



## Short communication

Migration of di(2-ethylhexyl)phthalate (DEHP) and di-*n*-butylphthalate (DBP) from polypropylene food containersHaiqin Fang <sup>a, b</sup>, Jun Wang <sup>a, \*</sup>, Robert A. Lynch <sup>a</sup><sup>a</sup> Department of Occupational and Environmental Health, College of Public Health, University of Oklahoma Health Sciences Center, Oklahoma City, OK 73126, United States<sup>b</sup> Key Laboratory of Food Safety Risk Assessment of Ministry of Health, China National Center for Food Safety Risk Assessment, Beijing 100021, China

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## ABSTRACT

Di(2-ethylhexyl)phthalate (DEHP) and di-*n*-butylphthalate (DBP) exposure from food packaging material migration can adversely affect the reproductive, developmental, immune, and endocrine systems. The migration of DEHP and DBP from polyvinyl chloride plastic food containers was well documented. However, supposedly “green” polypropylene plastic food containers have not been examined. The objective of this preliminary study was to determine the level of phthalate migration from commercially available polypropylene food containers into food-alike aqueous solutions. The liquid samples were retrieved from polypropylene containers under four different pH values (3, 5, 7, 9) resembling acidic to basic conditions, with a heating time of 0–5 min. The results showed that both DEHP and DBP had the highest migration under strong acidity (pH=3), with the highest cumulative concentrations of 159.8 and 104.9 µg/L, respectively. Migration also increased with prolonged heating time. The highest migration of DBP from the polypropylene food container (0.6 mg/kg) exceeded specific migration limit.

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## 1. Introduction

Plasticizers are commonly added to polymer materials used in food manufacturing, processing, and packaging to improve plasticity, fluidity, flexibility, and durability of these materials (Cadogan & Howick, 2000). Phthalate plasticizers, namely di(2-ethylhexyl)phthalate (DEHP) and di-*n*-butyl phthalate (DBP), are widely used due to their low cost and high performance (Cao, 2010). The practice of blending phthalate plasticizers with polymer materials, such as polyvinyl chloride (PVC), for food packaging has lasted several decades (Page & Lacroix, 1995). Both DEHP and DBP have been detected in various types of retail foods (Lau & Wong, 2000). The most likely explanation for the occurrence of phthalates in retail foods is the frequent use or unintended presence of phthalates in various food contact materials during processing, storing, transportation, and preparation (Castle, Mayo, & Gilbert, 1989; de Fátima Poças & Hogg, 2007). Fasano, Bono-Blay, Cirillo, Montuori, and Lacorte (2012) analyzed chemical compounds migration in eleven common food packaging using specific food simulants such as

water, acid, and ethanol, and the findings showed various phthalates migrated from food packaging, with concentrations ranged from ng L<sup>-1</sup> to µg L<sup>-1</sup>. Although these phthalate compounds were approved for use in food packaging, if found in food with high concentrations, may produce adverse health effects in the exposed population.

Phthalate plasticizers are usually not chemically bonded to the polymer matrix (Haishima et al., 2004), due to their mobile and migratory nature. Leaching, migration, and evaporation of phthalates (Arvanitoyannis & Bosnea, 2004; Inoue et al., 2005) into liquid and solid foods results in human exposure through ingestion, inhalation, and dermal contact during interaction with contaminated foods (Abb, Heinrich, Sorkau, & Lorenz, 2009; Koniecki, Wang, Moody, & Zhu, 2011; Latini, 2005). Among these three pathways, ingestion was considered to be the most frequent pathway for phthalate plasticizers exposure. The exposure can be lifetime, beginning at the intrauterine development stage (Cirillo, Fasano, Esposito, Montuori, & Amodio Cocchieri, 2013; Haishima et al., 2004; Haishima et al., 2005). This lifetime exposure represents a high health risk, particularly to vulnerable groups such as infants, pregnant women, and elderly people (Marsee, Woodruff, Axelrad, Calafat, & Swan, 2006; Swan et al., 2005).

