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

Wei Wang, ALEXANDROS GEORGE ASIMAKOPOULOS, Khalid Abualnaja, Adrian Covaci, Bondi Gevao, Boris Johnson-Restrepo, Taha Kumosani, Govindan Malarvannan, Tu Binh Minh, Hyo-Bang Moon, Haruhiko Nakata, Ravindra K Sinha, and Kurunthachalam Kannan

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2 **homes and microenvironments**

3

4 **Wei Wang<sup>1</sup>, Alexandros G. Asimakopoulos<sup>1</sup>, Khalid O. Abualnaja<sup>2</sup>, Adrian Covaci<sup>3</sup>,**  
5 **Bondi Gevao<sup>4</sup>, Boris Johnson-Restrepo<sup>5</sup>, Taha A. Kumosani<sup>2</sup>, Govindan**  
6 **Malarvannan<sup>3</sup>, Tu Binh Minh<sup>6</sup>, Hyo-Bang Moon<sup>7</sup>, Haruhiko Nakata<sup>8</sup>, Ravindra K.**  
7 **Sinha<sup>9</sup>, and Kurunthachalam Kannan<sup>1,2,\*</sup>**

8

9 <sup>1</sup>Wadsworth Center, New York State Department of Health, and Department of  
10 Environmental Health Sciences, School of Public Health, State University of New York at  
11 Albany, Empire State Plaza, P.O. Box 509, Albany, New York 12201-0509, United States

12

13 <sup>2</sup>Biochemistry Department, Faculty of Science, Experimental Biochemistry Unit, King Fahd  
14 Medical Research Center and Bioactive Natural Products Research Group, King Abdulaziz  
15 University, Jeddah, Saudi Arabia

16 <sup>3</sup>Toxicological Center, University of Antwerp, Universiteitsplein 1, 2610 Wilrijk-Antwerp,  
17 Belgium

18

19 <sup>4</sup>Environmental Management Program, Environment and Life Sciences Center, Kuwait  
20 Institute for Scientific Research, P.O. Box 24885, Safat 13109, Kuwait

21

22 <sup>5</sup>Environmental and Chemistry Group, Sede San Pablo, University of Cartagena, Cartagena,  
23 Bolívar 130015, Colombia

24

25 <sup>6</sup>Faculty of Chemistry, Hanoi University of Science, Vietnam National University, Hanoi, 19  
26 Le Thanh Tong, Hoan Kiem, Hanoi, Vietnam

27 <sup>7</sup>Department of Marine Sciences and Convergent Technology, College of Science and  
28 Technology, Hanyang University, Ansan, South Korea

29

30 <sup>8</sup>Graduate School of Science and Technology, Kumamoto University, 2-39-1 Kurokami,  
 31 Kumamoto 860-8555, Japan

32

33 <sup>9</sup>Department of Zoology, Patna University, Patna, 800 005, India

34

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

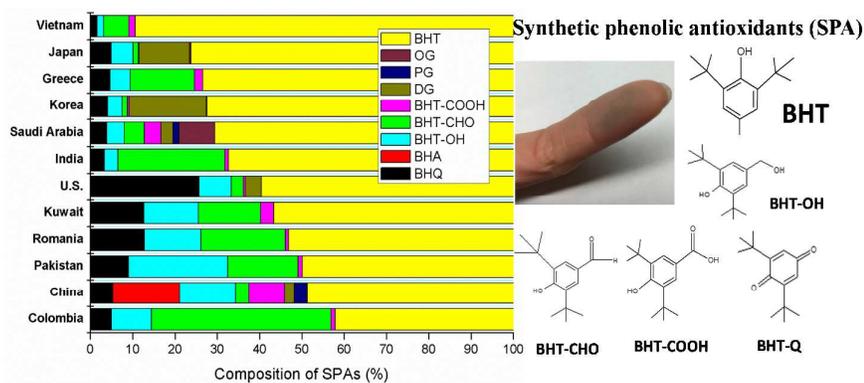
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41 **TOC**

42



44 **Abstract**

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

62

63

64 **Introduction**

65 Synthetic phenolic antioxidants (SPAs) are the most frequently used antioxidants in many  
66 consumer products including foodstuffs.<sup>1</sup> The U.S. Food and Drug Administration (FDA)  
67 and the European Union (EU) regulate the use of SPAs, including 2,6-di-tert-butyl-4-  
68 hydroxytoluene (BHT), 2-tert-butyl-4-methoxyphenol (BHA), propyl (PG)-, octyl- (OG) and  
69 dodecyl- (DG) gallate as food additives.<sup>2,3</sup> SPAs are widely used in food and feed industries  
70 including confectionery and edible oil industry. BHT is also used in a wide range of  
71 cosmetics.<sup>4</sup> Furthermore, SPAs are currently used in a wide range of products including  
72 packing materials, rubber, plastics, hand-washing soap, pet foods, chewing gum and as anti-  
73 skinning agents in paints and inks<sup>1</sup>. SPAs might be released into the indoor environment  
74 from various household commodities and indoor dust can be a source of human exposure.

