Company 2014). DEHTP is used in products to replace other phthalates including di-2-ethylhexyl phthalate (DEHP). Because of its toxicity in animal studies, the use of DEHP in toys and food contact materials has been restricted in Europe and in the USA (CPSC 2014; European Union 2005). Of interest, general population data from the National Health and Nutrition Examination Survey (NHANES) suggest that these restrictions may have already impacted exposures to DEHP in the United States. For example, adjusted geometric mean concentrations of the sum of DEHP metabolites decreased 37% between 2001–2002 and 2009–2010 (Zota et al. 2014). Furthermore, estimates of daily intake dose and several cumulative risk metrics obtained using NHANES biomonitoring data for six phthalates, including DEHP, showed a shift from exposure to relatively more-toxic phthalates such as DEHP (based on their Tolerable Daily Intake values) to relatively less-toxic phthalates between 2005 and 2014 (Reyes and Price 2018).

One of those relatively less-toxic phthalates is DEHTP, a structural isomer of DEHP. In Sprague-Dawley rats administered DEHTP in the diet, DEHTP did not induce major adverse effects at doses up to 600 mg/kg bw/day (Barber and Topping 1995). Similarly, in male and female rats with continuous intravenous infusion of DEHTP over 4 weeks at 38.2, 114.5 or 381.6 mg/kg, DEHTP had no effect on survival, hematotoxicity or immunotoxicity, or effects on hepatic, thyroidal and reproductive functions or organs (Wirnitzer et al. 2011). Although DEHTP toxicity data in humans do not exist, because DEHTP is considered a safer alternative to DEHP, the use of DEHTP appears to be on the rise (Nagorka et al. 2011). At the same time, as select chemicals, such as DEHTP, replace others (e.g., DEHP) in consumer markets, increasing the understanding of exposures to these replacement chemicals is gaining scientific and public interest, particularly because for some of the

chemicals only limited exposure potential and/or toxicity information exists (LaKind and Birnbaum 2010).

Two oxidative metabolites of DEHTP, namely mono-2-ethyl-5-hydroxyhexyl terephthalate (MEHHTP) and mono-2-ethyl-5-carboxypentyl terephthalate (MECPTP), have been identified as adequate biomarkers of exposure to DEHTP (Lessmann et al. 2016a; Lessmann et al. 2016b; Lessmann et al. 2018; Silva et al. 2015). Together, these two metabolites represent about 15% (MECPTP, 13%; MEHHTP, 2%) of the oral dose of DEHTP excreted in urine (Lessmann et al. 2016b). Other possible DEHTP metabolites only represent a small fraction (<1%) of the excreted parent compound, and their usefulness as exposure biomarkers is questionable (Lessmann et al. 2018). Interestingly, the MEHHTP and MECPTP analogous DEHP metabolites, mono-2-ethyl-5-hydroxyhexylphthalate (MEHHP) and mono-2-ethyl-5-carboxypentylphthalate (MECPP) represent about 42% (MECPP, 18.5%; MEHHP, 23.3%) of the DEHP excreted urinary dose (Koch et al. 2005; Koch et al. 2006), thus suggesting important differences in the metabolism of DEHTP and DEHP. Concentrations in urine of MEHHP and MECPP, the two widely studied DEHP exposure biomarkers, are often detected in the U.S. general population since the mid-2000s (CDC 2018). On the other hand, the frequent detection of urinary concentrations of MEHHTP and MECPTP in convenience populations of adults in the USA (Silva et al. 2017) and Germany (Lessmann et al. 2016a) suggest exposure to DEHTP. Yet, U.S. general population exposure data for these two DEHTP biomarkers do not exist.

Because of the potential increase in use of DEHTP in consumer products, interest exist in understanding the extent of human exposure to this compound and whether exposure may change with time. To establish a baseline assessment of exposure to DEHTP, a critical step to evaluate potential future exposure trends, we present here the first nationally representative data on urinary concentrations of two biomarkers of DEHTP in the U.S. general population 3 years of age and older, stratified by age group, sex, and race/ethnicity.

2. Materials and methods

2.1. Study population

The National Health and Nutrition Examination Survey (NHANES) is designed to assess the health and nutritional status of the civilian noninstitutionalized population of the United States by using a combination of interviews, physical examinations, and laboratory analysis of biological specimens (CDC 2016). Sociodemographic information and medical histories of the participants and their families are collected during household interviews. Spot urine and blood samples are collected from each participant (some urine samples may be first-morning-voids) during one of three daily examination periods (morning 08.30-12.00 hr; afternoon 12.30-16.00 hr; evening 16.30-20.00 hr) at the NHANES mobile examination center. Collection follows NHANES approved protocols, comprehensively detailed on the NHANES website, developed to ensure the integrity of all biospecimens for the quantification of clinical, nutritional, and environmental chemical biomarkers (CDC 2013). Since 1999, the Centers for Disease Control and Prevention (CDC) uses some of these biological specimens to assess exposure to select environmental chemicals (CDC 2018).

