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Synthetic phenolic antioxidants and their metabolites in indoor dust from homes and microenvironments

Wei Wang¹, Alexandros G. Asimakopoulos¹, Khalid O. Abualnaja², Adrian Covaci³, Bondi Gevao⁴, Boris Johnson-Restrepo⁵, Taha A. Kumosani², Govindan Malarvannan³, Tu Binh Minh⁶, Hyo-Bang Moon⁷, Haruhiko Nakata⁸, Ravindra K. Sinha⁹, and Kurunthachalam Kannan¹²,*

¹Wadsworth Center, New York State Department of Health, and Department of Environmental Health Sciences, School of Public Health, State University of New York at Albany, Empire State Plaza, P.O. Box 509, Albany, New York 12201-0509, United States
²Biochemistry Department, Faculty of Science, Experimental Biochemistry Unit, King Fahd Medical Research Center and Bioactive Natural Products Research Group, King Abdulaziz University, Jeddah, Saudi Arabia
³Toxicological Center, University of Antwerp, Universiteitsplein 1, 2610 Wilrijk-Antwerp, Belgium
⁴Environmental Management Program, Environment and Life Sciences Center, Kuwait Institute for Scientific Research, P.O. Box 24885, Safat 13109, Kuwait
⁵Environmental and Chemistry Group, Sede San Pablo, University of Cartagena, Cartagena, Bolivar 130015, Colombia
⁶Faculty of Chemistry, Hanoi University of Science, Vietnam National University, Hanoi, Le Thanh Tong, Hoan Kiem, Hanoi, Vietnam
⁷Department of Marine Sciences and Convergent Technology, College of Science and Technology, Hanyang University, Ansan, South Korea
Supplementary Information

8Graduate School of Science and Technology, Kumamoto University, 2-39-1 Kurokami, Kumamoto 860-8555, Japan
9Department of Zoology, Patna University, Patna, 800 005, India

* Corresponding author at: Wadsworth Center, Empire State Plaza, P.O. Box 509, Albany, NY 12201-0509, USA. Tel.: +1 518 474 0015, fax: +1 518-473- 2895, E-mail address: Kurunthachalam.kannan@health.ny.gov (K. Kannan).

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TOC

Synthetic phenolic antioxidants (SPA)

Composition of SPAs (%)
Abstract

Synthetic phenolic antioxidants (SPAs), including 2,6-di-tert-butyl-4-hydroxytoluene (BHT), are extensively used in food, cosmetic and plastic industries. Nevertheless, limited information is available on human exposures, other than the dietary sources, to SPAs. In this study, occurrence of nine SPAs and their metabolites/degradation products was determined in 339 indoor dust collected from 12 countries. BHT was found in 99.5% of indoor dust samples from homes and microenvironments at concentrations that ranged from <LOQ to 118 µg/g and 0.10 to 3460 µg/g, respectively. This is the first study to measure BHT metabolites in house dust (0.01-35.1 µg/g) and their concentrations accounted for 9.2% to 58% of the sum concentrations (∑SPA). 3,5-di-tert-butyl-4-hydroxybenzaldehyde (BHT-CHO), 2,6-di-tert-butyl-4-(hydroxymethyl)phenol (BHT-OH), 2,6-di-tert-butyl-1,4-benzoquinone (BHT-Q) were the major derivatives of BHT found in dust samples. The concentrations of gallic acid esters (gallates) in dust from homes and microenvironments ranged from <LOQ to 18.2 and <LOQ to 684 µg/g, respectively. The concentrations and profiles of SPAs varied among countries and microenvironments. Significantly elevated concentrations of SPAs were found in dust from an e-waste workshop (1530 µg/g). The estimated daily intake (EDI) of BHT via house dust ingestion ranged from 0.40 to 222 ng/kg/d (95th percentile).
Introduction

Synthetic phenolic antioxidants (SPAs) are the most frequently used antioxidants in many consumer products including foodstuffs. The U.S. Food and Drug Administration (FDA) and the European Union (EU) regulate the use of SPAs, including 2,6-di-tert-butyl-4-hydroxytoluene (BHT), 2-tert-butyl-4-methoxyphenol (BHA), propyl (PG)-, octyl- (OG) and dodecyl- (DG) gallate as food additives. SPAs are widely used in food and feed industries including confectionery and edible oil industry. BHT is also used in a wide range of cosmetics. Furthermore, SPAs are currently used in a wide range of products including packing materials, rubber, plastics, hand-washing soap, pet foods, chewing gum and as anti-skinning agents in paints and inks. SPAs might be released into the indoor environment from various household commodities and indoor dust can be a source of human exposure.