75 In recent years, concerns with regard to the safety of SPAs have increased, due to  
76 their potential toxicity.<sup>4</sup> Nevertheless, considerable controversy surrounds with regard to the  
77 link between BHT/BHA and carcinogenicity.<sup>5,6</sup> BHA has been shown to possess estrogenic  
78 properties in breast cancer cells, and has been shown to disrupt estrogen receptor  
79 functions.<sup>4,6</sup> A few other studies have not found such estrogenic effects.<sup>7,8</sup> The metabolites of  
80 BHT have been reported to induce peroxides in mice and rats, which results in cellular DNA  
81 damage and instigate cancer.<sup>9</sup> BHT has been reported to be metabolized to 3,5-di-tertbutyl-4-

82 hydroxybenzoic acid (BHT-COOH) through oxidation of alkyl group via the corresponding  
83 alcohol (BHT-OH) and aldehyde (BHT-CHO) or to 2,6-di-tert-butylcyclohexa-2,5-diene-1,4-  
84 dione (BHT-Q) through oxidation of the  $\pi$ -system.<sup>10</sup> In addition, BHT-OH and BHT-CHO  
85 are photoproducts of BHT.<sup>11</sup>

86 Although SPAs are considered safe for human health at recommended doses (for  
87 instance, the acceptable daily intake of BHT has been set at 250  $\mu\text{g}/\text{kg}/\text{day}$ ), its ubiquitous  
88 presence and the controversial toxicological data suggest the need for more information on  
89 these classes of chemicals. A few studies have reported the occurrence of SPAs in surface  
90 water, wastewater and foodstuffs.<sup>4,12,13,14,15</sup> However, no information is available on the  
91 occurrence of SPAs and their metabolites in indoor environments. Because SPAs are used  
92 in a variety of consumer products, including adhesives, personal care products and  
93 pharmaceuticals<sup>1</sup>, humans can be exposed to these compounds via both oral ingestion and  
94 inhalation of settled dust.<sup>16,17</sup> In this study, a wide range of SPAs and their metabolites were  
95 determined in indoor dust samples collected from 12 countries, for the first time, to  
96 elucidate the occurrence, sources and human exposure profiles through dust ingestion.

97

## 98 **Materials and Methods**

99 **Sample Collection.** A total of 339 indoor dust samples were collected from 12 countries,  
100 with 241 samples from homes and 98 from other microenvironments (laboratories, offices,

101 cars, and e-waste workshop) (Table S1; Supporting Information). House dust samples (5-50  
102 g) were collected from select cities in China (CN, number of samples: n = 26), U.S. (US,  
103 14), India (IN, 30), Japan (JP, 10), Greece (GR, 20), Colombia (CO, 40), Pakistan (PK, 22),  
104 Saudi Arabia (SA, 10), South Korea (KR, 26), Kuwait (KW, 15), Romania (RO, 20), and  
105 Vietnam (VN, 8) during 2012 to 2014. Dust samples from laboratories, offices, cars, and  
106 public areas were collected from South Korea (lab, n = 10; office, 14), Kuwait (car, 15),  
107 Pakistan (car, 6; office 31), Saudi Arabia (car, 10), and Vietnam (e-waste work shop, 4;  
108 market, 8). Floor dust samples were obtained from vacuum cleaner bags in each of the  
109 sampling sites following the same sampling protocol, with the exception of samples from  
110 China and India, which were obtained by sweeping the floor. The vacuum and the sweeping  
111 tool were pre-cleaned before each sampling. Only bedrooms and living rooms of homes and  
112 apartments (all countries) were selected for sampling. We employed volunteers to collect  
113 samples in each country, and these volunteers sampled sites for which they had access. This  
114 approach of opportunistic sampling is not expected to be fully representative of the country,  
115 but it can obtain a sufficient sample size in the variety of different types of  
116 microenvironments (homes, offices, cars, etc.) desired to meet the objectives of the study.  
117 All samples were transported to the laboratory at Wadsworth Center, sieved through a 150  
118  $\mu\text{m}$  sieve, homogenized, packed in clean aluminum foil, and stored at 4 °C until analysis.