For the present study, we analyzed 2,970 spot urine specimens collected from children 3-5 years old (N=465), and from a one-third subsample (N=2,505) of 2015–2016 NHANES participants 6 years of age and older. Because the sub-sample was random, the representative design of the survey was maintained. The National Centers for Health Statistics (NCHS) Research Ethics Review Board reviewed and approved the study protocol. All participants gave written informed consent; parents or guardians provided consent for participants younger than 18 years of age.

2.2. Urinary concentrations of DEHTP biomarkers

The urine samples were shipped on dry ice to CDC's National Center for Environmental Health, and stored at or below −20 °C until analyzed. Briefly, the glucuronide conjugates of MEHHTP and MECPTP in 100 μL of urine were hydrolyzed using β-glucuronidase from E. coli-K12, and the concentrations of the target analytes were quantified using on-line solid-phase extraction, separation with high-performance liquid chromatography, and detection by isotope-dilution negative ion electrospray ionization tandem mass spectrometry as described before (Silva et al. 2007; Silva et al. 2013). Spiked urine was repeatedly analyzed to determine the method limit of detection (LOD), accuracy, and precision for each analyte. The LODs, 0.4 μg/L (MEHHTP) and 0.2 μg/L (MECPTP), were calculated as $3S_0$, where S_0 (determined from the replicate analysis of low-level standards) was the standard deviation as the concentration approaches zero (Taylor 1987). The mean accuracy (standard deviation), calculated from the recovery at three spiking levels (2.5, 6.3, 15.6 μg/L), was 99.4% (6.8%) for MECPTP and 95.9% (3.6%) for MEHHTP. We prepared low-concentration (2.5 μg/L–5 μg/L) and high-concentration (8 μg/L–12 μg/L) quality control (QC) materials with pooled human urine. The precision of measurements, expressed as the relative standard deviation of inter- and intraday measures of these QC materials in a period of approximately 8 months, ranged from 6.0% to 9.5%, depending on the metabolite and concentration range. The CDC laboratory is certified by the Health Care Financing Administration to comply with the requirements set forth in the Clinical Laboratory Improvement Act of 1988 (CLIA '88) and is recertified annually. Therefore, the analytical measurements followed strict CLIA-recommended quality control/quality assurance protocols. For example, in addition to the NHANES samples, each analytical run included calibration standards, high- and low-concentration QC materials, and reagent blanks to assure data accuracy and reliability. The concentrations of the high-concentration QCs and the low-concentration QCs, averaged to obtain one measurement of high-concentration QC and low-concentration QC for each run, were evaluated using standard statistical probability rules. If the QC samples failed the statistical evaluation, all of the samples in the run were re-extracted. As with any other CLIA-certified analytical method used for the analysis of NHANES biospecimens, the details of the procedure used to quantify MEHHTP and MECPTP are available at https://wwwn.cdc.gov/nchs/data/nhanes/2015-2016/labmethods/PHTHTE_I_MET.pdf.

2.3. Statistical analysis

We used SAS surveymeans, surveyfreq, surveyreg (version 9.4; SAS Institute Inc.; Cary, North Carolina) and SUDAAN (version 11; Research Triangle Institute; Research Triangle Park, North Carolina) to perform statistical analyses. SAS and SUDAAN incorporate the sample population weights and calculate variance estimates that account for the complex

design of NHANES. The survey-specific sample weights were designed for the subset of participants 3 years of age and older of the full survey. As recommended by NCHS, we used the environmental subsample B population weights (provided in the data release file) to produce estimates that are representative of the U.S. population. For metabolite concentrations below the LOD, we imputed a value equal to the LOD divided by the square root of 2 (Hornung and Reed 1990). Statistical significance was set at $p < 0.05$.

For the descriptive statistics, we stratified age, reported in years at the last birthday, in five groups (3–5 years, 6–11 years, 12–19 years, 20–59 years, and 60 years and older). On the basis of self-reported information, we categorized race/ethnicity as non-Hispanic black, non-Hispanic white, all-Hispanic, and Other (Table 1); 301 of the 443 persons included in the Other racial category were Asian. For each sex, and age and race/ethnicity group, we calculated the geometric mean (GM) and distribution percentiles for both volume-based (μg/L) and creatinine-corrected concentrations (μg/g creatinine).

The concentration distributions of the two DEHTP metabolites were right skewed. Before log transformation, skewness and kurtosis were 8.3 and 8.8, and 110 and 102, for MEHHTP and MECPTP, respectively. After log transformation, skewness and kurtosis became 0.335 and 0.126, and −0.009 and −0.03, for MEHHTP and MECPTP, respectively (<0.7 for skewness and <0.2 for kurtosis for normal distributions). We also determined the weighted Pearson correlation coefficient (r) among the concentrations (log_{10} transformed) of MECPTP and MEHHTP. Of note, NHANES participants attending the morning examination session reported fasting longer (mean ± standard error, 10.5 ± 0.22 hr) compared to participants attending afternoon (3.1 ± 0.33 hr) and evening (2.6 ± 0.24 hr) sessions. Furthermore, self-reported fasting duration increased with age (3.5 ± 0.31 hr for 3–5 year olds vs. 8.1 ± 0.24 hr for >60 years old). Lastly, more children attended the morning (weighted percentage, 40.63%) and afternoon (39.52%) examination sessions than the evening session (19.85%). Therefore, we also evaluated the relationship between self-reported fasting duration (at the time of the examination) and urine collection time (using the examination period information).