In recent years, concerns with regard to the safety of SPAs have increased, due to their potential toxicity. Nevertheless, considerable controversy surrounds with regard to the link between BHT/BHA and carcinogenicity. BHA has been shown to possess estrogenic properties in breast cancer cells, and has been shown to disrupt estrogen receptor functions. A few other studies have not found such estrogenic effects. The metabolites of BHT have been reported to induce peroxides in mice and rats, which results in cellular DNA damage and instigate cancer. BHT has been reported to be metabolized to 3,5-di-tertbutyl-4-
hydroxybenzoic acid (BHT-COOH) through oxidation of alkyl group via the corresponding alcohol (BHT-OH) and aldehyde (BHT-CHO) or to 2,6-di-tert-butylcyclohexa-2,5-diene-1,4-dione (BHT-Q) through oxidation of the π-system. In addition, BHT-OH and BHT-CHO are photoproducts of BHT.

Although SPAs are considered safe for human health at recommended doses (for instance, the acceptable daily intake of BHT has been set at 250 µg/kg/day), its ubiquitous presence and the controversial toxicological data suggest the need for more information on these classes of chemicals. A few studies have reported the occurrence of SPAs in surface water, wastewater and foodstuffs. However, no information is available on the occurrence of SPAs and their metabolites in indoor environments. Because SPAs are used in a variety of consumer products, including adhesives, personal care products and pharmaceuticals, humans can be exposed to these compounds via both oral ingestion and inhalation of settled dust. In this study, a wide range of SPAs and their metabolites were determined in indoor dust samples collected from 12 countries, for the first time, to elucidate the occurrence, sources and human exposure profiles through dust ingestion.

Materials and Methods

Sample Collection. A total of 339 indoor dust samples were collected from 12 countries, with 241 samples from homes and 98 from other microenvironments (laboratories, offices,
cars, and e-waste workshop) (Table S1; Supporting Information). House dust samples (5-50 g) were collected from select cities in China (CN, number of samples: n = 26), U.S. (US, 14), India (IN, 30), Japan (JP, 10), Greece (GR, 20), Colombia (CO, 40), Pakistan (PK, 22), Saudi Arabia (SA, 10), South Korea (KR, 26), Kuwait (KW, 15), Romania (RO, 20), and Vietnam (VN, 8) during 2012 to 2014. Dust samples from laboratories, offices, cars, and public areas were collected from South Korea (lab, n = 10; office, 14), Kuwait (car, 15), Pakistan (car, 6; office 31), Saudi Arabia (car, 10), and Vietnam (e-waste workshop, 4; market, 8). Floor dust samples were obtained from vacuum cleaner bags in each of the sampling sites following the same sampling protocol, with the exception of samples from China and India, which were obtained by sweeping the floor. The vacuum and the sweeping tool were pre-cleaned before each sampling. Only bedrooms and living rooms of homes and apartments (all countries) were selected for sampling. We employed volunteers to collect samples in each country, and these volunteers sampled sites for which they had access. This approach of opportunistic sampling is not expected to be fully representative of the country, but it can obtain a sufficient sample size in the variety of different types of microenvironments (homes, offices, cars, etc.) desired to meet the objectives of the study. All samples were transported to the laboratory at Wadsworth Center, sieved through a 150 µm sieve, homogenized, packed in clean aluminum foil, and stored at 4 °C until analysis.
Chemicals and Reagents. Target analytes and their structure are shown in Table S2. BHT, BHT-d21, BHT-OH, BHT-Q, BHT-CHO, BHT-COOH, DG and PG were obtained from Sigma-Aldrich (St. Louis, MO) and OG was purchased from Chem Cruz (Dallas, Texas). Isotopically-labeled $^{13}$C$_{12}$-methyl paraben, ($^{13}$C$_{12}$-MeP) and $^{13}$C$_{12}$-propyl paraben ($^{13}$C$_{12}$-PrP) (RING-$^{13}$C$_{12}$, 99%) were obtained from Cambridge Isotope Laboratories (Andover, MA) and Wellington Laboratories (Guelph, Ontario, Canada). HPLC grade methanol was supplied by J.T. Baker (Phillipsburg, NJ). Ultra-pure water (18.2Ω) was generated using a Milli-Q system (Millipore, Billerica, MA).