119       **Chemicals and Reagents.** Target analytes and their structure are shown in Table S2.  
120       BHT, BHT-d21, BHT-OH, BHT-Q, BHT-CHO, BHT-COOH, DG and PG were obtained  
121       from Sigma-Aldrich (St. Louis, MO) and OG was purchased from Chem Cruz (Dallas,  
122       Texas). Isotopically-labeled  $^{13}\text{C}_{12}$ -methyl paraben, ( $^{13}\text{C}_{12}$ -MeP) and  $^{13}\text{C}_{12}$ -propyl paraben  
123       ( $^{13}\text{C}_{12}$ -PrP) (RING- $^{13}\text{C}_{12}$ , 99%) were obtained from Cambridge Isotope Laboratories  
124       (Andover, MA) and Wellington Laboratories (Guelph, Ontario, Canada). HPLC grade  
125       methanol was supplied by J.T. Baker (Phillipsburg, NJ). Ultra-pure water (18.2 $\Omega$ ) was  
126       generated using a Milli-Q system (Millipore, Billerica, MA).

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

137       **Instrumental Analysis.** BHT was analyzed using a GC (Agilent Technologies 6890)

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

149 **Quality Assurance and Quality Control (QA/QC).** With every set of 20 samples  
150 analyzed, a procedural blank, a pair of pre-extraction matrix spike sample (fortified before  
151 extraction), a pair of matrix match (fortified after extraction) and duplicate samples were  
152 analyzed. Trace levels of BHT-CHO (approximately 0.25 and 0.34 ng/g, respectively) were  
153 found in procedural blanks in one batch, and background subtraction was performed for this  
154 batch of samples. Recoveries of SPAs in spiked dust matrices ranged from 69 ± 22% for OG  
155 to 106 ± 12% for BHT (Table S4). Duplicate analysis of randomly selected samples (n = 12)  
156 showed a coefficient of variation of <20%. Quantification of SPAs was performed by an

157 isotope-dilution method based on the response of BHT-d21 (for BHT),  $^{13}\text{C}_{12}$ -MeP (for BHT-  
158 Q, BHA, BHT-OH, BHT-CHO, and BHT-COOH),  $^{13}\text{C}_{12}$ -PrP (for OG, PG and DG). The  
159 limits of quantification (LOQs) were 0.12 ng/g for BHT-CHO and BHT-COOH, 0.6 ng/g for  
160 BHA, 1.2 ng/g for BHT, BHT-Q and BHT-OH, and 2.4 ng/g for DG, OG and PG (Table S4),  
161 which were calculated from the lowest acceptable calibration standard and a nominal sample  
162 weight of 0.25 g (LOQs for LC/MS/MS analyses were corrected based on diluted  
163 subsamples). A midpoint calibration standard (in methanol) was injected as a check for  
164 instrumental drift in sensitivity after every 20 samples, and a pure solvent (methanol) was  
165 injected as a check for sample carry-over. Instrumental calibration was verified by injection  
166 of 10 calibration standards (ranging from 0.02 to 100 ng/g), and the linearity of the  
167 calibration curve ( $r^2$ ) was  $> 0.99$ . The concentrations of BHT-CHO in the third extraction of  
168 30 randomly selected dust samples were  $< 1\%$  of the values found in the first three  
169 extractions while others are undetectable, which indicated that the extraction cycles used in  
170 this study completely extracted the target chemicals. For ease of discussion and exposure  
171 assessment, dust from homes and other microenvironments were segregated.

172 **Statistical Analysis.** Statistical analyses were performed with Origin ver. 8 (for profile  
173 analyses) and SPSS 16.0 software (for correlation analyses, test for normality and ANOVA).  
174 Normality of the data was checked by Shapiro-Wilk test. The 95% upper confidence limit  
175 (UCL) was calculated using ProUCL 4.0. Differences between groups were compared using

176 a one-way ANOVA followed by a Tukey test. Prior to one-way ANOVA, the data were log-  
177 transformed to meet the normality assumptions. The probability value of  $p \leq 0.05$  was set for  
178 statistical significance.

179

## 180 **Results and Discussion**

181 **SPAs in House Dust.** BHT was found in 99.5% of house dust samples and the  
182 concentrations varied by five orders of magnitude, from  $<1.2$  ng/g to  $118$   $\mu\text{g/g}$  (Table 1).  
183 Highest concentrations of BHT were found in house dust collected from Japan (range:  $3.19$ -  
184  $33.9$   $\mu\text{g/g}$ ) and South Korea ( $2.27$ - $118$   $\mu\text{g/g}$ ), which were 2-3 orders of magnitude higher  
185 than the concentrations found in countries with the lowest levels, Romania ( $0.04$ - $1.59$   $\mu\text{g/g}$ )  
186 and Vietnam ( $0.09$ - $0.74$   $\mu\text{g/g}$ ). SPAs are used as preservatives or additives in household  
187 products,<sup>15,18</sup> which can contribute to their occurrence in settled dust. BHT is also widely  
188 used in plastic materials as an antioxidant to stabilize the polymer during processing and to  
189 protect plastics through their lifespan<sup>15</sup>. High concentrations of BHT found in both house  
190 dust (median  $1.55$   $\mu\text{g/g}$ ) and sewage sludge (median  $2.35$   $\mu\text{g/g}$ ) from China indicate the  
191 widespread usage of this compound in China.<sup>19</sup>

192 BHA, a endocrine disrupting chemical (EDC) with potential as a tumor promoter,<sup>20,21</sup>  
193 was found only in house dust from China (ranged from  $0.01$  to  $7.44$   $\mu\text{g/g}$  for five cities),  
194 whereas this compound was not found in house dust from the other eleven countries studied.

