Development of a personal dual-phase air sampling method for phthalate diesters

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Phthalates are used as plasticizers in many industrial and consumer products. Urinary biomonitoring has shown widespread human exposure to phthalates, with workers having especially high exposures. Phthalates can be present in workplace air as either aerosols or vapors depending on source materials, vapor pressure, and processing temperatures. We sought to develop a dual-phase air sampling method for 6 phthalates, dimethyl phthalate (DMP), diethyl phthalate (DEP), di-*n*-butyl phthalate (DBP), benzyl butyl phthalate (BzBP), di(2-ethylhexyl) phthalate (DEHP), and di-*n*-octyl phthalate (D*n*OP), adaptable to aerosol inlets with known particle collection characteristics. Collection media consisted of a quartz fiber filter and XAD-2 resin. Limit of detection (LOD) and limit of quantification (LOQ) were determined for each phthalate. Phthalate recoveries were evaluated at 3×, 10× and 30× the LOQ, and after storage at −21 °C and 21 °C. Media were Soxhlet extracted in 10% diethyl ether in hexanes along with an extraction surrogate, di-*n*-pentyl phthalate-d_4. Gas chromatography/mass spectrometry was performed to quantify the phthalate diesters using di(2-ethylhexyl) phthalate-d_4 as an internal standard. Estimated LODs were 1 μg per sample (BzBP, DEHP, and D*n*OP), 2 μg per sample (DMP and DBP), and 5 μg per sample (DEP). Mean recoveries under static conditions were 85–104% for DBP, BzBP, DEHP, and D*n*OP; but <70% for DMP and DEP at 3× and 10× the LOQ. After air was pulled through spiked samples, DMP and DEP recoveries improved to 74–81%. After storage for 62 days, phthalate recovery was better at −21 °C than at 21 °C. Method accuracy was best for DBP, BzBP, DEHP, and D*n*OP (range 11–18%), and less so for DMP (28%) and DEP (29%).

Introduction

Phthalates are widely used in industrial, medical, and consumer products to impart flexibility (*e.g.* in vinyl and rubber materials) or as a solvent and vehicle (*e.g.* in fragrances and cosmetics).[1,2] Phthalates are liquids at room temperature. Certain phthalates, such as dibutyl phthalate (DBP) and di(2-ethylhexyl) phthalate (DEHP), are reproductive and developmental toxicants in rats, and in humans, phthalates may also act as endocrine disruptors and immune system modulators.[3–9] Phthalate exposure is widespread in the US general population,[10] with diet, ambient air, personal care products, and materials in the home likely sources of exposure.[1,11–14] Sub-populations such as infants in neonatal care units, plasma/platelet donors, and dialysis patients may also be exposed to phthalates during medical procedures.[15–19] Occupational sources can also contribute to total phthalate exposure.[20–28]

In polymers, phthalates are not covalently bound and can migrate to the environment over time. As a result, phthalates have been measured in residential, workplace, and ambient air,[24–27,29–32] and in home and office dust.[31,33–36] Inhalation may be an especially important exposure route for workers. Phthalate loss to the ambient air can be accelerated when heat is

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Environmental impact

Phthalates are widely used in industrial and consumer products. Some phthalates cause reproductive and developmental effects in rats. Phthalates are not covalently bound to their matrix and can leach into the environment. While some phthalate exposure is dietary, inhalation is also an important exposure route, especially in the workplace where phthalates may be associated with dust-generating processes and heated materials. Under these conditions, phthalates can be present as either aerosols and/or vapors. Traditional phthalate air sampling methods have used either single phase or dual-phase samplers, not designed to collect aerosols of known particle-size collection characteristics. In this paper, we describe the evaluation of a personal dual-phase air sampler for phthalates that can be adapted for use with several well-characterized aerosol inlets.

applied to phthalate-containing materials, especially for materials with large surface areas (*e.g.* films, sheets), a condition often found in the workplace. Phthalate vapor pressure, which is inversely related to alkyl chain length,[37] can also influence phthalate air concentrations.

Phthalates are found in three principal forms in the workplace: as a liquid (raw) material, as a dispersion of phthalate and resin (*i.e.* a plastisol), and as a dry (granular or powder) material where phthalate is incorporated (*i.e.* compounded) into a resin or rubber.[38] The handling of liquid phthalate is primarily limited to the manufacturing (production) of phthalates and to compounding operations. Although phthalates are manufactured in closed heated reactors, worker exposure can occur while taking process samples and while performing maintenance. Liquid phthalates used in compounding and plastisols can be dispensed by either opened (generally manual) or closed (generally automated) systems.

The handling of liquid phthalates and plastisols could result in phthalate exposure by both inhalation and dermal contact. Phthalate exposure during compounding, and any subsequent milling, extrusion, or calendering operations, could also arise from inhaling vapors or condensation particles. Because phthalates may be present in the workplace air as both particles and vapors, air sampling methods are needed that can capture both physical states in order to measure total airborne phthalate exposure.