Sample Preparation. Briefly, 0.25 g of dust sample was weighed and transferred into 15 mL glass tube. After spiking with BHT-d21, $^{13}$C$_{12}$-MeP and $^{13}$C$_{12}$-PrP (as internal standards, IS), sample was extracted with a 5 mL solvent mixture of dichloromethane/hexane (3:1, v/v) by shaking for 60 min. The mixture was centrifuged at 2000 x g for 10 min (Eppendorf Centrifuge 5804, Hamburg, Germany), and the supernatant was transferred into a glass tube. The extraction repeated twice with the same amount of solvent, and the extracts were combined, concentrated and solvent exchanged to 300 µL ethyl acetate. Prior to analysis by high performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS), 50 µL of the extract was diluted to 250 µL with methanol in HPLC vials and the remaining 250 µL of the extract was analyzed on a gas chromatograph-mass spectrometer (GC-MS).

Instrumental Analysis. BHT was analyzed using a GC (Agilent Technologies 6890)
coupled to a MS (Agilent Technologies 5973) in the selected ion monitoring (SIM) mode. A fused-silica capillary column (DB-5; 30 m × 0.25 mm i.d. × 0.25 µm film thickness) was used for separation. Other SPAs were determined using an Agilent 1260 HPLC (Agilent Technologies Inc., Santa Clara, CA) interfaced with an Applied Biosystems QTRAP 4500 mass spectrometer (ESI-MS/MS; Applied Biosystems, Foster City, CA). An analytical column (Betasil® C18, 100 × 2.1 mm column; Thermo Electron Corporation, Waltham, MA), connected to a Javelin guard column (Betasil® C18, 20 × 2.1 mm) was used for separation. The negative ion multiple reaction monitoring (MRM) mode was used. The MS/MS parameters were optimized by infusion of individual compounds into the MS through a flow injection system (Table S3). The MRM transitions of the target chemical monitored are listed in Table S4. Nitrogen was used as both curtain and collision gas.

Quality Assurance and Quality Control (QA/QC). With every set of 20 samples analyzed, a procedural blank, a pair of pre-extraction matrix spike sample (fortified before extraction), a pair of matrix match (fortified after extraction) and duplicate samples were analyzed. Trace levels of BHT-CHO (approximately 0.25 and 0.34 ng/g, respectively) were found in procedural blanks in one batch, and background subtraction was performed for this batch of samples. Recoveries of SPAs in spiked dust matrices ranged from 69 ± 22% for OG to 106 ± 12% for BHT (Table S4). Duplicate analysis of randomly selected samples (n = 12) showed a coefficient of variation of <20%. Quantification of SPAs was performed by an
isotope-dilution method based on the response of BHT-d21 (for BHT), $^{13}$C$_{12}$-MeP (for BHT-Q, BHA, BHT-OH, BHT-CHO, and BHT-COOH), $^{13}$C$_{12}$-PrP (for OG, PG and DG). The limits of quantification (LOQs) were 0.12 ng/g for BHT-CHO and BHT-COOH, 0.6 ng/g for BHA, 1.2 ng/g for BHT, BHT-Q and BHT-OH, and 2.4 ng/g for DG, OG and PG (Table S4), which were calculated from the lowest acceptable calibration standard and a nominal sample weight of 0.25 g (LOQs for LC/MS/MS analyses were corrected based on diluted subsamples). A midpoint calibration standard (in methanol) was injected as a check for instrumental drift in sensitivity after every 20 samples, and a pure solvent (methanol) was injected as a check for sample carry-over. Instrumental calibration was verified by injection of 10 calibration standards (ranging from 0.02 to 100 ng/g), and the linearity of the calibration curve ($r^2$) was > 0.99. The concentrations of BHT-CHO in the third extraction of 30 randomly selected dust samples were < 1% of the values found in the first three extractions while others are undetectable, which indicated that the extraction cycles used in this study completely extracted the target chemicals. For ease of discussion and exposure assessment, dust from homes and other microenvironments were segregated.