We used multiple regression models to examine the associations between the two DEHTP biomarkers and several variables (i.e., age (continuous), sex, race/ethnicity, household income, time of urine collection, fasting duration, log-transformed creatinine). Study participants reported annual household income (INDFMIN2) in increments of $5000 from < $5000 to ≥$75,000; to obtain a comparable number of participants per group, we categorized income as <$20,000, $20,000–<$45,000, $45,000–<$75,000, and ≥$75,000. Participants with missing data for covariates (of the 240 missing, 238 were for household income) were excluded from those analyses. Because time of urine collection and fasting duration highly correlated (data not shown), we chose to keep only time of urine collection in the model to minimize bias (i.e., fasting duration is self-reported). For the multiple regression models, we used the above variables and all their possible two-way interactions to calculate the adjusted GM concentrations of MEHHTP and MECPTP (in μg/L). To arrive at the final models, we removed non-significant interactions one at a time by backward elimination with SUDAAN. We then removed covariates with non-significant main effects one at a time, and rerun the models to determine whether the beta coefficients for the significant main effects or

interactions changed by >10%. If any did, we retained the non-significant main effect in the model. Once we completed the backward procedure, we added back main effects and interactions into the model one at a time to determine whether any were significant. We retained all significant main effects and their interactions in the final models.

We calculated the adjusted geometric means of MEHHTP and MECPTP concentrations and the molar concentration ratios of MEHHTP and MECPTP for ages 4, 8.5, 15.5, 39.5 and 72.5 years (the mid-point of each of the five age groups described above). We also compared the adjusted GM concentrations of MEHHTP and MECPTP with those of their corresponding DEHP metabolite analogs, MEHHP and MECPP, respectively.

3. Results

We quantified the urinary concentrations of two DEHTP metabolites, MEHHTP and MECPTP, in 2,970 NHANES 2015–2016 participants. We present the distribution of concentrations of MEHHTP (Table 1) and MECPTP (Table 2), including GM and select percentiles, with and without creatinine adjustment stratified by age group, sex, and race/ethnicity. The weighted detection frequency of MEHHTP (concentration range: >0.4 μg/L–876 μg/L) was 96%. The weighted detection frequency and concentration range of MECPTP were 99.9% and >0.2 μg/L–4,312 μg/L, respectively. Weighted bivariate Pearson's correlation analysis showed statistically significant correlations ($p < 0.0001$) between the $\log_{10}$-transformed concentrations of MEHHTP and MECPTP ($r = 0.89$; Figure 1).

In Table 3, we present the adjusted GM concentrations for select demographic variables after adjustment for all other covariates. The final linear multivariate regression models included sex, household income, age, and log-creatinine. Compared to males, females had significantly higher adjusted GM concentrations of MEHHTP (5.48 μg/L vs 4.9 μg/L, p=0.04) and MECPTP (24.85 μg/L vs 20.25 μg/L, p=0.002). The adjusted GM for persons with household income <$20K was 4.13 μg/L (MEHHTP) and 18.92 μg/L (MECPTP), and was 6.98 μg/L (MEHHTP) and 30.83 μg/L (MECPTP) for persons with household income ≥ $75K (Table 3, Figure S1). The differences between the three lowest household income groups and the highest (≥$75K) were statistically significant (Table S1).

The least square regression analysis showed a downward trend in adjusted GM concentrations of the DEHTP metabolite with age ($\beta_{MEHHTP} = -0.006$ ($p<.001$); $\beta_{MECPTTP} = -0.01$ ($p<0.001$)) (Figure 2a), but an upward trend of the ratio of molar concentrations of MEHHTP and MECPTP (Figure 2b). We also found a significant association between the [MEHHTP]:[MECPTP] molar concentration ratio and the time of urine collection. The adjusted GM concentration ratio was significantly higher in samples collected in the morning (0.29) than those collected in the afternoon (0.24, p=0.002) or in the evening (0.22, $p<0.0001$).

The adjusted GM concentration of MECPTP was significantly higher in samples collected in the evening (29.9 μg/L) than in the morning (18.37 μg/L, p=0.002) or afternoon (20.56 μg/L, p=0.0054), but differences between concentrations from morning and afternoon collections did not reach statistical significance (p=0.3491). Similarly, the adjusted GM concentrations

of MEHHTP were highest in samples collected in the evening (6.19 μg/L), but differences did not reach statistical significance (Table 3, Table S1).

Using the data publicly available on the NHANES website, we calculated the GM (95% confidence interval [CI]) concentrations (in μg/L) of MECPP and MEHHP in NHANES 2015–2016: 8.69 (7.96–9.48) and 5.59 (5.27–5.93), respectively, much lower than their concentrations (MECPP: 34.7 (31.0–38.9); MEHHP: 21.7 (19.3–24.4)) in NHANES 2003–2004, in agreement with previously reported downward concentration trends for DEHP metabolites (Zota et al. 2014). The final linear multivariate regression model for MECPP only included household income (p=0.0294); no covariates were significantly associated with the concentrations of MEHHP. Persons in the highest household income category (≥ $75K) had the lowest adjusted GM concentrations of MECPP (7.85 μg/L, Table S2); differences in MECPP adjusted GM between persons with household income <$20K and for persons with household income ≥$75K did not reach statistical significance (p=0.1422, Table S2). The GM concentrations of MECPP and MEHHP were lowest in the samples collected during the evening examination period (Table S3); however, none of the differences reached statistical significance.