The National Institute for Occupational Safety and Health (NIOSH), as part of its research on phthalate exposure in the workplace, sought a sampling and analytical method for phthalates that could capture both particles and vapors, and was adaptable to aerosol inlets with known particle collection characteristics, preferably inlets conforming to particle-size fractions meeting either ISO 1995 (inhalable, thoracic, and respirable) or EPA ($PM_{2.5}$ and PM_{10}) criteria.[39,40] Other desired method characteristics included suitability for multiple phthalates, an 8–24 h sampling time (typical range for workplace and residential air sampling), and good analyte stability on stored samples. Because phthalate analysis is susceptible to laboratory-introduced contamination, eliminating or reducing phthalate sources in the laboratory was also important.[41–43]

Various sampling approaches have been used for collecting phthalates in air, including Tenax,[44] charcoal,[45] silica gel,[46] and Florisil[47] sorbents, polyurethane foam,[31] and ethylene glycol traps.[48] Analysis for these methods was typically by gas chromatography (GC) with detection by mass spectrometry (MS), flame photometry, or electron capture. The draft NIOSH air sampling method for phthalates (Method 5045, unpublished) uses a 0.8 μm pore size cellulose ester membrane filter in a 37 mm polystyrene closed-faced cassette with a 4 mm inlet, at a sampling rate of 1–3 L min^{-1}. While this sampler collects particles, it is not designed to capture vapors. The Occupational Safety and Health Administration (OSHA) phthalate air sampling method (Method 104)[49] uses a two-stage sampler, the OSHA Versatile Sampler (OVS), containing an 11 mm glass fiber filter followed by two sections of Tenax (140 mg front, 70 mg back, part no. 226-56, SKC Inc., Eighty Four, PA, USA). The OVS sampler has a 13 mm inlet and is operated at 1 L min^{-1}. Analysis for both the NIOSH and the OSHA methods is by GC with flame ionization detection. Neither the 37 mm cassette nor the OVS sampler was designed to collect particles in accordance with either the ISO 1995 or EPA size-selection criteria.

The URG Personal Pesticide Sampler (URG, Chapel Hill, NC, USA) has been used for collecting semi-volatile compounds, including phthalates, in both particle and vapor phases.[35,36,50] In these studies, the URG sampler consisted of a PM_{10} impactor inlet followed in sequence by a 25 mm quartz fiber filter and a 3 g bed of XAD-2 resin, with a flow rate of 4 L min^{-1}. Analysis was by GC/MS. Although the method had been applied to a large number of semi-volatile compounds, it had not been optimized for the detection and quantification of phthalates. We selected the URG sampler as a starting point for our phthalate method development because it was commercially available with either a $PM_{2.5}$ or PM_{10} inlet, and could be adapted to use the "button" sampler (SKC Inc., Eighty Four, PA, USA), an inlet designed to collect the ISO 1995 inhalable fraction.[51] The button sampler consists of a spherical shell "…with numerous, identical, evenly spaced holes that act as sampling orifices and give the sampler a multidirectional sampling capability" and uses a 25 mm filter.[52] The PM_{10} size fraction is essentially equivalent to the ISO 1995 thoracic fraction, while the $PM_{2.5}$ inlet collects a smaller particle-size fraction than the ISO 1995 respirable fraction (median aerodynamic diameter of 4.25 μm).[53]

In this paper, we describe a sensitive and specific dual-phase personal air sampling method for 6 phthalate diesters: dimethyl phthalate (DMP, CAS No. 131-11-3), diethyl phthalate (DEP, CAS No. 84-66-2), di-*n*-butyl phthalate (DBP, CAS No. 84-74-2), benzyl butyl phthalate (BzBP, CAS No. 85-68-7), di(2-ethylhexyl) phthalate (DEHP, CAS No. 117-81-7), and di-*n*-octyl phthalate (D*n*OP, CAS No. 117-84-0). We present recovery, limit of detection (LOD) and limit of quantification (LOQ), storage stability, and blank contamination results for these 6 phthalates.

Methods

Reagents and materials

Commercial solutions of the 6 phthalate diesters were purchased from Protocol Analytical (Middlesex, NJ, USA) and Ultra-Scientific (North Kingston, RI, USA) and used without further purification. High purity methanol, 1-octanol, diethyl ether, hexanes, acetone, and toluene were purchased from Fisher Scientific (Fairlawn, NJ, USA) and Honeywell Burdick & Jackson (Muskegon, MI, USA). The extraction surrogate, di-*n*-pentyl phthalate-d_4 (D*n*PP-d_4), was obtained from C/D/N Isotopes (Pointe-Claire, Quebec, Canada), and the internal standard, di(2-ethylhexyl) phthalate-d_4 (DEHP-d_4), from Chem Service (West Chester, PA, USA) and Cambridge Isotope Laboratories (Andover, MA, USA).

The extraction solvent was 10% diethyl ether (v/v) in hexanes. Stock standard solutions (1–2 mg mL^{-1}) of the internal standard di(2-ethylhexyl) phthalate-d_4 and the extraction surrogate di-*n*-pentyl phthalate-d_4 were prepared in methanol and/or hexanes. A low level internal standard solution (500 ng μL^{-1}) was also prepared by dilution with hexanes. Working standards of the 6 phthalate diesters were prepared at five concentrations (approximate range 2–40 ng μL^{-1}) by diluting stock standard solutions with extraction solvent. The internal standard was added to working standards and sample extracts at a concentration of 10 ng μL^{-1}.

The URG Personal Pesticide Sampler was obtained from URG (Chapel Hill, NC, USA). Sampling media for the URG sampler consisted of a quartz microfiber filter (26 mm diameter) followed by 3 g of XAD-2 resin (Supelco, Bellefonte, PA) held in place by two, 25.4 mm cylinders of polyurethane foam (PUF) plugs (22 mm diameter and 25.4 mm length) (Fig. 1). The 26 mm diameter quartz microfiber filters were die-cut at Southwest Research Institute (San Antonio, TX) from 102 mm diameter QMA filters (Whatman International, Maidstone, England). The PUF plugs were also die-cut at Southwest Research Institute from a 76 mm thick sheet of polyurethane foam (0.0224 g cm^{-3}) (San Antonio Foam Fabricators, San Antonio, TX, USA) and re-cut into 25.4 mm lengths. The dimensions of the assembled URG sampler were od 35 mm and length 160 mm. The back pressure of the fully assembled cartridge when operated at 4 L min^{-1} was 8″ H_2O.