Statistical Analysis. Statistical analyses were performed with Origin ver. 8 (for profile analyses) and SPSS 16.0 software (for correlation analyses, test for normality and ANOVA). Normality of the data was checked by Shapiro-Wilk test. The 95% upper confidence limit (UCL) was calculated using ProUCL 4.0. Differences between groups were compared using
a one-way ANOVA followed by a Tukey test. Prior to one-way ANOVA, the data were log-
transformed to meet the normality assumptions. The probability value of $p \leq 0.05$ was set for
statistical significance.

Results and Discussion

**SPAs in House Dust.** BHT was found in 99.5% of house dust samples and the
concentrations varied by five orders of magnitude, from $<1.2$ ng/g to 118 µg/g (Table 1).
Highest concentrations of BHT were found in house dust collected from Japan (range: 3.19-
33.9 µg/g) and South Korea (2.27-118 µg/g), which were 2-3 orders of magnitude higher
than the concentrations found in countries with the lowest levels, Romania (0.04-1.59 µg/g)
and Vietnam (0.09-0.74 µg/g). SPAs are used as preservatives or additives in household
products,\textsuperscript{15,18} which can contribute to their occurrence in settled dust. BHT is also widely
used in plastic materials as an antioxidant to stabilize the polymer during processing and to
protect plastics through their lifespan\textsuperscript{15}. High concentrations of BHT found in both house
dust (median 1.55 µg/g) and sewage sludge (median 2.35µg/g) from China indicate the
widespread usage of this compound in China.\textsuperscript{19}

BHA, an endocrine disrupting chemical (EDC) with potential as a tumor promoter,\textsuperscript{20,21}
was found only in house dust from China (ranged from 0.01 to 7.44 µg/g for five cities),
whereas this compound was not found in house dust from the other eleven countries studied.
Propyl-, octyl- and dodecyl- gallates are often used as antioxidants in cosmetics and food industry (especially in oils and fats to prevent oxidation).\textsuperscript{22,23} In dust samples, distribution pattern for gallates was different from that of other SPAs, indicating the different usage and sources of gallates. OG was only detected in house dust from China (<LOQ-0.04 µg/g), Korea (<LOQ-0.14), Saudi Arabia (0.09-0.75) and Japan (<LOQ-0.11), whereas PG was only found in China (<LOQ-1.25) and Saudi Arabia (<LOQ-0.11). DG was found in house dust from China (<LOQ-0.32), Korea (0.31-7.56), the U.S. (<LOQ-0.76), Japan (<LOQ-18.2) and Saudi Arabia (0.01-11.9). Gallates were not found in house dust from Greece, Romania, Kuwait, India, Colombia and Vietnam.

**BHT Metabolites in House Dust.** BHT metabolites were found in all house dust samples at total concentrations (\(\sum\text{MTs}\)) that ranged from 0.01 to 35.1 µg/g. The most abundant metabolites of BHT were BHT-CHO, BHT-OH and BHT-Q, with median concentration ranges of 0.01 to 0.41, <LOQ to 0.93 and <LOQ to 1.86 µg/g, respectively, across twelve countries. The detection frequencies of BHT-Q, BHT-OH, BHT-COOH and BHT-CHO ranged from 38 to 100%, 91 to 100%, 87 to 100%, and 75 to 100%, respectively, across twelve countries. In general, BHT-Q, BHT-OH, BHT-CHO, and BHT-COOH collectively accounted for, on average, 9 to 58% of the sum of concentrations of SPAs and their metabolites (\(\sum\text{SPA}\)). BHT-COOH was found at the lowest concentration in dust. Compared
with other countries studied, higher concentrations of BHT-COOH were found in dust samples from China (median: 0.27 µg/g) and Saudi Arabia (0.13), and BHT-Q was dominant in dust from the U.S. (1.86 µg/g), Japan (0.87), and Korea (0.47). Similar to the distribution of BHT, the highest median concentration of ∑MTs was determined in house dust from the U.S. (3.02 µg/g), Japan (1.94 µg/g), and South Korea (1.37 µg/g). The toxic effects BHT-metabolites including DNA damage and carcinogenicity have been reported in several studies. The widespread occurrence of BHT-metabolites in indoor dust at high concentrations suggests the need for further studies on potential health effects of these metabolites.