4. Discussion

For the first time, we report concentrations of two DEHTP metabolites in a nationally representative population, including children aged 3-5 years, in the United States. Detection of both biomarkers in over 95% of the samples analyzed suggest widespread exposure to DEHTP in the United States. Not surprisingly, because MECPTP and MEHHTP are both metabolites of DEHTP, their urinary concentrations were highly correlated.

In a human metabolism study, approximately 13.0% of the applied DEHTP dose was excreted as MECPTP in urine compared to approximately 1.8% for MEHHTP, suggesting that MECPTP is the major urinary metabolite of DEHTP (Lessmann et al. 2016b). In agreement with these results, urinary concentrations of MECPTP were several times higher than those of MEHHTP among all NHANES demographic groups examined. These results are also in agreement with a previous study involving a convenience sampling of non-occupationally exposed U.S. adults (N=149) collected in 2016 (Silva et al. 2017).

Because DEHTP may replace DEHP in certain uses, comparing concentration patterns for the biomarkers of DEHTP and DEHP may be useful to increase the understanding of exposure determinants. For instance, adjusted urinary concentrations of DEHTP biomarkers, but not of the DEHP metabolites, decreased significantly with age. These differences may relate to children-specific behaviors compared with those of adults. Because DEHTP is widely used in certain plastics (PubChem 2018), use of plastic toys may have contributed to exposure to DEHTP among young children. On the other hand, the Consumer Products Safety Commission restricted use of DEHP in certain children toys (CPSC 2014), thus somewhat supporting the absence of age-related differences for the DEHP biomarkers.

In the evening, concentrations of MECPTP and MEHHTP were highest while those of the corresponding DEHP metabolites, MECPP and MEHHP, were lowest. Of interest, in a study

of 48 Norwegian mothers and their children, urinary concentrations of MECPP and MEHHP (DEHTP metabolites were not measured) were also higher in samples collected in the morning time-period (overnight–8.00 hr) compared to those collected in early day (8.00–12.00 hr) and afternoon (12.00–16.00 hr) periods (Sakhi et al. 2017). We speculate that the different concentration patterns between DEHP and DEHTP biomarkers by sample collection time period may relate, at least in part, to differences in the use of these two phthalates, differences in the biomarkers elimination half-lives, or a combination of both.

Despite the fact that MECPTP and MEHHTP have rather similar elimination half-lives (~7 hr) from the human body (Lessmann et al. 2016b), and that within each person, in general, MECPTP concentrations were higher than those of MEHHTP, we observed that the ratio of molar concentrations of MEHHTP and MECPTP was significantly lower in samples collected in the evening compared to those collected in afternoon and morning collections. Also, more children attended the morning and afternoon examination sessions than the evening session. Interestingly, we observed a gradual increase in the ratio of molar concentrations of MEHHTP and MECPTP with age, and the trend remained significant even after including sample collection session in the model. Noteworthy, a similar increase in ratio of molar concentrations of the analogous metabolites of DEHP (i.e., MEHHP, MECPP), which have longer elimination half-lives (10–15 hr) than the DEHTP metabolites (Koch et al. 2005; Koch et al. 2006), was reported for Finnish infants from 3 days to 14 months of age, and was associated to maturation of physiological metabolism processes as infants aged (Frederiksen et al. 2014). Therefore, we speculate that differences in enzyme activities specific for ω−1 oxidation (the pathway for the formation of MEHHTP and MEHHP) and/or ω–oxidation (the pathway for the formation of MECPTP and MECPP) with age (Becker et al. 2004; Frederiksen et al. 2014) may have contributed to the observed trends.

Interestingly, DEHTP metabolites concentrations increased with household income, and were significantly higher in households with the highest income compared to the other income groups. By contrast, the concentrations of the analogous DEHP metabolites did not change with household income (MEHHP) or were lowest among persons in the highest household income group (MECPP). Furthermore, although DEHTP and DEHP are not known to be used in personal care products where differences in the use by sex may occur, females had significantly higher concentrations of DEHTP metabolites than males, but we found no associations between concentrations of the DEHP metabolites and sex. The reasons for such differences in concentrations by household income and sex, and the fact that these factors may influence exposures to DEHP and DEHTP differently remain unknown.

Data on human exposure to DEHTP are rather limited (Lessmann et al. 2016a; Lessmann et al. 2017; Silva et al. 2015). In particular, only one study has reported DEHTP biomarker concentrations in children (Lessmann et al. 2017). Median MECPTP urinary concentrations in 68 Portuguese children 4-11 years old recruited in 2014-2015 were 4.03 μg/L compared to 38.2 μg/L among NHANES 2015-2016 children 6-11 years of age. Among 34 German adults aged between 25 and 61 recruited in 2014, the median MECPTP concentrations was 0.9 μg/L compared to 14.6 among NHANES 2015-2016 adults 20-59 years of age (Lessmann et al. 2016a). Exposure to DEHP and other phthalates vary among countries

because of differences in the manufacture and commercial use of phthalates around the world. Therefore, the higher concentrations of MCEPTP in U.S. children and adults likely reflect differences in the use of DEHTP in commercial products and applications among countries. Future studies evaluating exposure to DEHTP in various countries will increase the understanding of factors that impact exposure to this compound.