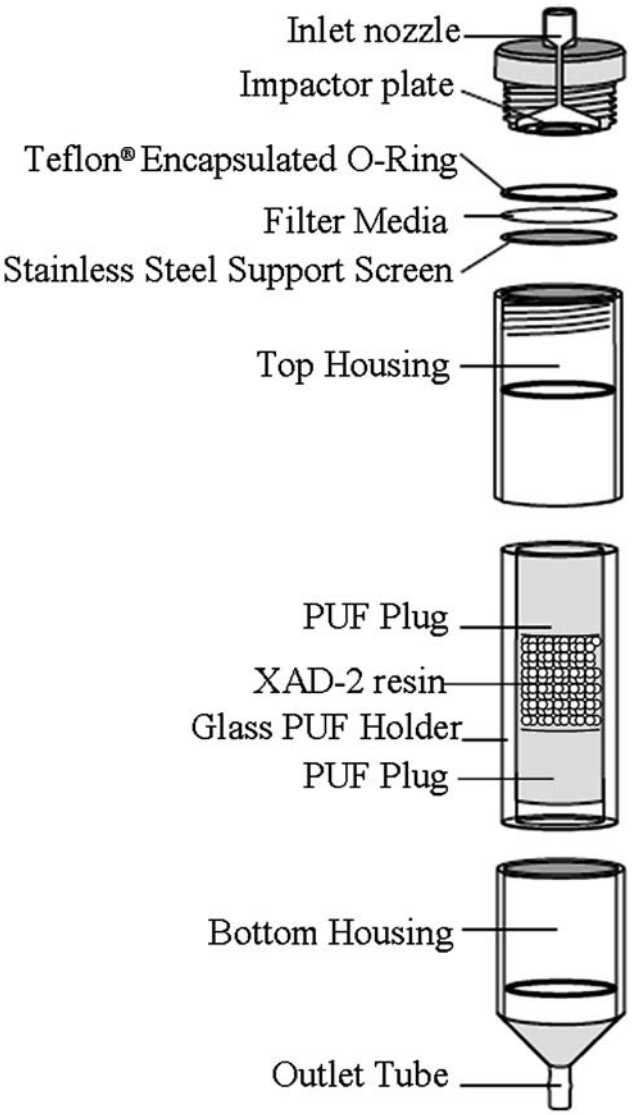

Fig. 1 Schematic of the URG sampler with 25 mm quartz fiber filter and 3 g of XAD-2 resin held in place by two polyurethane foam plugs.

Measures to minimize phthalate contamination in the laboratory

Phthalates may be present in personal care products, soaps, detergents, fragrances, and some laboratory materials. Therefore, special precautions were adopted during all laboratory procedures to minimize exogenous phthalate contamination. Individuals handling or extracting samples for phthalates were instructed to avoid using cosmetics, nail polish, hand lotion, and perfumes. After using soap or hand cleaning products, hands were thoroughly rinsed with water. Rubber glove use was also minimized in the laboratory. Only new rubber pipette bulbs pre-rinsed with extraction solvent and air-dried were used. Glass transfer pipettes were also pre-rinsed with extraction solvent and oven-dried at 130–150 °C for at least 2 h.

Filters, XAD-2 resin, and PUF plugs were taken from lots of acceptable pre-cleaned media. PUF plugs were cleaned by Soxhlet extraction with acetone for 24 h, with hexanes for 48 h and again with acetone for 24 h, and then dried under ultra high purity nitrogen. XAD-2 was washed with deionized water, then cleaned by Soxhlet extraction with methanol for 24 h and with dichloromethane for 48 h, and then dried under zero nitrogen. Filters were cleaned by Soxhlet extraction with acetone : hexanes (1 : 1) for 24 h. Lots were accepted provided that measured amounts of each target phthalate were low (<0.3 μg of DEP, <0.2 μg of DEHP, and <0.1 μg of other phthalates) in representative cleaned media. The glass and screen parts of the URG sampler were washed with hot water and detergent, and rinsed sequentially with hot water, deionized water, acetone, and deionized water. The plastic and Teflon parts of the URG sampler were washed with hot water and detergent, rinsed sequentially with hot water, deionized water, acetone, hexanes, and then air-dried. The glass tube was kiln-dried at 400 °C and the metal components (impactor plate and stainless steel support screen) were oven-dried at 60 °C. Before each extraction, the Soxhlet apparatus was pre-rinsed with extraction solvent for 4 h to remove any phthalate residue remaining in the condenser unit from previous extractions.

Spiking solution and procedure

Spiking solutions of the 6 phthalate diesters were prepared in methanol : 1-octanol (84 : 16) at a concentration range of 400 μg L^{-1} to 1600 μg L^{-1} for the recovery and storage stability studies, and in toluene at a concentration of 20 μg L^{-1} (DEP) and 10 μg L^{-1} (other phthalate diesters) for the LOD determination study. A total of 100 μL of spiking solution were spiked onto the sampling media, half (50 μL) onto the XAD-2 resin and half (50 μL) onto the quartz fiber filter. The URG cartridge was capped within 1–2 min, except where noted, to minimize phthalate evaporation. This spiking procedure was used for all experiments.