195 Propyl-, octyl- and dodecyl- gallates are often used as antioxidants in cosmetics and food  
196 industry (especially in oils and fats to prevent oxidation).<sup>22,23</sup> In dust samples, distribution  
197 pattern for gallates was different from that of other SPAs, indicating the different usage and  
198 sources of gallates. OG was only detected in house dust from China (<LOQ-0.04 µg/g),  
199 Korea (<LOQ-0.14), Saudi Arabia (0.09-0.75) and Japan (<LOQ-0.11), whereas PG was  
200 only found in China (<LOQ-1.25) and Saudi Arabia (<LOQ-0.11). DG was found in house  
201 dust from China (<LOQ-0.32), Korea (0.31-7.56), the U.S. (<LOQ-0.76), Japan (<LOQ-  
202 18.2) and Saudi Arabia (0.01-11.9). Gallates were not found in house dust from Greece,  
203 Romania, Kuwait, India, Colombia and Vietnam.

204

205 **BHT Metabolites in House Dust.** BHT metabolites were found in all house dust samples  
206 at total concentrations ( $\Sigma$ MTs) that ranged from 0.01 to 35.1 µg/g. The most abundant  
207 metabolites of BHT were BHT-CHO, BHT-OH and BHT-Q, with median concentration  
208 ranges of 0.01 to 0.41, <LOQ to 0.93 and <LOQ to 1.86 µg/g, respectively, across twelve  
209 countries. The detection frequencies of BHT-Q, BHT-OH, BHT-COOH and BHT-CHO  
210 ranged from 38 to 100%, 91 to 100%, 87 to 100%, and 75 to 100%, respectively, across  
211 twelve countries. In general, BHT-Q, BHT-OH, BHT-CHO, and BHT-COOH collectively  
212 accounted for, on average, 9 to 58% of the sum of concentrations of SPAs and their  
213 metabolites ( $\Sigma$ SPA). BHT-COOH was found at the lowest concentration in dust. Compared

214 with other countries studied, higher concentrations of BHT-COOH were found in dust  
215 samples from China (median: 0.27  $\mu\text{g/g}$ ) and Saudi Arabia (0.13), and BHT-Q was dominant  
216 in dust from the U.S. (1.86  $\mu\text{g/g}$ ), Japan (0.87), and Korea (0.47). Similar to the distribution  
217 of BHT, the highest median concentration of  $\Sigma\text{MTs}$  was determined in house dust from the  
218 U.S. (3.02  $\mu\text{g/g}$ ), Japan (1.94  $\mu\text{g/g}$ ), and South Korea (1.37  $\mu\text{g/g}$ ). The toxic effects BHT-  
219 metabolites including DNA damage and carcinogenicity have been reported in several  
220 studies<sup>24,25,26,27,28</sup>. The widespread occurrence of BHT-metabolites in indoor dust at high  
221 concentrations suggests the need for further studies on potential health effects of these  
222 metabolites.

223 **SPAs in Dust from Various Microenvironments.** The concentrations of  $\Sigma\text{SPAs}$  in  
224 indoor dust from various microenvironments varied widely (Table S5), with the highest  
225  $\Sigma\text{SPA}$  mean concentrations found in an e-waste workshop (4670  $\mu\text{g/g}$ ) in Vietnam. The  
226 median concentrations of  $\Sigma\text{SPAs}$  in car dust (3.76  $\mu\text{g/g}$ ) from Saudi Arabia were similar to  
227 those reported for house dust from the same country (3.93  $\mu\text{g/g}$ ). Nevertheless,  $\Sigma\text{SPA}$   
228 concentrations in house dust from rural homes (range: 0.64-10.9  $\mu\text{g/g}$ ) in Pakistan were  
229 significantly lower than those from urban (1.58-14.6  $\mu\text{g/g}$ ) homes, which might be attributed  
230 to different lifestyles including the usage of consumer products. The concentrations of BHT  
231 in dust from laboratories and offices in South Korea (range: 2.32-73.8, median: 22.9 and  
232 33.0  $\mu\text{g/g}$ , respectively) were significantly ( $p < 0.05$ ) higher than those in homes (median:

233 8.21  $\mu\text{g/g}$ ). As one of the widely used stabilizers, SPAs are present in plastics at levels of  
234 hundreds to a few thousand mg per kg,<sup>29</sup> which might explain for the high concentrations  
235 found in numerous microenvironments, such as car, office, and e-waste workshop. Similarly,  
236 significantly ( $p < 0.05$ ) higher BHT-metabolite concentrations were found in dust from  
237 offices (2.70-29.9  $\mu\text{g/g}$ ) and laboratories (3.60-25.1  $\mu\text{g/g}$ ) than in homes (0.51-5.86  $\mu\text{g/g}$ ) in  
238 South Korea. However, higher concentrations of gallates were found in homes (0.31-7.58  
239  $\mu\text{g/g}$ ) than in laboratories (0.23-2.48  $\mu\text{g/g}$ ) and offices (0.04-5.79  $\mu\text{g/g}$ ). These differences in  
240 the profiles of SPAs suggest that gallates might be primarily used in household products. The  
241 use of SPAs in petroleum products and plastics such as electronic equipment and cables, that  
242 are widely found in offices/laboratories, is a possible source of their occurrence in these  
243 microenvironments. However, dust samples from Pakistan did not show a significant  
244 difference in SPA concentrations between offices and homes. The nature and magnitude of  
245 indoor products (such as computer, furniture, personal care products, food packages, interior  
246 decorations and building material) and ventilation can possibly contribute to variations in  
247 SPA profiles in different microenvironments. The highest BHT, gallate and  $\sum\text{SPA}$   
248 concentrations were found in dust from an e-waste workshop in Vietnam, in the  
249 concentration ranges of 425 - 3460, 0.02 - 684, and 429 - 4670  $\mu\text{g/g}$ , respectively; these  
250 values were four orders of magnitude ( $p < 0.05$ ) higher than those found in dust from homes  
251 and offices in Vietnam. The use of BHT in plastic components of e-waste might explain the

252 high concentrations found in dust from e-waste workshop<sup>4</sup>. The high contamination of SPAs  
253 in e-waste workshop found in this study suggests the need for further investigations on  
254 occupational exposures in e-waste workshops.

255 **SPAs and Their Metabolite Profiles.** A significant correlation was found between BHT  
256 and  $\sum$ MTs in house dust samples from China ( $p < 0.05$ ) and Colombia ( $p < 0.05$ ), which  
257 indicated that the dominant source of BHT-metabolites is degradation of BHT itself;  
258 however, no significant relationship was found between BHT and  $\sum$ MTs in dust from other  
259 countries, possibly due to the existence of other sources and transformation pathways. For  
260 all the 224 house dust samples, significant correlations ( $p < 0.05$ ) were found among BHT  
261 metabolites (Table S6), including BHT-Q, BHT-OH and BHT-COOH, except for BHT-  
262 CHO. The contribution of each of the target compounds to the sum concentrations of  
263  $\sum$ SPAs analyzed in dust is presented in [Figure 1](#). BHT accounted for up to 89% of  $\sum$ SPA  
264 concentrations in dust from Vietnam, followed by Japan (76%) > Greece (73%) > Korea  
265 (72%) > Saudi Arabia (71%) > India (67%) > the U.S. (60%) > Kuwait (57%) > Romania  
266 (53%) > Pakistan (50%) > China (49%) > Colombia (42%).  $\sum$ MTs accounted for 58% of  
267 the total concentrations in dust from Colombia, followed by Pakistan (50%) > Romania  
268 (47%) > Kuwait (43%) > the U.S. (37%) > India (33%) > China (30) > Greece (27%) >  
269 Saudi Arabia (17%) > Japan (12%) > Vietnam (11%) > Korea (9%). The highest

270 contributions of BHT-Q, BHT-OH, BHT-CHO and BHT-COOH to  $\Sigma$ MTs were found in  
271 dust from the U.S. (70%), Pakistan (47%), India (78%), and China (28%), respectively.

272 The proportion of BHT was significantly elevated in dust from an e-waste workshop in  
273 Vietnam, which suggested that electronic products are an important source for this chemical.  
274 Different profiles were found for the contribution of BHT in dust samples from offices,  
275 laboratories, and homes in Korea, with the lowest contribution of  $\Sigma$ MTs found in offices,  
276 which suggested different emission sources between homes and the workplace  
277 microenvironment. A higher proportion of  $\Sigma$ MTs was found in urban than rural homes in  
278 Pakistan, with elevated contribution from BHT-Q in urban homes possibly attributed to  
279 differences in the transformation processes. Elevated contribution of OG and PG was found  
280 in dust from homes than cars in Saudi Arabia. The proportion of DG was significantly  
281 higher in house dust than laboratory and office dusts in Korea. OG, PG and DG are mainly  
282 used in foodstuffs, cosmetics and personal care products<sup>22,23</sup>.