In summary, we report the first nationally representative population-based MEHHTP and MECPTP urinary concentrations for select demographic groups in the United States from NHANES 2015–2016. These results suggest exposure to DEHTP in all population categories, including young children 3–5 years of age. More importantly, the data demonstrating widespread exposure to DEHTP in the U.S. general population represent a baseline assessment of exposure to DEHTP that can serve as reference to assess future exposure trends, and to provide the foundation for additional research to evaluate potential health effects upon exposure to DEHTP.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

CDC	Centers for Disease Control and Prevention
CI	Confidence interval
GM	Geometric mean
LOD	Limit of detection
NCHS	National Center for Health Statistics
NHANES	National Health and Nutrition Examination Survey

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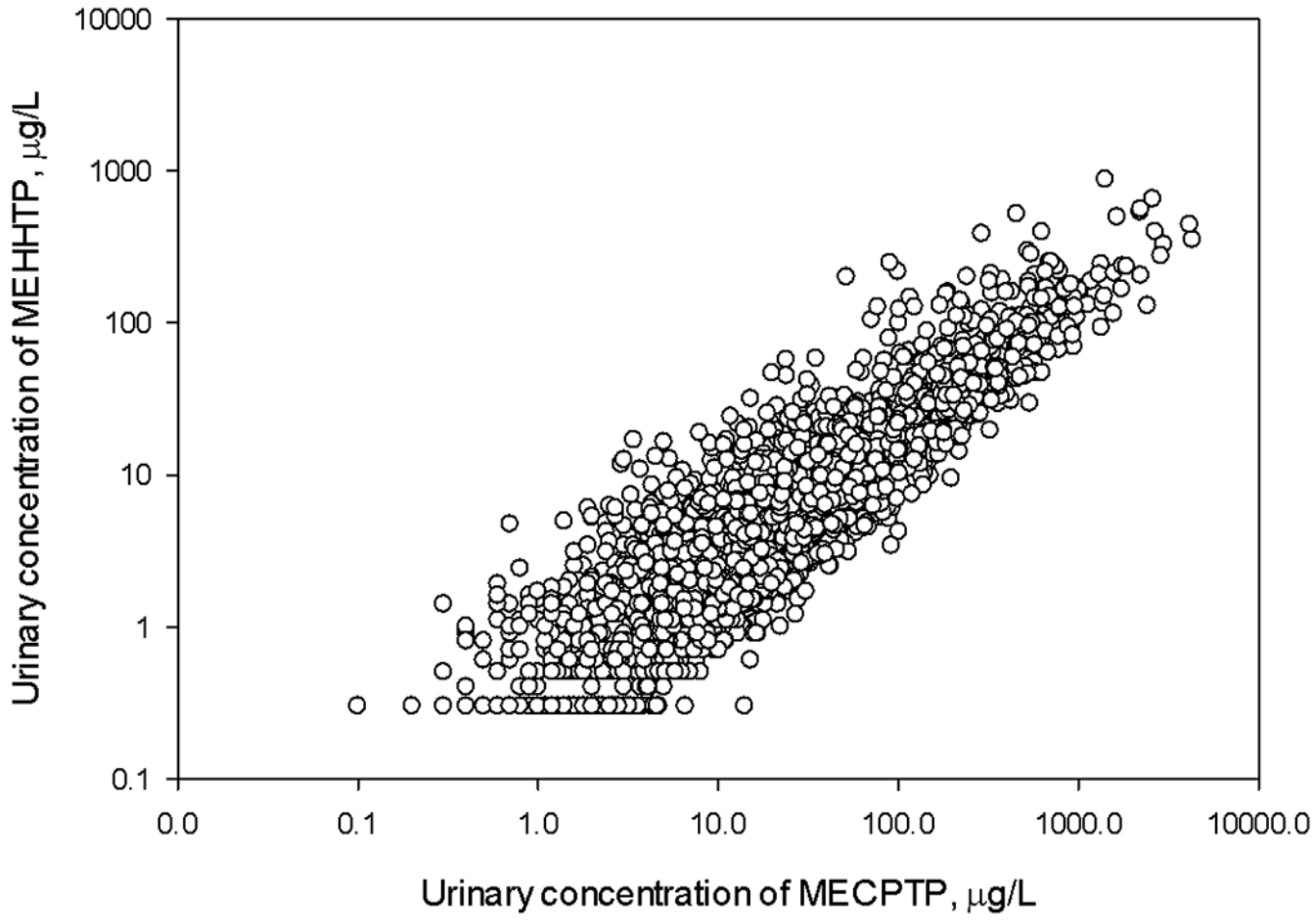

Figure 1.
Correlation plot of urinary concentrations of DEHTP biomarkers, mono-2-ethyl-5-hydroxyhexyl terephthalate (MEHHTP) and mono-2-ethyl-5-carboxypentyl terephthalate (MECPTP) in the U.S. population from NHANES 2015-2016.