Extraction procedure

In preliminary optimization tests, both dichloromethane and 10% diethyl ether (v/v) in hexanes gave acceptable extraction recoveries (*i.e.* >90%); however, when PUF separators are used, 10% diethyl ether (v/v) in hexanes is a better solvent as dichloromethane can partially dissolve PUF leaving interfering residues.[54] The PUF, XAD-2 resin, and quartz fiber filter were

placed in a pre-rinsed Soxhlet extractor (50 mL extractor capacity) followed by the addition of 200 mL of 10% diethyl ether (v/v) in hexanes. A total of 100 μL of an extraction surrogate solution of di-*n*-pentyl phthalate-d_4 (100 μg mL^{-1} or 1000 μg mL^{-1} in hexanes depending on anticipated phthalate level) were added, half to the filter and half to the XAD-2. Extraction surrogate was also added to all matrix and solvent blanks. Sampling media were extracted for at least 16 h. Each extract was initially concentrated to 15 mL using a 500 mL Kuderna-Danish (K-D) concentrator with an 18 mL receiver and a 3 ball Synder column. The extract was further concentrated under zero nitrogen to a final volume of 1.0 mL (adjusted using extraction solvent).

Matrix and solvent blanks

Each experiment included matrix and solvent blanks. Matrix blanks consisted of pre-cleaned XAD-2 resin, PUF, and quartz fiber pre-filters from the same media lots. Recoveries were computed after subtracting the mean amount of phthalate in the matrix blanks as determined in each experiment.

Gas chromatography/mass spectrometry

Full scan (45–525 *m/z*) gas chromatography/mass spectrometry (GC/MS) was performed to detect and quantify the 6 phthalate diesters. Separation was achieved using an Agilent DB-5ms (or DB-5.625 in early runs) capillary column (30 m × 0.25 mm i.d., 0.25 μm film thickness) (Agilent Technologies, Santa Clara, CA, USA) and a Phenomenex ZB-5 ms capillary column (30 m × 0.25 mm i.d., 0.25 μm film thickness) (Phenomenex, Torrance, CA, USA). The carrier gas was helium (chromatography grade) at 1.2 mL min^{-1}. The injector temperature was 250 °C and the transfer line temperature was 280 °C. An injection volume of 0.5 μL in a pulsed splitless mode was used. The initial column temperature was held at 60 °C for 0.5 min, and then ramped at 25 °C min^{-1} to 310 °C where it was held for 2 min. We observed excellent resolution among the 6 phthalates (Fig. 2).

Each run included at least five calibration standards (LOD study: DEP 1–64 ng μL^{-1}, other phthalates 0.5–32 ng μL^{-1} and recovery and storage stability studies: DEP 2–60 ng μL^{-1}, other phthalates 1–30 ng μL^{-1}). Calibration curves for each phthalate were linear, with all relative standard deviations <25% in each initial calibration. Di(2-ethylhexyl) phthalate-d_4 was used as an internal standard and added to sample extracts and calibration standards at 10 ng μL^{-1}. Quantitation and confirmation ions are provided in Table 1.

Each analytical sequence of up to 20 sample extracts also included associated matrix and solvent blanks and a mid-level continuing calibration verification standard analyzed at the beginning and ending of the sequence. A second calibration curve was prepared by a different analyst using different lot numbers for most of the targeted phthalates and analyzed against the original calibration curve as verification.

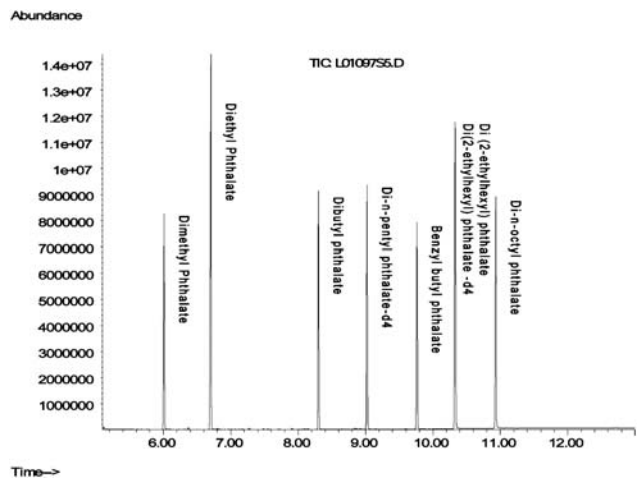

Fig. 2 Chromatogram of 6 phthalate diesters on a Phenomenex ZB-5 ms capillary column (30 m × 0.25 mm × 0.25 μm film thickness).

Determination of limits of detection and quantification

LODs and LOQs were determined according to NIOSH SOP 018.[55] A total of 7 sets of at least 6 replicates in each set were prepared by spiking the 6 phthalates onto the sampling media. Spiking levels were 0.5× (2 sets), 1× (2 sets), 5× (1 set), and 10× (2 sets) the expected LOD (4 μg for DEP and 2 μg for other phthalates), a 20-fold range. Spiking solutions were prepared separately for each set. A total of 14 matrix blanks and 7 solvent blanks were also prepared. Spiked samples and blanks were extracted and analyzed by GC/MS as previously described. Linear regression analysis was performed in Quattro Pro (Corel Corp., Fremont, CA, USA) where the dependent variable was the amount of phthalate recovered from the spiked sample minus the mean matrix blank amount, and the independent variable was the spiked amount of phthalate. Matrix blanks provide the best estimates of lab-introduced phthalate contamination for each set with contributions from the cleaned matrices, solvent systems, glassware, and contamination from handling. The LOD and LOQ were calculated using the results of the regression analysis as specified in NIOSH SOP 018.[55]

Recovery studies

The recovery efficiency of the phthalates from the sampling media was determined at 3×, 10×, and 30× the rounded LOQ. Six replicates were spiked at each level, 3 replicates on one day, and 3 replicates two days later. A total of 6 matrix blanks and 4 solvent blanks were prepared. The elapsed time from spiking until capping the assembled cartridge was 2–13 min for the replicates prepared on the first day, and ≤1 min for replicates prepared on the second day. Spiked media were held inside the capped URG cartridge at room temperature (21 °C) for 16 h. Extraction and analysis were performed as previously described.

