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ARTICLE *in* ENVIRONMENTAL SCIENCE & TECHNOLOGY · SEPTEMBER 2011

Impact Factor: 5.33 · DOI: 10.1021/es202507f · Source: PubMed

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Widespread Occurrence of Bisphenol A in Paper and Paper Products: Implications for Human Exposure

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Supporting Information

ABSTRACT: Bisphenol A (BPA) is used in a variety of consumer products, including some paper products, particularly thermal receipt papers, for which it is used as a color developer. Nevertheless, little is known about the magnitude of BPA contamination or human exposure to BPA as a result of contact with paper and paper products. In this study, concentrations of BPA were determined in 15 types of paper products (n = 202), including thermal receipts, flyers, magazines, tickets, mailing envelopes, newspapers, food contact papers, food cartons, airplane boarding passes, luggage tags, printing papers, business cards, napkins, paper towels, and toilet paper, collected from several cities in the USA. Thermal receipt papers also were collected from Japan, Korea, and Vietnam. BPA was found in 94% of thermal receipt papers (n = 103) at concentrations ranging from below the limit of quantitation (LOQ, 1 ng/g) to 13.9 mg/g (geometric mean: 0.211 mg/g). The majority (81%) of other paper products (n = 99) contained BPA at concentrations ranging from below the LOQ to 14.4 μg/g (geometric mean: 0.016 μg/g). Whereas thermal receipt papers contained the highest concentrations of BPA (milligram-per-gram), some paper products, including napkins and toilet paper, made from recycled papers contained microgram-per-gram concentrations of BPA. Contamination during the paper recycling process is a source of BPA in paper products. Daily intake (DI) of BPA through dermal absorption was estimated based on the measured BPA concentrations and handling frequency of paper products. The daily intake of BPA (calculated from median concentrations) through dermal absorption from handling of papers was 17.5 and 1300 ng/day for the general population and occupationally exposed individuals, respectively; these values are minor compared with exposure through diet. Among paper products, thermal receipt papers contributed to the majority (>98%) of the exposures.

INTRODUCTION

Bisphenol A (BPA) is an endocrine-disrupting chemical and has been implicated in a wide variety of adverse health outcomes in humans.[1−6] Due to its toxicity and widespread human exposure, BPA has received the attention of regulatory agencies across the globe.[1] An oral reference dose (RfD) for BPA of 50 μg/kg body weight (bw)/day has been established by the United States Environmental Protection Agency (USEPA) and the European Food Safety Authority (EFSA).[7,8] Nevertheless, some studies have reported that BPA can stimulate cellular responses and toxic effects at exposure doses below the currently recommended RfD.[1−3] The low-dose exposures and toxicity of BPA are subjects of debate.[6,9]

Produced in quantities of over 8 billion pounds each year worldwide, BPA is one of the most widely used chemicals, as the base chemical in the manufacture of polycarbonate plastics and the resin lining of food and beverage cans.[10,11] BPA can leach out of products, through the hydrolysis of ester bonds linking BPA monomers, under acidic or basic conditions.[12] BPA has been reported to occur in various environmental matrices, including air, water, sewage sludge, soil, dust, foodstuffs, and soft drinks.[2,3,13−15] Biomonitoring studies have reported widespread occurrence of BPA at ng/g or ng/mL levels in human tissues and fluids, including urine, blood (maternal blood, cord blood, and fetal blood), and other bodily fluids (amniotic fluid, follicle fluid, saliva, and breast milk).[1−3,16−21]

There are multiple sources that contribute to human exposure to BPA.[3,9] Diet, however, appears to be a major source of human exposure to BPA.[18,22−24] The U.S. National Toxicology Program reported that oral exposure from foods of adults in the USA to BPA ranged from 0.008 to 1.5 μg/kg bw/day.[22] On the basis of the leaching levels from consumer products and consumption of canned foods, BPA exposures have been estimated to range from <1 to 5 μg/kg bw/day.[3,21] However, recent studies indicate that human exposure doses to BPA have been underestimated because the contribution of nondietary sources to BPA exposure is not well understood. Nonfood sources that are presumed to be

Received: July 20, 2011
Accepted: September 23, 2011
Revised: September 12, 2011
Published: September 23, 2011

important sources of exposure include inhalation and dermal absorption, especially in occupational settings.[13] BPA is present in some cigarette filters [25] and there exits an association between smoking and urinary BPA concentrations.[26] A joint expert meeting held in 2010 by the Food and Agriculture Organization and the World Health Organization estimated inhalation exposure to BPA at 0.003 μg/kg bw/day and soil/dust ingestion at 0.0001 to 0.03 μg/kg bw/day for the general population.[27]

Additional sources of human exposure to BPA include thermal papers and paper currencies,[28,29] medical devices,[30] dental sealants,[31] and printing ink.[32] The thermal papers used in direct thermal printing process typically consist of two layers: the base paper (a standard paper formulation) and the thermal sensitive layer.[28] The thermal sensitive layer typically consists of three components: the thermochromic dye, a weakly acidic color developer (traditionally BPA), and a solvent (generally a long-chain aliphatic compound such as fatty acid, amide, alcohol). When the thermal sensitive layer is heated above the melting point of the solvent by a printing stylus, BPA (the developer) interacts with the thermochromic dye, donating protons which open the rings of the dye and increase the conjugation of the system, resulting in a color.[28] Large amounts of BPA have been used in the production of thermal receipt papers due to its efficacy, availability, and low cost.[28] Very high levels of BPA, of up to 3 to 22 mg/g, have been reported in thermal receipt papers.[28,29] Thermal receipt papers are produced in large quantities for use in cash register receipts, luggage tags, and tickets (bus/train and lottery).[28]