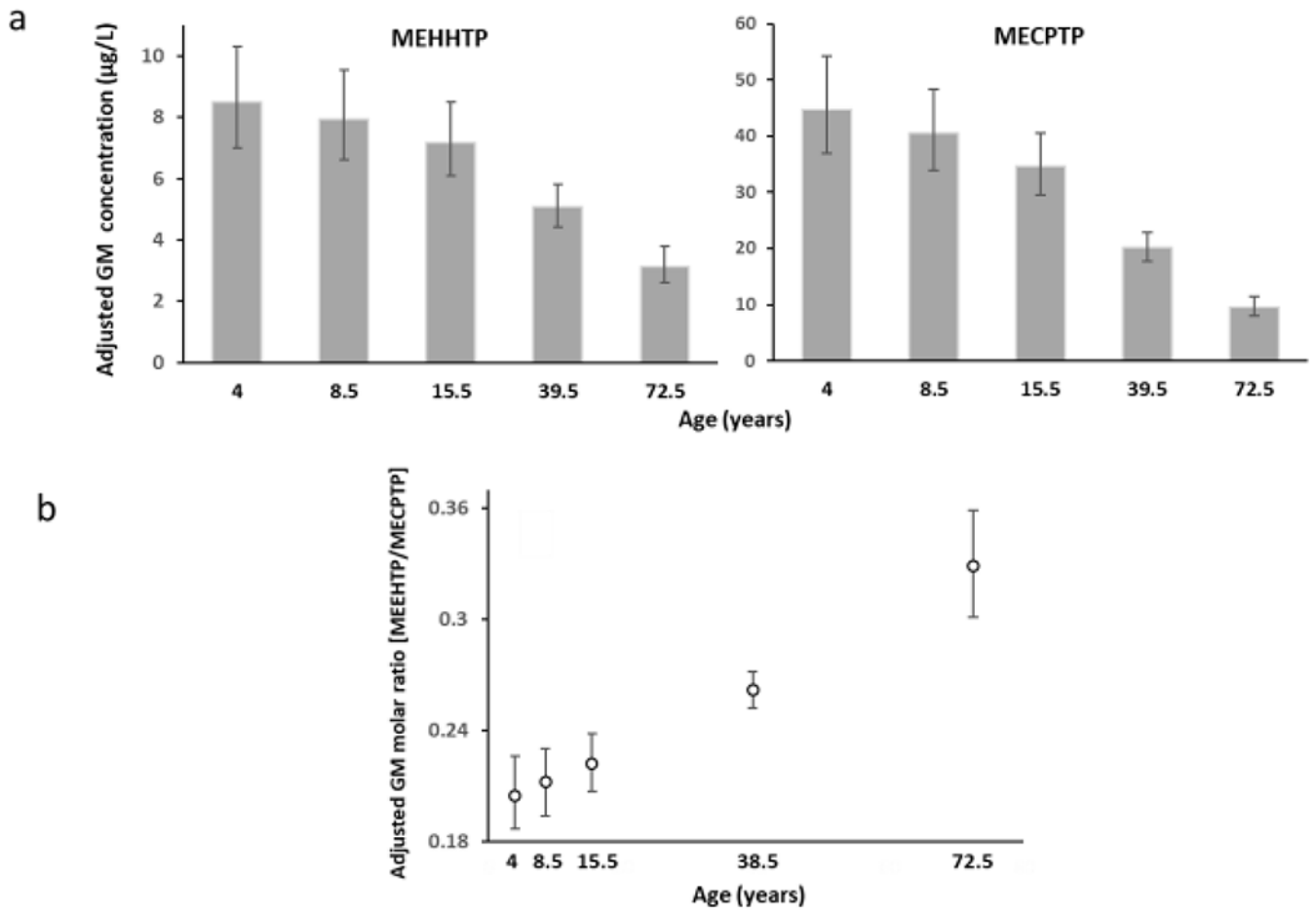

Figure 2.

(a) Adjusted geometric mean (GM) urinary concentrations (in µg/L) of mono-2-ethyl-5-hydroxyhexyl terephthalate (MEHHTP) and mono-2-ethyl-5-carboxypentyl terephthalate (MECPTP) and (b) adjusted GM of the ratio of the molar concentrations of MEHHTP and MECPTP by age at the mid-point of each age group from NHANES 2015-2016 . Error bars represent the lower and upper 95% confidence intervals.

Table 1.

Geometric mean and selected percentiles of mono-2-ethyl-5-hydroxyhexyl terephthalate (MEHHTP) concentrations in urine in μg/L (first line) and in μg/g creatinine (second line) for the U.S. population 3 years of age and older from NHANES 2015-2016 (N=2,970).