Results from toxicological animal and human studies indicated

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that phthalate plasticizer exposure caused severe developmental and reproductive toxicities (Duty, Calafat, Silva, Ryan, & Hauser, 2005; Latini, Del Vecchio, Massaro, Verrotti, & De Felice, 2006; Singh & Li, 2011). In short- and long-term rodent studies, dose-related adverse effects were found primarily in the liver and kidney, with some effects on thyroid and testes. Significant differences in doses were detected among different species and between males and females (Heudorf, Mersch-Sundermann, & Angerer, 2007). The National Toxicology Program Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR (NTP, 2003a, 2003b, 2003c, 2003d, 2005; Shelby, 2006); evaluated the impact of various phthalate plasticizers on human reproduction and development. The results revealed that human exposure to phthalates might cause decreased sperm counts, histological changes in testes, and reduced fertility.

Most phthalates exhibit a low acute toxicity, with LD<sub>50</sub> values ranging from 1 to 30 g/kg bodyweight. In recent years, concerns arose about possible endocrine disruption (Heudorf et al., 2007) and immune effects (Kimber & Dearman, 2010) of phthalates. Exposure to DBP showed developmental (Sathyanarayana, 2008) and reproductive (Swan, 2008) toxicity at exposure as low as 100 mg/kg bodyweight/day. Many phthalates are not carcinogenic: the International Agency for Research on Cancer (IARC, 2000) re-evaluated DEHP and changed its classification from 'possibly carcinogenic to humans' to 'not classifiable as to carcinogenicity in humans'.

Most food safety guidelines primarily focus on microbiological contamination. Evidence suggests that food packaging materials could represent an important source of chemical contamination through the migration and leaching of phthalates into food (Cirillo et al., 2013; Fierens, Vanermen, Van Holderbeke, De Henauw, & Sioen, 2012; Lau & Wong, 2000). Regulatory authorities worldwide have recognized that it is necessary to control such contamination, and many, such as the European Union (EU), have enacted extensive legislation. Meanwhile, various studies regarding the exposure from the migration of plasticizer in plastic packaging materials have been conducted. However, most of these studies focused only on PVC (Haishima et al., 2004; Inoue et al., 2005; Ito et al., 2005; Takatori et al., 2008; Takehisa et al., 2005), as it is the most popular food packaging material, and few have been conducted with polypropylene. Polypropylene is an allegedly environmental friendly material, is considered safer than PVC, and contains fewer toxins, such as chlorine. Theoretically, polypropylene plastic requires less plasticizer additives than does PVC, due to the softness and flexibility from polypropylene's molecule structure. This characteristic makes polypropylene a desirable food container material.

Although several previous studies were conducted to verify phthalates leaching and migrating from specific food containers such as baby bottle made from polypropylene (Onghena et al., 2014; Simoneau, Van den Eede, & Valzacchi, 2012), the scarcity of studies on the application of polypropylene in many other types of food containers is still existed and could be attributed to the difficulty of trace-level phthalates analysis in the complex food matrix, and variables during the lifetime of a food container (Franco, Prevedouros, Alli, & Cousins, 2007; García, Silva, Cooper, Franz, & Losada, 2006). For the purposes of food safety risk assessment, it is critical to precisely determine the exposure to evaluate any significant risk of DEHP and DBP, and to establish the intake value of DEHP and DBP from understudied materials, such as polypropylene.

The objective of this study was to examine DEHP and DBP migration from commercially available polypropylene plastic food containers. This study simulated the effects of food pH (acidity and basicity) variation and microwave heating time on migration. The

amount of DEHP and DBP migrating into aqueous solutions were determined using an immunoassay method. The worst-case daily intakes from ingesting processed food in polypropylene plastic food containers were calculated and compared with the existing standards.

## 2. Materials and methods

### 2.1. Testing conditions

In the present study, the matrix effects of pH and heating time on the migration of DBP and DEHP were examined through a factorial design that incorporated pH values from 3 to 9 and heating times from 1 to 5 min. Clear polypropylene food containers (Red-itainer brand, 16 oz. bowl, 3 inches tall, 4.6-inch diameter at top, 3.3-inch diameter at base) with lids were purchased from Amazon.com. The description on the retailer's website claimed that the food containers were microwaveable, dishwasher safe, and reusable. Based on the reviews, the customers who bought these food containers were mostly take-out and deli restaurant owners, whose customers often re-heated food. The re-heating time in a household microwave oven was usually under 5 min. Therefore, the heating experiment was designed to simulate typical microwave heating times of 1–5 min.

Although most common foods fall in the mid-pH/neutral range (U.S. FDA, 2012), the pH of some fruits and juices can be as low as 2.2, and the pH of egg whites can be as high as 9.0. Hence, the selected pH range represented the majority of pHs included in the human diet. Solutions of known pH (3, 5, 7, and 9) were made from sodium hydroxide and hydrochloric acid to represent different acidity and basicity of food. The pH was verified through a pH meter (Hach, Loveland, CO).