To assess whether low recovery of the two most volatile phthalates, DMP and DEP, under static conditions was due to volatilization or condensation losses after spiking, a limited evaluation was performed that included two matrix blanks and two replicates spiked at 3× and 10× the rounded LOQ for a total of 6 samples. After the sampling media were spiked and the URG cartridge assembled, laboratory air was pulled through the samplers at 4 L min^{-1} for 8 h at room temperature (21 °C). The elapsed time from spiking the media, through cartridge assembly, to initial air flow was 95–100 s for the four spiked samplers. The

Table 1 Gas chromatography/mass spectrometry quantitation and confirmation ions for the evaluated phthalate diesters

Phthalate	CAS No.	Formula	VP/ mm Hg, 25 °C (ref. 37)	Quantitation ion	Confirmation ion
DEHP-d_4 (internal standard)				153	171
DMP	131-11-3	$C_{10}H_{10}O_4$	2.0×10^{-3}	163	194, 164
DEP	84-66-2	$C_{12}H_{14}O_4$	1.0×10^{-3}	177	149, 222
DBP	84-74-2	$C_{16}H_{22}O_4$	2.7×10^{-5}	223	149, 205
BzBP	85-68-7	$C_{19}H_{20}O_4$	5.0×10^{-6}	149	206, 91
DEHP	117-81-7	$C_{24}H_{38}O_4$	1.0×10^{-7}	149	167, 279
D*n*OP	117-84-0	$C_{24}H_{38}O_4$	1.0×10^{-7}	149	279
D*n*PP-d_4 (extraction surrogate)				241	153

samplers were arranged in a rectangular grid, with at least a 30 cm separation between the downward facing inlets. The duration of air flow through the 6 samplers was 453–492 min and the total air volume was 1.8–2.0 m^3. The spiked media and matrix blanks were extracted and analyzed as previously described.

Each spiked replicate was adjusted (by subtraction) for background phthalate air contamination in addition to the matrix blank. The phthalate concentration in the room air was estimated by dividing the amount of phthalate recovered on the two air sample blanks by the air volume pulled through each blank. These two air concentrations were averaged to obtain the mean phthalate concentration in the room air during the trial: 0.70 μg m^{-3} (DEP), 0.27 μg m^{-3} (DBP), 0.13 μg m^{-3} (BzBP), 0.10 μg m^{-3} (DEHP), and <0.05 μg m^{-3} (DMP and D*n*OP).

Storage stability study

A matrix storage stability study was conducted at 10× LOQ and at two temperatures (21 °C and −21 °C). Six matrix blank replicates in URG cartridges were prepared on day 0, and 6 replicates of spiked media in URG cartridges were prepared on each of three days (day 0, day 30, and day 55). The staggered days allowed all samples to be extracted at the same time to minimize the confounding of actual storage losses with day-to-day variation in extraction, and with analytical personnel or performance. URG cartridges were capped within 23–60 s of spiking. Three replicates from each set (including matrix blanks) were stored at room temperature (21 °C) and 50% relative humidity, and the other three replicates were stored in a freezer (−21 °C). Both room temperature and −21 °C sets were held until day 62. On day 62, all replicates, including blanks, were extracted. Three additional replicates were also spiked at 10× LOQ on day 62 and extracted at the same time as the other replicates. All extracts were analyzed as previously described in a balanced sequence across the replicate sets.

Results

Matrix and solvent blank evaluation

Matrix and solvent blank results from the LOD study are given in Table 2. All 6 phthalates were presumed detected at ≥0.001 μg per sample in all matrix and solvent blanks, except DMP was detected in only 2 of 7 solvent blanks and DBP was not detected in any solvent blanks. DEP was detected at >0.2 μg per sample in all 14 matrix blanks (mean ± SD: 0.51 ± 0.26 μg per sample) and in 5 of 7 solvent blanks (0.32 ± 0.24 μg per sample). DBP was detected at >0.1 μg per sample in 5 of 14 matrix blanks, but not in any solvent blanks (<0.001 μg per sample). Mean levels of DEP were the highest of any phthalate in both matrix and solvent blanks. In matrix blanks, mean levels of DMP, DBP, BzBP, DEHP, and D*n*OP were 6- to 70-fold lower than DEP. Because levels of DEP, BzBP, DEHP, and D*n*OP were as high or higher in the solvent blanks as in the matrix blanks, much of the matrix blank contamination of these 4 phthalates may have been due to the solvent or present in the laboratory air during the Soxhlet extraction. The presence of DBP in matrix but not solvent blanks suggests that the various media (XAD-2, PUF, or filters) were the source(s) of DBP contamination. Similar matrix and solvent blank results were seen in subsequent analyses.