		Select percentile (95% confidence interval)				
	Geometric mean (95% conf. limit)	**50th**	**75th**	**90th**	**95th**	**Sample size**
Total	5.15 (4.41-6.02)	4.6 (3.90-5.30)	13.8 (11.8-16.9)	42.3 (30.0-55.1)	85.7 (61.4-124)	2970
	5.33 (4.58-6.21)	4.47 (3.72-5.39)	12.3 (10.3-15.6)	34.6 (26.9-46.4)	67.5 (52.8-84.1)	2969
Age group						
3-5 years	5.74 (4.90-6.73)	5.2 (4.30-6.30)	10.8 (8.90-14.2)	28.1 (19.4-37.5)	45.2 (30.8-59.2)	465
	13.7 (11.4-16.6)	12.5 (10.6-14.6)	24.5 (19.5-28.9)	58.6 (36.4-81.9)	89.2 (60.2-118)	464
6-11 years	7.35 (5.70-9.48)	7.0 (5.20-10.0)	16 (12.6-22.5)	34.6 (23.0-63.1)	74.7 (34.6-111)	413
	9.5 (7.72-11.7)	8.86 (7.13-11.2)	16.9 (14.1-20.6)	41.5 (27.6-57.8)	64.3 (47.3-123)	413
12-19 years	8.11 (6.24-10.5)	7.3 (5.90-9.50)	23.5 (13.9-35.6)	70.2 (33.1-144)	126 (54.5-209)	403
	6.3 (5.00-7.95)	5.66 (3.54-7.99)	16.9 (10.7-25.5)	44.2 (27.6-59.5)	59.5 (44.3-71.8)	403
20-59 years	5.34 (4.38-6.51)	4.7 (3.80-5.70)	15.6 (11.2-20.1)	47.7 (32.0-61.4)	93.1 (65.1-128)	1146
	5.22 (4.32-6.31)	4.32 (3.42-5.89)	12.0 (9.23-15.9)	33.1 (23.6-47.1)	66.2 (49.4-86.5)	1146
60 years and older	3.18 (2.41-4.20)	2.5 (1.80-3.70)	8.1 (4.90-11.8)	22.6 (13.4-41.9)	51.8 (23.6-156)	543
	3.61 (2.79-4.67)	2.94 (2.32-3.77)	6.18 (4.68-10.1)	25.0 (13.3-61.6)	76.4 (30.9-92.3)	543
Sex						
Males	5.85 (4.89-6.99)	5.2 (4.20-6.60)	16 (12.3-20.0)	44.3 (30.0-63.5)	95.0 (65.1-144)	1472
	5.22 (4.38-6.21)	4.66 (3.63-5.69)	12 (9.32-16.0)	33.1 (25.2-46.4)	64.9 (47.2-81.9)	1472
Females	4.56 (3.88-5.36)	3.8 (3.20-4.70)	12.5 (10.5-15.1)	40.0 (26.8-54.5)	78.4 (52.1-124)	1498
	5.45 (4.66-6.39)	4.39 (3.67-5.56)	13.4 (10.5-15.9)	36.1 (26.3-51.5)	73.4 (47.1-95.4)	1497
Race/ethnicity						
All Hispanic	4.56 (3.39-6.13)	4.4 (3.10-5.80)	11.9 (8.50-15.7)	30.8 (22.9-47.6)	58.1 (44.5-94.4)	969
	4.81 (3.62-6.38)	4.32 (2.93-6.58)	11.5 (8.28-16.9)	27.8 (21.4-40.2)	50.2 (33.1-85.9)	969

	Geometric mean (95% conf. limit)	Select percentile (95% confidence interval) 50th	75th	90th	95th	Sample size
Non-Hispanic Blacks	6.0 (4.78-7.53)	5.9 (4.50-7.40)	15.3 (11.5-20.0)	39.6 (29.4-53.9)	72.4 (56.3-101)	697
	4.78 (4.04-5.65)	4.18 (3.29-5.67)	10.8 (8.6-13.2)	26.7 (21.4-34.8)	50.7 (34.0-69.9)	696
Non-Hispanic Whites	5.32 (4.45-6.37)	4.5 (3.60-5.50)	16.0 (12.3-19.9)	46.5 (30.0-76.0)	111 (71.1-156)	861
	5.72 (4.79-6.84)	4.88 (3.81-5.92)	14.1 (10.2-18.8)	44.3 (32.4-52.5)	79.8 (57.8-101)	861
Other	4.33 (3.27-5.73)	4.2 (3.30-5.00)	10.1 (6.70-14.2)	26.4 (18.7-46.8)	58.0 (29.7-115)	443
	4.75 (3.81-5.92)	3.64 (3.00-5.27)	9.4 (7.24-12.0)	26.1 (20.3-35.5)	43.1 (27.8-61.6)	443

Table 2.

Geometric mean and selected percentiles of mono-2-ethyl-5-carboxypentyl terephthalate (MECPTP) concentrations in urine in μg/L (first line) and in μg/g creatinine (second line) for the U.S. population 3 years of age and older from NHANES 2015-2016 (N=2970).