Each polypropylene container was filled with 200 mL of pre-determined pH solutions and was heated in a countertop microwave oven (Sharp 1200W, Mahwah, NJ) for 1, 3, and 5 min, respectively. For each pH group, a non-heated sample was used as a control group, and also represented storage effects. The 200 mL solution covered each bowl to a 1.2-inch depth, or approximately 40% of the total depth. The evaporation loss from each container was measured after heating. Each combination of pH and heating time was repeated at least three times ( $n = 3$ ), and mean values with standard deviation were acquired.

### 2.2. Chemical analysis

After heating, the aqueous samples were cooled and stored in glass tubes at 4 °C before chemical analysis. The concentrations of DEHP and DBP were determined using customized enzyme-linked immunosorbent assays (ELISA, NeoScientific, Woburn, MA). ELISA assay has shown advantages over the traditional chromatograph methods (such as GC-MS or LC-MS/MS) with easy operability, and adequate sensitivity and accuracy. Two 100  $\mu$ L samples of each sample were dispensed into the incubation plate and incubated with enzyme horseradish peroxidase (HRP) conjugate at 37 °C. DEHP and DBP in samples competed with the HRP conjugate on binding to the phthalate-specific antibody. The presence of DEHP and DBP reduced the amount of HRP conjugate and led to a reduced signal. Binding of HRP conjugate formed a colorimetric reaction product that was visually detected with a microplate reader (Lonza ELX808LBS, Allendale, NJ). An absorbance of 450 nm was used to determine the concentrations of HRP conjugate and, later, to calculate the levels of DEHP and DBP. The method limit of detection (LOD) of the assay was determined to be 0.1  $\mu$ g/L. The calibration curve was constructed using standard solutions from 5  $\mu$ g/L to 100  $\mu$ g/L with  $R^2 > 0.9998$ . Cumulative concentrations of migration

( $\mu\text{g/L}$ ) were calculated for each combination of pH and heating time. The highest migration was used as a worst-case scenario estimate and compared with the European Food Safety Authority (EFSA) tolerable daily intake (TDI) and European Union (EU) specific migration limit (SML). Since migration is a surface phenomenon and a contact-area-mediated process, migration concentrations were also normalized to concentration per unit of wetted area (measured prior to heating), and are provided in the supplemental tables.

### 2.3. Quality assurance and statistics

Acid and base chemicals (Fisher Scientific, Waltham, MA) were analytical grades or higher purity, and at their original concentrations. Water used for dilution and cleaning was purified by a reverse osmosis system (Barnstead D12651, Boston, MA). Labware was ultrasonically cleaned and dried in an isotemp oven before and after analysis to prevent potential residual contamination. To avoid experimental artifacts from ubiquitous phthalate in plastics, the use of plastic labware was minimized. Lab blanks that only contained reagent solutions were tested to examine background contamination. No interference was found.

All samples were collected in triplicate per each combination of pH and heating time. Two-way analysis of variance (ANOVA) was used to test treating pH and heating time dependency. Post-hoc pairwise *t*-tests were used to compare different combinations with a significance level of  $p = 0.05$ . Statistical analyzes were performed using SPSS 23.0 (Chicago, IL).

## 3. Results and discussion

### 3.1. DEHP and DBP migration

The cumulative concentrations of DEHP and DBP in the samples are shown in Figs. 1 and 2, respectively. Details and concentrations per wetted area are listed in the Supplemental Tables S-1 and S-2. DEHP was not detected in most non-heated samples, except under strongly acidic conditions ( $\text{pH} = 3$ ). The concentration of DEHP in heated samples ranged from  $33.3 \pm 21.1 \mu\text{g/L}$  ( $\text{pH} = 5$ , 1-minute heating) to  $159.8 \pm 21.1 \mu\text{g/L}$  ( $\text{pH} = 3$ , 5-minutes heating). DBP was detected in all samples, regardless of heating conditions. Acidic conditions produced DBP migration of  $66.1 \pm 3.9 \mu\text{g/L}$ , even without heating. DBP migration from heated samples ranged from  $10.2 \pm 3.3 \mu\text{g/L}$  ( $\text{pH} = 5$ , 1-minute heating) to  $104.9 \pm 3.6 \mu\text{g/L}$  ( $\text{pH} = 3$ , 5-minutes heating). Some of the variations indicated by the high standard deviation might be caused by the impurity across different container samples since they were consumer grades with low quality control.