**SPAs in Dust from Various Microenvironments.** The concentrations of ∑SPAs in indoor dust from various microenvironments varied widely (Table S5), with the highest ∑SPA mean concentrations found in an e-waste workshop (4670 µg/g) in Vietnam. The median concentrations of ∑SPAs in car dust (3.76 µg/g) from Saudi Arabia were similar to those reported for house dust from the same country (3.93 µg/g). Nevertheless, ∑SPA concentrations in house dust from rural homes (range: 0.64-10.9 µg/g) in Pakistan were significantly lower than those from urban (1.58-14.6 µg/g) homes, which might be attributed to different lifestyles including the usage of consumer products. The concentrations of BHT in dust from laboratories and offices in South Korea (range: 2.32-73.8, median: 22.9 and 33.0 µg/g, respectively) were significantly ($p < 0.05$) higher than those in homes (median:
As one of the widely used stabilizers, SPAs are present in plastics at levels of hundreds to a few thousand mg per kg, which might explain for the high concentrations found in numerous microenvironments, such as car, office, and e-waste workshop. Similarly, significantly ($p < 0.05$) higher BHT-metabolite concentrations were found in dust from offices (2.70-29.9 µg/g) and laboratories (3.60-25.1 µg/g) than in homes (0.51-5.86 µg/g) in South Korea. However, higher concentrations of gallates were found in homes (0.31-7.58 µg/g) than in laboratories (0.23-2.48 µg/g) and offices (0.04-5.79 µg/g). These differences in the profiles of SPAs suggest that gallates might be primarily used in household products. The use of SPAs in petroleum products and plastics such as electronic equipment and cables, that are widely found in offices/laboratories, is a possible source of their occurrence in these microenvironments. However, dust samples from Pakistan did not show a significant difference in SPA concentrations between offices and homes. The nature and magnitude of indoor products (such as computer, furniture, personal care products, food packages, interior decorations and building material) and ventilation can possibly contribute to variations in SPA profiles in different microenvironments. The highest BHT, gallate and $\sum$SPA concentrations were found in dust from an e-waste workshop in Vietnam, in the concentration ranges of 425 - 3460, 0.02 - 684, and 429 - 4670 µg/g, respectively; these values were four orders of magnitude ($p < 0.05$) higher than those found in dust from homes and offices in Vietnam. The use of BHT in plastic components of e-waste might explain the
high concentrations found in dust from e-waste workshop. The high contamination of SPAs in e-waste workshop found in this study suggests the need for further investigations on occupational exposures in e-waste workshops.

**SPAs and Their Metabolite Profiles.** A significant correlation was found between BHT and \( \sum \text{MTs} \) in house dust samples from China \((p < 0.05)\) and Colombia \((p < 0.05)\), which indicated that the dominant source of BHT-metabolites is degradation of BHT itself; however, no significant relationship was found between BHT and \( \sum \text{MTs} \) in dust from other countries, possibly due to the existence of other sources and transformation pathways. For all the 224 house dust samples, significant correlations \((p < 0.05)\) were found among BHT metabolites (Table S6), including BHT-Q, BHT-OH and BHT-COOH, except for BHT-CHO. The contribution of each of the target compounds to the sum concentrations of \( \sum \text{SPAs} \) analyzed in dust is presented in Figure 1. BHT accounted for up to 89% of \( \sum \text{SPA} \) concentrations in dust from Vietnam, followed by Japan (76%) > Greece (73%) > Korea (72%) > Saudi Arabia (71%) > India (67%) > the U.S. (60%) > Kuwait (57%) > Romania (53%) > Pakistan (50%) > China (49%) > Colombia (42%). \( \sum \text{MTs} \) accounted for 58% of the total concentrations in dust from Colombia, followed by Pakistan (50%) > Romania (47%) > Kuwait (43%) > the U.S. (37%) > India (33%) > China (30%) > Greece (27%) > Saudi Arabia (17%) > Japan (12%) > Vietnam (11%) > Korea (9%). The highest
contributions of BHT-Q, BHT-OH, BHT-CHO and BHT-COOH to ∑MTs were found in dust from the U.S. (70%), Pakistan (47%), India (78%), and China (28%), respectively.