		Select percentile (95% confidence interval)				
	Geometric mean (95% conf. limit)	**50th**	**75th**	**90th**	**95th**	**Sample size**
Total	19.7 (16.9-23.1)	16.5 (14.2-20.0)	59.8 (50.3-70.6)	196 (155-226)	369 (291-500)	2970
	20.4 (17.5-23.9)	18.1 (14.4-21.9)	58.8 (49.5-68.7)	166 (147-199)	361 (277-410)	2969
Age group						
3-5 years	39.7 (33.8-46.7)	38.6 (30.1-44.8)	72.8 (62.8-98.5)	207 (135-266)	282 (230-450)	465
	95.1 (79.2-114)	86.8 (67.5-107)	175 (143-217)	397 (304-537)	716 (413-1080)	464
6-11 years	41.4 (32.5-52.8)	38.2 (28.5-52.6)	100 (75.3-140)	228 (157-360)	401 (229-708)	413
	53.5 (44.5-64.3)	49.0 (42.0-60.4)	109 (82.2-138)	253 (183-339)	443 (302-710)	413
12-19 years	38.1 (29.4-49.3)	32.1 (23.5-44.9)	123 (79.4-214)	373 (187-628)	628 (361-846)	403
	29.6 (23.2-37.8)	23.7 (16.4-35.4)	88.6 (52.3-144)	244 (206-305)	395 (302-455)	403
20-59 years	18.8 (15.5-22.7)	14.6 (11.8-19.2)	59 (45.7-72.1)	188 (142-251)	367 (273-532)	1146
	18.4 (15.2-22.2)	15.5 (12.4-19.8)	51.7 (39.5-64.4)	146 (114-165)	277 (182-373)	1146
60 years and older	10.8 (8.29-14.1)	8.3 (7.00-10.8)	30.1 (19.7-40.9)	107 (51.2-142)	214 (108-358)	543
	12.3 (9.37-16.1)	11.2 (8.03-13.9)	27.1 (20.3-47.7)	110 (56.7-227)	346 (126-487)	543
Sex						
Males	20.7 (17.7-24.3)	17.8 (15.1-23.1)	62.9 (49.1-77.0)	190 (139-244)	374 (292-475)	1472
	18.5 (15.6-21.8)	15.5 (12.6-19.6)	54.8 (41.8-74.9)	148 (133-192)	302 (218-368)	1472
Females	18.8 (15.7-22.5)	15.7 (12.6-19.6)	57.9 (47.8-69.0)	198 (151-229)	361 (255-532)	1498
	22.5 (18.9-26.9)	20.3 (15.6-24.3)	61.1 (56.7-73.5)	182 (149-241)	426 (251-487)	1497
Race/ethnicity						
All Hispanic	19.1 (14.2-25.9)	17.9 (12.9-25.2)	58.8 (41.9-75.6)	156 (117-192)	288 (192-401)	969

	Geometric mean (95% conf. limit)	Select percentile (95% confidence interval) 50th	75th	90th	95th	Sample size
	20.2 (15.1-27.0)	19.0 (13.1-27.1)	59.8 (42.8-80.0)	153 (110-212)	282 (180-395)	969
Non-Hispanic Blacks	25.8 (20.5-32.6)	24.1 (19.7-29.9)	73.1 (54.5-95.8)	211 (167-266)	343 (265-502)	697
	20.6 (16.9-25.1)	18.4(13.6-24.4)	58.1 (45.1-77.8)	142 (108-188)	290 (204-364)	696
Non-Hispanic Whites	19.4 (16.0-23.7)	15.6 (12.4-20.3)	60.1 (49.1-78.5)	218 (148-282)	404 (291-600)	861
	20.9 (17.1-25.5)	18.5 (14.0-23.2)	59.7 (47.7-76.7)	197 (149-244)	426 (253-494)	861
Other	16.4 (12.4-21.8)	14.5 (10.0-18.5)	43.3 (30.0-69.3)	137 (81.9-218)	277 (145-506)	443
	18.0 (14.0-23.3)	14.8 (11.8-22.5)	48.9 (30.7-69.9)	138 (81.5-191)	203 (142-260)	443

Table 3.

Adjusted geometric mean (GM) urinary concentrations of mono-2-ethyl-5-hydroxyhexyl terephthalate (MEHHTP) and mono-2-ethyl-5-carboxypentyl terephthalate (MECPTP) in the U.S. population from NHANES 2015-2016.

	MEHHTP, µg/L	**MECPTP, µg/L**
	Adjusted GM (95% confidence interval)	**Adjusted GM (95% confidence interval)**
Age (years)		
4	8.48(6.98-10.31)	44.76(36.9-54.28)
8.5	7.95(6.62-9.54)	40.44(33.79-48.4)
15.5	7.18(6.08-8.48)	34.54(29.4-40.57)
39.5	5.07(4.42-5.81)	20.11(17.71-22.84)
72.5	3.14(2.61-3.79)	9.56(7.97-11.47)
Sex		
Female	5.48(4.75-6.32)	24.85(21.41-28.85)
Male	4.9(4.22-5.69)	20.25(17.86-22.97)
Household income (U.S. $)		
<20K	4.13(3.39-5.03)	18.92(15.57-22.99)
20K-<45K	4.84(4.01-5.83)	20.48(17.28-24.28)
45K-<75K	5.16(4.62-5.77)	21.21(18.25-24.65)
≥75K	6.98(5.67-8.61)	30.83(24.2-39.28)
Examination period		
Morning (8.00-12.00 hr)	4.87(4.21-5.64)	18.37(16.02-21.07)
Afternoon (12.30-16.00 hr)	4.61(3.93-5.41)	20.56(17.05-24.79)
Evening (16.30-20.00 hr)	6.19(4.89-7.83)	29.9(23.77-37.61)