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

288 Korea and Pakistan. BHT-COOH was the minor contributor of BHT metabolites, which was  
289 a secondary degradation product from BHT-CHO.

290 **Potential Indoor Sources of SPAs and Metabolite Products.** The results of this study  
291 suggests that phenolic antioxidants are widespread in indoor house dust, possibly due to  
292 their high production volumes and usage in several consumer products and foodstuffs. SPAs  
293 are weakly bound to their substrate, and are thus easily leached from products and enter the  
294 environment<sup>30</sup>. BHT is relatively less stable in the indoor environment, which results in  
295 abiotic degradation to products such as BHT-CHO, BHT-OH and BHT-Q, which are found  
296 at high concentrations in dust. However, the variations in metabolite profiles in different  
297 indoor environments and countries suggest the influence of various environmental factors,  
298 and further studies are needed to understand the mechanism of transformation of BHT.

299 The occurrence of OG (dr: 0-100%), PG (dr: 0-90%), and DG (dr: 0-100%) in dust from  
300 several countries indicates potential sources originating from consumer applications such as  
301 cosmetics, hair care products, soaps, shampoos, skin lotions, deodorants, adhesives,  
302 margarine, peanut butter and lubricants<sup>22</sup>. Among the three gallates, DG was found as the  
303 dominant contributor with the highest detection frequency (detected from six countries) and  
304 residue concentrations (< LOQ – 18.2 µg/g), indicating high usage of DG. DG is used as an  
305 anti-ageing agent in polymers.<sup>31</sup> The differences in the distribution of gallates, BHA and  
306 BHT in house dust indicate the existence of multiple sources for these compounds.

307           **Exposure Assessment.** We estimated the daily intake (EDI) of SPAs via dust  
308 ingestion for different age groups. Median and high exposure scenarios were assessed for  
309 BHT,  $\Sigma$ MTs and SPAs based on the median and 95<sup>th</sup> percentile concentrations determined  
310 in dust from household and microenvironments (For details, see supporting information  
311 section S1.3; S2.1; Table S7-S9; Figure S2, S3). The acceptable dietary intake (ADI) of  
312 BHT has been established by European Food Safety Authority (EFSA) in 2012 at 0.25  
313 mg/kg/d.<sup>32</sup> Compared with the mean EDI for BHT via dietary exposure for the general  
314 population in Korea reported to be 40  $\mu$ g/kg bw/day and for the U.S. population at 0.39 and  
315 0.78 mg/kg/d for mean and high exposure scenarios reported by the Joint FAO/WHO  
316 Expert Committee on Food Additives (JECFA) (2000)<sup>4,33</sup>, the EDIs from house dust were  
317 minor (222 ng/kg/d - maximum). However, since no estimation of EDI of BHT metabolites  
318 has been carried out yet., this study assessed the EDI for  $\Sigma$ MTs via house dust exposure and  
319 the highest EDI was estimated for toddlers from the U.S. with 152 ng/kg/d. Overall,  
320 contribution of dust ingestion to SPA exposure was two to three orders of magnitude lower  
321 than that from dietary route and the ADI.

322           Although this is the first study to report occurrence of a chemical that was not  
323 originally suspected to be present in indoor dust, our study has several limitations. First, our  
324 small sample size available for each microenvironment (e.g, e-waste workshop) limits our  
325 ability to draw inference on the sources and transformation pathways of SPAs. However, it

326 should be noted that the validity of our results are not affected and further studies with larger  
327 sample sizes are needed for the characterization of SPAs in microenvironments. The  
328 sampling approach was designed to meet the objective of providing accurate measurements  
329 for an emerging class of chemical contaminant in indoor dust. Second, although detailed  
330 instructions were provided, household dust samples were collected by local participants and  
331 volunteers. Variability in the types of vacuums and sweeping tools used can introduce  
332 measurement variations and potential contamination. However, we selected specific particle  
333 sizes by sieving the samples in the laboratory which is expected to reduce potential variance  
334 introduced by sample collection.

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

342

### 343 **Associated Content**

344 Supporting Information

345 Supporting data for this article includes additional details of methods, discussion on  
346 exposure assessment, as well as sampling information (Table S1), chemical and instrument  
347 parameters (Table S2, S3), summary statistics for LOQs and recoveries (Table S4), SPAs  
348 concentrations in microenvironments (Table S5), correlation analyses (Table S6), exposure  
349 analyses parameters (Table S7), and compound specific exposure estimates (Table S8, S9).  
350 Profile plot for BHT metabolites and EDI estimates for compound specific exposure are  
351 contained therein.