The proportion of BHT was significantly elevated in dust from an e-waste workshop in Vietnam, which suggested that electronic products are an important source for this chemical. Different profiles were found for the contribution of BHT in dust samples from offices, laboratories, and homes in Korea, with the lowest contribution of ∑MTs found in offices, which suggested different emission sources between homes and the workplace microenvironment. A higher proportion of ∑MTs was found in urban than rural homes in Pakistan, with elevated contribution from BHT-Q in urban homes possibly attributed to differences in the transformation processes. Elevated contribution of OG and PG was found in dust from homes than cars in Saudi Arabia. The proportion of DG was significantly higher in house dust than laboratory and office dusts in Korea. OG, PG and DG are mainly used in foodstuffs, cosmetics and personal care products.

The profiles of four BHT metabolites in house dust showed a geographical difference among the 12 countries studied, which can be attributed to different emission sources and degradation processes in the indoor environments (Figure S1). The highest contribution (70% of BHT metabolites) of BHT-Q was found in dust from the U.S., whereas BHT-CHO was found elevated in dust from India, Greece, and Colombia and BHT-OH in China, Japan,
Korea and Pakistan. BHT-COOH was the minor contributor of BHT metabolites, which was a secondary degradation product from BHT-CHO.

Potential Indoor Sources of SPAs and Metabolite Products. The results of this study suggests that phenolic antioxidants are widespread in indoor house dust, possibly due to their high production volumes and usage in several consumer products and foodstuffs. SPAs are weakly bound to their substrate, and are thus easily leached from products and enter the environment. BHT is relatively less stable in the indoor environment, which results in abiotic degradation to products such as BHT-CHO, BHT-OH and BHT-Q, which are found at high concentrations in dust. However, the variations in metabolite profiles in different indoor environments and countries suggest the influence of various environmental factors, and further studies are needed to understand the mechanism of transformation of BHT.

The occurrence of OG (dr: 0-100%), PG (dr: 0-90%), and DG (dr: 0-100%) in dust from several countries indicates potential sources originating from consumer applications such as cosmetics, hair care products, soaps, shampoos, skin lotions, deodorants, adhesives, margarine, peanut butter and lubricants. Among the three gallates, DG was found as the dominant contributor with the highest detection frequency (detected from six countries) and residue concentrations (< LOQ – 18.2 µg/g), indicating high usage of DG. DG is used as an anti-ageing agent in polymers. The differences in the distribution of gallates, BHA and BHT in house dust indicate the existence of multiple sources for these compounds.
Exposure Assessment. We estimated the daily intake (EDI) of SPAs via dust ingestion for different age groups. Median and high exposure scenarios were assessed for BHT, $\sum$MTs and SPAs based on the median and 95$^{\text{th}}$ percentile concentrations determined in dust from household and microenvironments (For details, see supporting information section S1.3; S2.1; Table S7-S9; Figure S2, S3). The acceptable dietary intake (ADI) of BHT has been established by European Food Safety Authority (EFSA) in 2012 at 0.25 mg/kg/d.\(^{32}\) Compared with the mean EDI for BHT via dietary exposure for the general population in Korea reported to be 40 $\mu$g/kg bw/day and for the U.S. population at 0.39 and 0.78 mg/kg/d for mean and high exposure scenarios reported by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) (2000)\(^{4,33}\), the EDIs from house dust were minor (222 ng/kg/d - maximum). However, since no estimation of EDI of BHT metabolites has been carried out yet., this study assessed the EDI for $\sum$MTs via house dust exposure and the highest EDI was estimated for toddlers from the U.S. with 152 ng/kg/d. Overall, contribution of dust ingestion to SPA exposure was two to three orders of magnitude lower than that from dietary route and the ADI.

Although this is the first study to report occurrence of a chemical that was not originally suspected to be present in indoor dust, our study has several limitations. First, our small sample size available for each microenvironment (e.g, e-waste workshop) limits our ability to draw inference on the sources and transformation pathways of SPAs. However, it
should be noted that the validity of our results are not affected and further studies with larger sample sizes are needed for the characterization of SPAs in microenvironments. The sampling approach was designed to meet the objective of providing accurate measurements for an emerging class of chemical contaminant in indoor dust. Second, although detailed instructions were provided, household dust samples were collected by local participants and volunteers. Variability in the types of vacuums and sweeping tools used can introduce measurement variations and potential contamination. However, we selected specific particle sizes by sieving the samples in the laboratory which is expected to reduce potential variance introduced by sample collection.