Cumulative migration categorized by pH and heating time was modeled with heating time and pH as fixed effects, with and without the inclusion of a heating time  $\times$  pH interaction effect. The result indicated no significant interaction effect between these two parameters. Thus, the interaction effect was excluded from further analysis.

Generally, DEHP and DBP concentrations increased with extended heating time, and were at a maximum with strong acidity ( $\text{pH} = 3$ ). At weak acidity ( $\text{pH} = 5$ ) and neutral ( $\text{pH} = 7$ ) conditions, the migration was at a minimum, with no significant difference between weak acidity and neutral for either DEHP or DBP concentration. It should be noted that DEHP migration is significantly different at basic conditions ( $\text{pH} = 9$ ) from other pH conditions (higher than  $\text{pH} = 5$  or 7, lower than  $\text{pH} = 3$ ,  $p < 0.01$ ). DBP leaching under basic conditions was not different from that observed under weak acidity and neutral conditions.

In addition, the linear effects of pH and heating time on the DEHP and DBP migration were determined. Both pH and heating time were statistically significantly correlated with migration, while migration at  $\text{pH} = 3$  was significantly higher than that observed under other conditions. This result is similar to the findings from many PVC migration studies, which concluded that acidic foods and longer heating time increased phthalate migration and presented the greatest risk. The findings on pH factor were also consistent with a previous study of the migration of phthalates from plastic containers into soft drinks and mineral water by Bošnjir et al. (2007), with DBP and DEHP showed highest level of migration into mineral water.

### 3.2. Worst-case estimation

TDI is an estimate of the daily intake of DEHP and DBP that can occur over a lifetime without appreciable risk. EFSA established a TDI of 0.05 mg/kg bodyweight/day (mg/kg BW/day) for DEHP (EFSA, 2005a) and 0.01 mg/kg BW/day for DBP (EFSA, 2005b). Since strong acidity ( $\text{pH} = 3$ ) represented the highest migration in this study and acid foods are commonly found in the human diet, a worst-case scenario was estimated based on the results of a strong acid condition. The potential phthalate dose as a percentage of TDI standards (%TDI) was calculated using the following equation:

$$\%TDI = \frac{C}{BW \times E} \times 100\%$$

where  $C$  ( $\mu\text{g/L}$ ) is the concentration of phthalate (DEHP/DBP) migrated in a single 0.2 serving,  $BW$  is the average body weight of an adult (60 kg), and  $E$  is the current EFSA TDI value converted to  $\mu\text{g/kg BW/day}$ . The findings are listed in Table 1.

Based on the worst-case estimate, a minimum of 93 servings of strong acid food with extensive heating must be consumed to approach the recommended DEHP TDI of 50  $\mu\text{g/kg BW/day}$ . Similarly, 29 servings are needed to reach the DBP TDI of 10  $\mu\text{g/kg BW/day}$  recommended by EFSA. These large numbers of servings are unlikely to occur in daily life. Additional standards for DEHP and DBP in food packaging are EU SML, which are measures of migration from certain weights of food packaging, processing, and serving materials into foods. According to the EU regulation (EU, 2011), the SMLs of DEHP and DBP are 1.5 and 0.3 mg/kg of packaging material, respectively. The highest migration of DEHP and DBP based on the container weights in the present study were 1.1 mg/kg and 0.6 mg/kg, respectively. Although DEHP migration was lower than the SML, the DBP migration level exceeded the SML and presented a potential risk.

To avoid overexposure to the DEHP and DBP migration in the worst-case scenario, phthalate substitute plasticizers should be considered when making food containers. Glycerol and citrate esters, have shown to increase the flexibility and improve the plasticizing effect (Lin, Chen, & Run-Chu, 2000; Shirai et al., 2013). Being the less toxic and more environmentally friendly chemical, citrate esters plasticizer was adopted in some plastic manufacturer and medical sectors. These phthalate substitutes were anticipated with more applications emerging in food packaging, pending with adequate migration and toxicological studies conducted.