352

### 353 **Author Information**

354 Corresponding Author

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

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

357 Notes

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359

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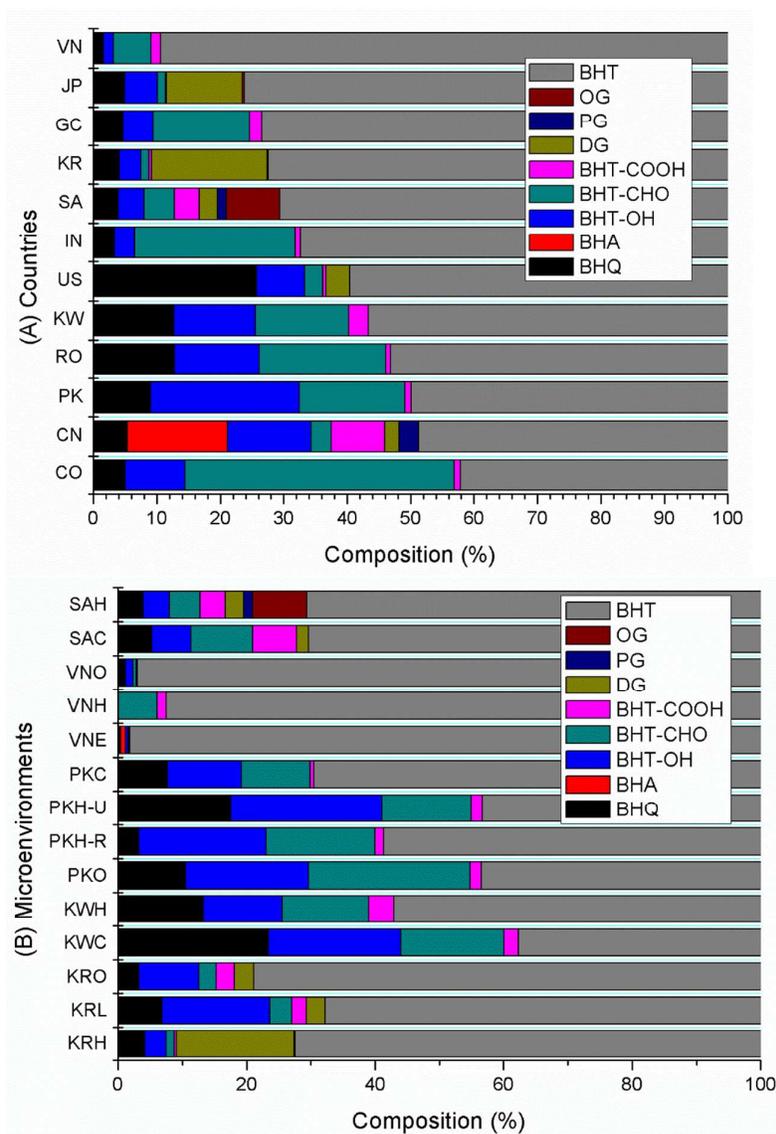
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**Figure 1.** Composition profiles of synthetic phenolic antioxidants in house dust from 12 countries (A) and indoor dust from various microenvironments (B) (SAH and SAC–house and car dust from Saudi Arabia; VNO, VNH and VNE–office, house and e-waste 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 ( $\mu\text{g/g}$  dr weight) from 12 countries