Table 2 Levels of phthalate diesters in matrix and solvent blanks[a,b]

Phthalate diester	Matrix blanks Mean ± SD/μg (n = 14)	Solvent blanks Mean ± SD/μg (n = 7)
DMP	0.011 ± 0.006	0.004 ± 0.007
DEP	0.51 ± 0.26	0.32 ± 0.24
DBP	0.079 ± 0.052	<0.001
BzBP	0.024 ± 0.009	0.021 ± 0.013
DEHP	0.048 ± 0.020	0.040 ± 0.014
D*n*OP	0.007 ± 0.004	0.010 ± 0.006

[a] Data from limit of detection study. [b] Blank amounts reported down to 1 ng by quantifying all peaks present in the phthalate retention windows. All phthalates were presumed detected at or above this level in all matrix blanks and solvent blanks, except DMP was detected in only 2 of 7 solvent blanks and DBP not detected in any solvent blanks. Non-detect values were set equal to zero for determination of mean and standard deviation.

LOD/LOQ determination

In the LOD study, mean recoveries of the 6 phthalates over the 4 spiking levels were 74–93% (DMP), 84–92% (DEP), 90–100% (DBP), 90–103% (BzBP), 88–105% (DEHP), and 96–104% (D*n*OP) (Table 3). Mean recoveries across all spiking levels and phthalates were generally ≥90% (80% of the time). The lowest mean recovery was for DMP (74%) at the highest spiking level (20 μg). All relative standard deviations (RSDs) were ≤10%, except DEP (12%) at the lowest spiking level (2 μg). The mean amount of DEP in the matrix and solvent blanks was equivalent to 25% and 16%, respectively, of the lowest DEP spiking level. In contrast, the mean amount of all other phthalates in the matrix and solvent blanks was less than 5% of the lowest spike level, except DBP where the matrix blank was 8% of the lowest DBP spike (1 μg). Extraction surrogate recoveries (75–119%) indicated acceptable extraction of spiked samples and blanks.

Table 3 Phthalate diester recovery efficiencies in limit of detection study. Spiking levels from 0.5 to 10 times expected LOD[a]

Spike level/μg	*n*	Recovery efficiency[b] (%) Mean ± SD DMP	DEP	DBP	BzBP	DEHP	D*n*OP
1 (2)[c]	12	93 ± 3	90 ± 12	100 ± 5	103 ± 2	105 ± 3	101 ± 5
2 (4)	12	77 ± 4	84 ± 6	90 ± 9	90 ± 6	88 ± 2	96 ± 4
10 (20)	6	80 ± 3	92 ± 4	90 ± 4	96 ± 3	99 ± 3	104 ± 3
20 (40)	14	74 ± 4	90 ± 4	98 ± 4	93 ± 2	96 ± 2	97 ± 2

[a] Expected LOD: 4 μg for DEP and 2 μg for other phthalates. [b] After subtracting matrix blank mean. [c] DEP spiking levels shown in parentheses.

The estimated LODs and LOQs for the 6 phthalates are given in Table 4. LODs were approximately 1 μg per sample for BzBP, DEHP, and D*n*OP, approximately 2 μg per sample for DMP and DBP, and approximately 5 μg per sample for DEP. These LODs were all higher than the lowest spike amount. For all phthalates except DEP, the LOD expressed as an air concentration (μg m^{-3})was ≤1 μg m^{-3} for 8 h of sampling, and <0.5 μg m^{-3} for 24 h of sampling (based on a flow rate of 4 L min^{-1}) (Table 4).

Recovery studies

Mean recoveries under static conditions for DBP, BzBP, DEHP, and D*n*OP were 85–104% across all spiking levels (Table 5). Mean static recoveries at 30× LOQ for DEP and DMP (83% and 76%, respectively) were acceptable (*i.e.* ≥75%), however, at 3× LOQ and 10× LOQ, mean recoveries were considerably lower for DEP (65% and 63%, respectively) and for DMP (57% and 56%, respectively) than at 30× LOQ. All spiked static recovery extracts were analyzed twice, by different analysts, two weeks apart, and the results averaged to verify low DMP and DEP recoveries. Across phthalates and spiking levels, RSDs were <10% (Table 5). Extraction surrogate recoveries (76–95%) indicated acceptable extraction of spiked samples and blanks.

When air had been pulled through the samplers post-spiking, mean recoveries for all phthalates at 3× LOQ and 10× LOQ exceeded 70%, with most recoveries ≥80% (Table 6). Although the sample size was small in this preliminary evaluation, recovery estimates were stable, with RSDs ≤4%. Air flow through the samples and blanks averaged 3.90–4.19 L min^{-1}, with a mean air volume ranging from 1282 L (pump failure at 322 min) to 1990 L. The elapsed time from spiking to initial air flow was kept as short as possible (95–110 s) to minimize volatilization losses of DMP and DEP. As expected, the air flow acted to minimize volatilization losses from the filter onto inner surfaces of the cartridge. Extraction surrogate recoveries (89–93%) indicated acceptable extraction of spiked samples and blanks.

Table 4 Phthalate diester limits of detection (LOD) and quantification (LOQ) (*n* = 44)

	S_y/μg[a]	Slope	Mass/μg per sample LOD	LOQ	Equivalent air concentration LOD/μg m^{-3} 8 h at 4 L min^{-1}	24 h at 4 L min^{-1}
DMP	0.439	0.735	1.8	6	0.9	0.31
DEP	1.457	0.909	4.8	16	2.5	0.84
DBP	0.723	0.990	2.2	7.3	1.1	0.36
BzBP	0.419	0.935	1.3	4.5	0.7	0.23
DEHP	0.390	0.968	1.2	4.0	0.6	0.21
D*n*OP	0.392	0.976	1.2	4.0	0.6	0.21

[a] S_y = Standard error of the regression.