## 4. Conclusions

These findings indicate that both pH and heating time affect DEHP and DBP migration from polypropylene food containers. Acidic foods and longer heating times increased phthalate migration and presented greater health risks, even with the supposedly

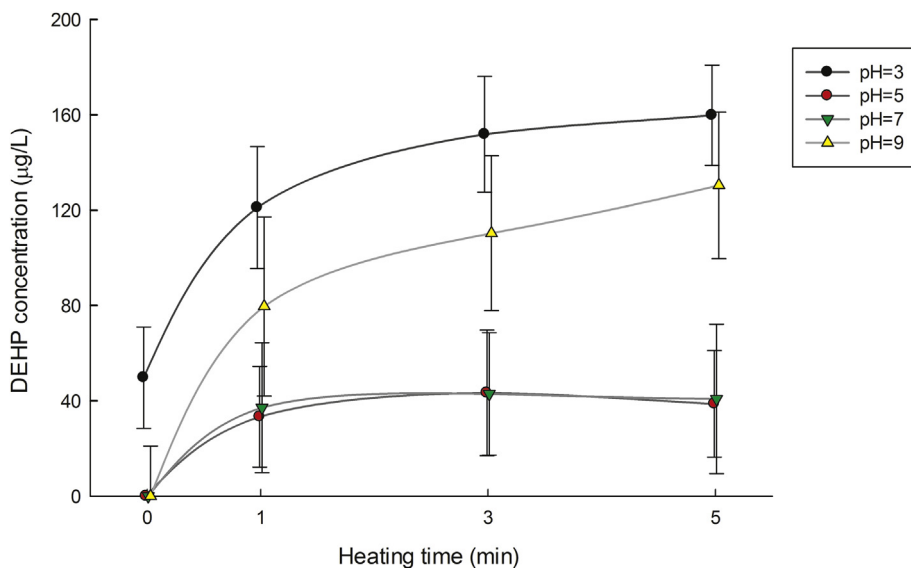


Fig. 1. Mean DEHP migration (µg/L; n = 6 for all samples), with error bars representing the standard deviation of the mean.

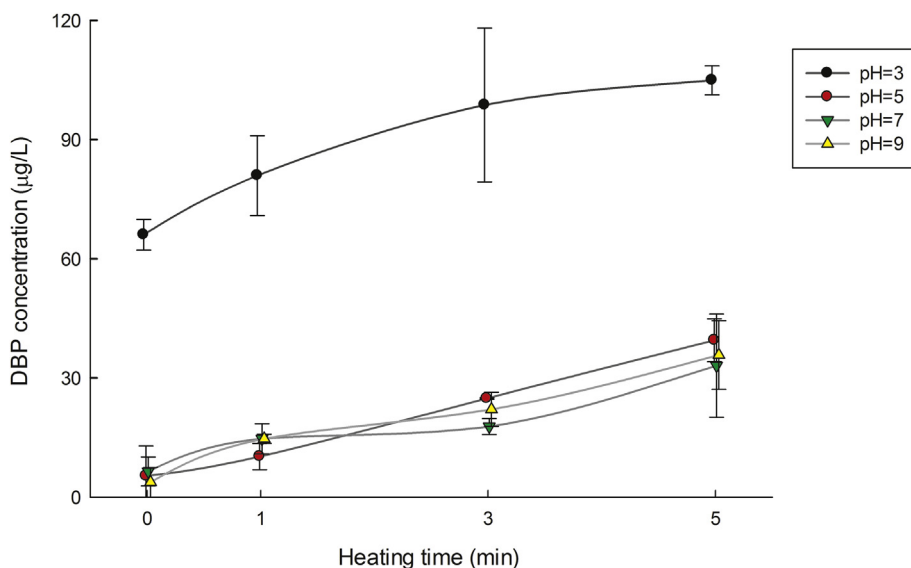


Fig. 2. Mean DBP migration (µg/L; n = 6 for all samples), with error bars representing the standard deviation of the mean.

Table 1

Estimated %TDI of DEHP and DBP for an adult (60 kg) intake 200 mL of food at pH = 3.

Heating time (minute)	DEHP		DBP	
	%TDI	Servings to reach TDI	%TDI	Servings to reach TDI
0	0.33	303	2.20	45
1	0.81	123	2.70	37
3	1.01	99	2.29	44
5	1.07	93	3.50	29

low-toxic polypropylene material. Besides pH and heating conditions, simulations such as ethanol in the food should also be studied in the future. Considering the ever-growing use of plastic containers for food processing, this preliminary study served as a basis for determining the most acceptable composition of plastic containers, and set the course for additional studies of human exposure to phthalates.

Conflict of interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://>

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