	BHQ	BHA	BHT-OH	BHT-CHO	BHT-COOH	DG	PG	OG	BHT	Gallate <sup>b</sup>	$\Sigma$ SPAs <sup>c</sup>	$\Sigma$ MTs <sup>d</sup>
<b>Greece (n=20)</b>												
median/df <sup>a</sup>	0.08/100	<LOQ/100	0.09/100	0.27/100	0.03/100	<LOQ/0	<LOQ/0	<LOQ/0	1.33/100	<LOQ/	1.74/	0.50/
range	0.02-0.42	<LOQ	0.02-0.38	0.06-0.86	0.003-0.18	<LOQ	<LOQ	<LOQ	0.08-4.56	<LOQ	0.84-5.03	0.16-1.69
<b>Pakistan (n=22)</b>												
median/df	0.18/95	<LOQ/0	0.48/90.9	0.34/100	0.02/95	<LOQ/0	<LOQ/0	<LOQ/0	1.01/100	<LOQ/	2.87/	1.18/
range	<LOQ-12.2	<LOQ	<LOQ-1.58	0.18-1.51	<LOQ-0.21	<LOQ	<LOQ	<LOQ	0.29-10.2	<LOQ	0.64-14.6	0.23-13.8
<b>Romania (n=20)</b>												
median/df	0.13/100	<LOQ/0	0.13/100	0.20/100	0.008/85	<LOQ/0	<LOQ/0	<LOQ/0	0.52/100	<LOQ/	1.16/	0.52/
range	0.04-0.31	<LOQ	0.07-0.29	0.0-0.62	<LOQ-0.10	<LOQ	<LOQ	<LOQ	0.04-1.59	<LOQ	0.39-2.05	0.24-0.85
<b>China (n=26)</b>												
median/df	0.17/84.6	0.50/100	0.42/96.2	0.10/87	0.27/100	0.07/62	0.10/76.9	<LOQ/42.3	1.55/96.2	0.24/	3.93/	1.07/
range	<LOQ-3.76	0.01-7.44	<LOQ-4.64	<LOQ-0.52	0.004-12.7	<LOQ-0.32	<LOQ-1.25	<LOQ-0.04	0.13-21.1	<LOQ-1.26	1.04-34.8	0.49-13.0
<b>Kuwait (n=15)</b>												
median/df	0.20/86.7	<LOQ/0	0.21/100	0.24/100	0.05/100	<LOQ/0	<LOQ/0	<LOQ/0	0.91/100	<LOQ/93.3	1.80/100	0.81/
range	<LOQ-2.48	<LOQ	0.03-2.33	0.11-0.56	0.006-0.51	<LOQ	<LOQ	<LOQ	0.35-17.4	<LOQ	0.79-18.8	0.28-5.25
<b>Korea (n=26)</b>												
median/df	0.47/93.8	<LOQ/0	0.38/100	0.14/100	0.05/93.8	2.07/100	<LOQ/0	0.018/77	8.21/100	2.11/100	11.5/	1.37/
range	<LOQ-2.36	<LOQ	0.11-1.73	0.02-3.02	0.003-1.06	0.31-7.56	<LOQ	<LOQ-0.14	2.27-118	0.31-7.58	3.21-121	0.51-5.86
<b>India (n=30)</b>												
median/df	0.05/93	<LOQ/0	0.048/100	0.38/100	0.01/87	<LOQ/0	<LOQ/0	<LOQ/0	1.02/100	<LOQ/	1.62/	0.53/
range	<LOQ-0.36	<LOQ	0.01-0.43	0.05-0.92	<LOQ-0.34	<LOQ	<LOQ	<LOQ	0.05-9.30	<LOQ	0.53-10.6	0.06-1.34
<b>U.S. (n=14)</b>												
median/df	1.86/88.9	<LOQ/0	0.55/88.9	0.21/100	0.04/89	0.27/89	<LOQ/0	<LOQ/0	4.31/100	0.23/	8.17/	3.02/
range	<LOQ-8.49	<LOQ	<LOQ-27	0.05-0.74	<LOQ-0.75	<LOQ-0.76	<LOQ	<LOQ	0.76-7.34	<LOQ-0.76	2.70-39.4	0.06-35.1
<b>Colombia (n=40)</b>												
median/df	0.049/98	<LOQ/0	0.09/98	0.41/100	0.01/87.5	<LOQ/0	<LOQ/0	<LOQ/0	0.41/93.9	<LOQ/	0.83/	0.59/
range	<LOQ-2.69	<LOQ	<LOQ-0.28	0.14-1.21	<LOQ-0.17	<LOQ	<LOQ	<LOQ	<LOQ-4.50	<LOQ	0.17-7.95	0.17-3.50
<b>Japan (n=10)</b>												
median/df	0.88/90	<LOQ/0	0.93/100	0.22/100	0.04/100	2.15/90	<LOQ/0	0.05/80	13.7/100	2.22/	20.7/	1.94/
range	0.366-1.461	<LOQ	0.03-1.45	0.006-1.58	0.001-0.08	<LOQ-18.2	<LOQ	<LOQ-0.11	3.19-33.9	<LOQ-18.2	4.29-43.7	0.03-3.80
<b>Saudi Arabia (n=10)</b>												
median/df	0.12/90	<LOQ/0	0.13/100	0.15/100	0.13/100	0.09/100	0.04/90	0.27/100	2.23/100	0.41/	3.93/	0.58/
range	<LOQ-0.39	<LOQ	0.03-0.37	0.05-0.33	0.03-2.66	0.01-11.9	<LOQ-0.11	0.09-0.75	0.40-6.34	0.14-12.2	1.43-16.3	0.30-2.79
<b>Vietnam (n=8)</b>												
median/df	<LOQ/38	<LOQ/0	<LOQ/38	0.01/100	0.003/75	<LOQ/0	<LOQ/0	<LOQ/0	0.17/100	<LOQ/	0.31/	0.02/
range	<LOQ-0.02	<LOQ	<LOQ-0.02	0.005-0.08	0.002-0.56	<LOQ	<LOQ	<LOQ	0.09-0.74	<LOQ	0.15-0.85	0.01-0.63

<sup>a</sup> detection frequency;<sup>b</sup> The sum concentrations of gallic acid esters (OG, PG and DG)<sup>c</sup> The sum concentrations of SPAs;<sup>d</sup> Total concentrations of BHT metabolites.

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