In summary, ubiquitous occurrence of several SPAs including BHT and its metabolites were found in indoor dust in this study. BHT was the major SPA in indoor dust samples analyzed from 12 countries (<LOQ-3460 µg/g). The variations in the profiles of SPAs and their metabolites among various countries and different microenvironments indicated multiple sources and transformation pathways for these compounds. The metabolites of BHT were found at elevated concentrations in dust, which suggest the need for further studies on the toxicity and health effects from exposure to BHT metabolites.

**Associated Content**

**Supporting Information**
Supporting data for this article includes additional details of methods, discussion on exposure assessment, as well as sampling information (Table S1), chemical and instrument parameters (Table S2, S3), summary statistics for LOQs and recoveries (Table S4), SPAs concentrations in microenvironments (Table S5), correlation analyses (Table S6), exposure analyses parameters (Table S7), and compound specific exposure estimates (Table S8, S9).

Profile plot for BHT metabolites and EDI estimates for compound specific exposure are contained therein.

Author Information

Corresponding Author

Tel.: +1 518 474 0015; fax: +1 518-473-2895;

E-mail address: Kurunthachalam.kannan@health.ny.gov (K. Kannan).

Notes

The authors declare no competing financial interests.

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References


(2) Food and Drug Administration, Code of Federal Regulations, Title 21: Food and Drugs, Office of the Federal Register, Washington, DC, 2001 (Chapter I).


and dust in home and the implications from human hair. Atmos. Environ. 2013, 73 (0), 204-213.


(22) Sharla, R. The truth about BHA, BHT, T BHT-Q and other antioxidants used as food additives. Tigmor Books 2009.


(29) Vitrac, O.; Challe, B.; Leblanc, J.C.; Feigenbaum, A. Contamination of packaged food by substances migrating from a direct-contact plastic layer: Assessment using a generic quantitative household scale methodology. Food Addit. Contam. 2007, 24 (1) 75-94.


Figure 1. Composition profiles of synthetic phenolic antioxidants in house dust from 12 countries (A) and indoor dust from various microenvironments (B) (SAH and SAC–house and car dust from Saudi Arabia; VNO, VNH and VNE-office, house and e-waste workshop dust from Vietnam; PKC, PKH-U, PKH-R, PKO-car, urban house, rural house and office dust from Pakistan; KWH and KWC-house and car dust from Kuwait; KRO, KRL, KRH-office, laboratory, and house dust from South Korea).
Table 1. Concentrations of synthetic phenolic antioxidants in house dust (µg/g dry weight) from 12 countries

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<td>0.34/100</td>
<td>&lt;LOQ/0</td>
<td>&lt;LOQ/0</td>
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<td>0.52/0.60</td>
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<tr>
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<td>0.04/0.31</td>
<td>&lt;LOQ/0</td>
<td>0.07/0.29</td>
<td>0.00/0.62</td>
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<td>0.24/0.85</td>
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<tr>
<td>India</td>
<td>0.47/93.8</td>
<td>&lt;LOQ/0</td>
<td>0.38/100</td>
<td>0.14/100</td>
<td>&lt;LOQ/0</td>
<td>&lt;LOQ/0</td>
<td>0.01/100</td>
<td>&lt;LOQ/0</td>
<td>0.27/0.62</td>
<td>0.10/0.76</td>
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<tr>
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<td>0.05/93</td>
<td>&lt;LOQ/0</td>
<td>0.04/0.10</td>
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<td>0.05/0.38</td>
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<td>1.86/88.9</td>
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<td>0.55/88.9</td>
<td>0.21/100</td>
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<td>0.04/0.29</td>
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<tr>
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<td>0.09/98</td>
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<td>&lt;LOQ/0</td>
<td>0.93/100</td>
<td>0.22/100</td>
<td>&lt;LOQ/0</td>
<td>&lt;LOQ/0</td>
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<td>20.7/1.94</td>
<td>1.94/1.62</td>
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<td>3.93/0.58</td>
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<td>Vietnam</td>
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<td>0.31/0.02</td>
<td>0.02/0.04</td>
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1 detection frequency;
2 The sum concentrations of gallic acid esters (OG, PG and DG)
3 The sum concentrations of SPAs;
4 Total concentrations of BHT metabolites.