Table 6 Phthalate diester recovery efficiencies after air drawn through spiked and matrix blank samples. Spiking levels at 3 and 10 times the LOQ[a] (*n* = 2)

	Recovery efficiency[b] 3× LOQ[b] Mean ± SD (%)	RSD	10× LOQ Mean ± SD (%)	RSD	Pooled RSD (S_r)[c]
DMP	78 ± 3	0.038	80 ± 1	0.012	0.025
DEP	74 ± 3	0.040	81 ± 0.4	0.005	0.022
DBP	87 ± 2	0.023	91 ± 0.5	0.006	0.014
BzBP	88 ± 1	0.011	88 ± 2	0.023	0.017
DEHP	84 ± 1	0.012	89 ± 0.1	0.001	0.006
D*n*OP	92 ± 0.4	0.004	90 ± 4	0.044	0.024

[a] LOQs in Table 4. [b] After subtracting mean concentration of sampled air. [c] RSDs at 3× and 10× LOQ were pooled; two samples at each level.

Table 5 Phthalate diester recovery efficiencies under static conditions. Spiking levels at 3, 10, 30 times the LOQ[a] (*n* = 6)

	Recovery efficiency[b] 3× LOQ Mean ± SD (%)	RSD	10× LOQ Mean ± SD (%)	RSD	30× LOQ Mean ± SD (%)	RSD	Pooled RSD (S_r)[c]
DMP[c]	57 ± 4	0.070	56 ± 4	0.071	76 ± 3	0.040	0.060
DEP	65 ± 4	0.062	63 ± 2	0.032	83 ± 2	0.024	0.039
DBP	88 ± 3	0.034	85 ± 2	0.024	99 ± 2	0.020	0.026
BzBP	94 ± 2	0.021	91 ± 2	0.022	102 ± 3	0.029	0.024
DEHP	88 ± 2	0.023	90 ± 2	0.022	98 ± 2	0.020	0.022
D*n*OP	99 ± 2	0.020	96 ± 1	0.010	104 ± 3	0.029	0.020

[a] LOQs in Table 4. [b] After subtracting matrix blank mean. [c] RSDs at 3×, 10×, and 30× the LOQ were pooled; 6 samples at each level.

Storage stability study

After freezer storage (−21 °C), mean recoveries of all phthalates were 89–98% (at 7 days), 78–94% (at 32 days), and 74–98% (at 62 days) (Table 7). The only mean recovery <75% at −21 °C was for DMP at 62 days (74%). Mean recoveries for all phthalates stored at rt were generally, if not substantially, lower at all time points than under freezer conditions. BzBP, DEHP, and D*n*OP had acceptable (*i.e.* ≥75%) mean recoveries after storage at rt for 7 days and 32 days. Mean recoveries of DEP and DBP after storage at rt for 7, 32, and 62 days were all <75%. Mean recovery of DMP after storage at rt was marginal over the 3 time points (71–79%). Although the mean recovery of DEP after storage at rt increased slightly with increasing storage duration (Table 7), the relatively large standard deviations suggest that the true mean DEP recovery efficiency was probably unchanged with increasing storage duration.

Accuracy of the method

The overall method accuracy was estimated for each phthalate over the range evaluated (3× to 30× the LOQ) using NIOSH criteria[55] (Table 8). Method accuracy is estimated from measures of the bias and precision (S_{rT}) of the method, the latter of which incorporates a term for air sampling pump measurement error of 5%. DBP, BzBP, DEHP, and D*n*OP had accuracy estimates ranging from 11–18%. Accuracy estimates for DMP and DEP were 28% and 29%, respectively. NIOSH generally considers accuracies of ≤25% to be acceptable. Using this criterion, the method was acceptable for DBP, BzBP, DEHP, and D*n*OP, but not for DMP and DEP.

Discussion

Methods to assess personal exposure to airborne phthalates require sampling devices that can be worn comfortably, are suitable for the chemical and physical state of the compounds as found in the environment, and conform to accepted particle-size sampling criteria. The URG sampler we evaluated for phthalate determination in air meets these desired characteristics. The sampler is adaptable for use with a $PM_{2.5}$, PM_{10} or inhalable aerosol inlet and contains a filter to collect particles and a sorbent bed for vapors. Interchangeable aerosol inlets enhance the versatility of the method. The method has an LOD of 1–2 μg for all phthalates, except DEP (~5 μg), and a corresponding equivalent air concentration LOD of ≤1 μg m^{-3} (except DEP, 2.5 μg m^{-3}) for an 8 h sample, and ≤0.4 μg m^{-3} (except DEP, 0.84 μg m^{-3}) for a 24 h sample. Minimizing laboratory-introduced contamination was most difficult for DEP despite procedures to eliminate potential sources, and most likely accounts for DEP having the highest LOD of the 6 phthalates.

The method is most accurate (using the NIOSH accuracy criterion) for DBP, BzBP, DEHP, and D*n*OP (range 11–18%), with lower accuracy for the two more volatile phthalates, DMP and DEP (28% and 29%, respectively). Air samples for DEP, DBP, BzBP, DEHP, and D*n*OP can be stored at −21 °C for at least 62 days before extraction, however, samples collected for DMP should be stored at −21 °C and extracted within 32 days of collection. Although recovery of BzBP, DEHP, and D*n*OP was acceptable (*i.e.* >75%) after storage at rt for up to 32 days, storage at −21 °C is recommended for the 6 phthalates because of generally improved recovery.

Volatilization losses during the 16 h hold period in the static recovery study possibly contributed to low DMP and DEP recoveries, especially at 3× and 10× the LOQ. DMP and DEP have the highest vapor pressures of the phthalates we evaluated.[37] DMP and DEP recoveries at 3× and 10× the LOQ improved when air was drawn through the samplers (as in actual sampling), although the DMP and DEP recoveries were still lower than the other phthalates evaluated. DBP, BzBP, DEHP, and D*n*OP recoveries were stable (within a few percent) between the recovery studies with and without air flow through the sampler.

Table 8 Accuracy, bias, and precision of the method

Phthalate	Bias	Method precision(S_{rT})[a]	Estimated Accuracy[b]
DMP[c]	−0.21	0.056	0.28
DEP[c]	−0.22	0.055	0.29
DBP	−0.093	0.056	0.18
BzBP	−0.043	0.056	0.13
DEHP	−0.080	0.055	0.16
D*n*OP	−0.003	0.054	0.11

[a] The precision of the method (S_{rT}) includes a term for pump error of 5%. S_{rT} = sqrt[$(S_r)^2$ + $(0.05)^2$]. [b] Estimated from nomogram in ref. 55. [c] Bias and precision for DMP and DEP from recovery study where air pulled through samplers post-spiking (Table 6); for all other phthalates, bias and precision from recovery study under static conditions (Table 5).

Table 7 Matrix storage study, $n = 3$. Spiked at 10 times the LOQ[a]

		Recovery [retention] efficiency[b], (mean ± SD, %)					
		Freezer (−21 °C)			Room temperature (21 °C)		
	Extraction efficiency (%)	7 days	32 days	62 days	7 days	32 days	62 days
DMP	90 ± 5	89 ± 6	78 ± 7	74 ± 4	71 ± 5	76 ± 10	79 ± 6
DEP	96 ± 5	96 ± 6	90 ± 5	88 ± 5	67 ± 6	71 ± 9	74 ± 5
DBP	99 ± 2	97 ± 4	94 ± 7	98 ± 5	72 ± 3	62 ± 2	60 ± 5
BzBP	92 ± 7	93 ± 3	86 ± 2	91 ± 6	87 ± 5	76 ± 3	74 ± 11
DEHP	93 ± 4	98 ± 3	90 ± 4	94 ± 4	92 ± 5	93 ± 4	86 ± 11
D*n*OP	91 ± 2	92 ± 8	86 ± 6	87 ± 5	88 ± 1	87 ± 7	83 ± 13

[a] LOQs in Table 4. [b] After subtracting matrix blank mean.

The process of spiking the phthalate solution onto the sample media differs considerably from the collection process during actual air sampling. During actual air sampling, vapor phase phthalate may adsorb onto airborne particles that will initially be collected on the filter. With continued air flow, some of this particle-adsorbed vapor may re-volatilize and migrate to the sorbent bed. The capacity of the small quartz fiber filter to retain the spiking solution is also important. If the capacity was insufficient, some fraction of the more volatile phthalates (*i.e.* DMP and DEP) could have evaporated inside the capped cartridge onto nearby exposed inner surfaces of the cartridge. Since the upper inner surfaces of the cartridge were not solvent-rinsed into the Soxhlet extractor, any phthalate residues on these surfaces would be lost.

Differences in GC/MS response factors for the spiking solution and calibration standard may also partly explain apparent static storage losses of DMP and DEP. The phthalate spiking solution and calibration standard were prepared from different sources of standards. An analysis of balanced duplicates of the spiking solution and the calibration standard for one sequence showed that the mean relative response factor was higher for the calibration standard than for the spiking solution for all 6 phthalates, by relative percent differences of 3.2% (DEHP), 3.9% (DOP), 5.4% (BzBP), 6.7% (DBP), 8.6% (DMP), and 10.4% (DEP) [data not shown]. Since the response factor is in the denominator of the quantification equation, the phthalate sample amounts obtained through analysis using the calibration standard will be low by these percentages relative to the calculated spiked phthalate amount. The response factor difference was largest for DMP and DEP.

An 8 h time-weighted average occupational exposure limit (OEL) of 5 mg m^{-3} for airborne exposure has been established for DMP, DEP, DBP, and DEHP by either the Occupational Safety and Health Administration,[56] NIOSH[57] or the American Conference of Governmental Industrial Hygienists.[58] The estimated LODs for 8 h at 4 L min^{-1} (range 0.6–2.5 μg m^{-3}) for the 6 phthalates are below the OEL by over three orders of magnitude.

Although combination samplers like the URG sampler described here can collect both particles and vapors, separate analysis of the filter and sorbent materials may not yield an accurate partition of the particle and vapor components as they entered the inlet. Vapor initially adsorbed onto particles could re-volatilize and pass to the sorbent bed, thereby underestimating the particle-associated phthalate fraction.[43,59] The capacity of the sampler has not been determined for each phthalate, although the URG sampler, as used in this evaluation, has a large XAD-2 sorbent bed (3 g) compared to the OSHA OVS sampler which has a total sorbent capacity of 0.21 g (front section 0.14 g and back section 0.07 g). Future work should also include field evaluation of the method.

Conclusions

In summary, we have developed a dual-phase air sampling method for 6 phthalate diesters, with LODs of 1–2 μg for all phthalates, except DEP (~5 μg). Over the range evaluated (3× to 30× the LOQ), the method was most accurate for DBP, BzBP, DEHP, and D*n*OP (range 11–18%), with somewhat lower accuracy for DMP and DEP (28% and 29%, respectively). We recommend that samples for phthalate determination be stored at −21 °C and extracted within approximately 30 days of collection. This method is adaptable to multiple aerosol inlets, including $PM_{2.5}$, PM_{10}, and the "button" inhalable sampler.

Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention (CDC). Mention of any company or product does not constitute endorsement by the National Institute for Occupational Safety and Health.

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