It has been reported that approximately 30% of thermal papers enter the paper recycling streams.[33] Recycling of thermal paper can introduce BPA into the cycle of paper production.[34] BPA can be absorbed into human skin during the handling of thermal receipt papers.[29] Because most people contact with thermal receipt papers and paper products on a daily basis, exposure of humans to BPA through dermal contact is expected.[35]

Two approaches have been used to derive estimates of daily intake of BPA. First, by summation or aggregation of the amount of BPA measured in various sources of exposure (e.g., food, food packaging, air, water, dust, paper products) for the estimation of total exposure ("aggregate sources" method).[36] Second, on the basis of biomonitoring data, such as the urinary BPA concentrations to estimate the total exposure that reflects all sources of exposure, both known and unknown ("back calculation" method).[17] Since BPA is biotransformed in the body, some uncertainties exist in the "back calculation" method of BPA exposure assessment.[17] Nevertheless, both of these approaches are dependent on various assumptions, such as body weight, skin surface area, amount of food or beverage consumed, daily volume of urine output, or ability of a single measurement to characterize general exposures.

Although a few studies have measured BPA in thermal receipt papers,[28,29] those studies involved small sample sizes ($n < 25$). Furthermore, exposure to BPA from the handling of papers was not estimated previously. In addition, BPA levels in other types of paper and paper products, such as flyers, magazines, tickets, mailing envelopes, newspapers, food contact papers (e.g., paper cups, plates), food cartons, napkins, kitchen rolls (i.e., paper towels), and toilet paper, that are frequently used in our daily lives, and the potential contribution of these paper types to BPA exposure remain unknown. In this study, we measured BPA concentrations in 202 samples, representing several types of papers and paper products, with the aim of establishing baseline concentrations in paper products and estimating potential exposure doses to BPA from the handling of papers.

MATERIALS AND METHODS

Sampling. Thermal receipt paper samples (n = 103) were collected from 58 locations, including supermarkets, grocery stores, banks, public libraries, gas stations, restaurants, and fast food restaurants in Albany, New York City, and Buffalo (New York), Boston (Massachusetts), Chicago (Illinois), Weston (Vermont), and Charlotte (North Carolina), in the USA in 2010 and 2011, and from retail stores in Matsuyama and Tokyo, Japan, Incheon, Korea, and Hanoi, Vietnam in 2010 and 2011. Other paper and paper products (n = 99) were grouped into 14 categories: flyers (e.g., advertisement brochures, store coupons, gift cards, bus schedule), magazines, tickets (e.g., train and bus tickets), mailing envelopes, newspapers, food contact papers (e.g., fast-food wrappers, paper cups, paper plates), food cartons (e.g., pizza paperboards, food buckets, snack food boxes), airplane boarding passes, airplane luggage tags, printing paper (i.e., regular copy paper), business cards, facial tissue (referred to as napkins in this study), paper towels (or kitchen rolls), and toilet paper. Most of the paper products were made from recycled paper.[32,34,37,38] These samples were collected mainly in Albany, New York, USA, and a few samples were collected in New York City and Buffalo (New York) and Boston (Massachusetts) in 2010 and 2011. Samples were individually wrapped in polyethylene bags and stored in a freezer at −20 °C until analysis.

Analysis. Paper and paper products were analyzed for BPA by following a method similar to that described earlier, with some modifications.[15] For thermal receipt papers, a circular spot (19 mm diameter) was taken in the middle of each receipt using a punch (Uchida Corp., Torrance, CA). After weighing the spot accurately ($\sim$ 0.0172 g), samples were cut into small pieces and extracted with methanol three times. Further details of the analysis are given in the Supporting Information. An Applied Biosystems API 2000 electrospray triple quadrupole mass spectrometer (ESI-MS/MS; Applied Biosystems, Foster City, CA) coupled with an Agilent 1100 Series HPLC system (Agilent Technologies Inc., Santa Clara, CA), consisting of a binary pump and an autosampler, was used for the measurement of BPA. An analytical column (Betasil C18, 100 × 2.1 mm column; Thermo Electron Corporation, Waltham, MA), connected in series with a Javelin guard column (Betasil C18, 20 × 2.1 mm; Thermo Electron Corporation), was used for analysis. Data were acquired using multiple reaction monitoring for the transitions of 227 > 212 for BPA (97%; Sigma-Aldrich, St. Louis, MO) and 239 > 224 for $^{13}C_{12}$−BPA (99%; Cambridge Isotope Laboratories, Andover, MA).

Quality Assurance and Quality Control (QA/QC). For each batch of 20 samples analyzed, a procedural blank, a spiked blank, a pair of matrix spiked samples, and duplicate samples were processed. The procedural blank, containing water in place of paper sample, was analyzed by passage through the entire analytical procedure as a check for interferences or laboratory contamination. BPA was not detected in procedural blanks or sample containers (i.e., polypropylene tube). The recoveries of BPA from spiked blanks and spiked matrices were 100 ± 15% and 101 ± 17% (mean ± SD), respectively. The relative standard deviation (RSD) of replicate analysis of samples was <10%. Eight thermal receipt samples and 10 samples from other paper types were randomly selected, and a fourth extraction was carried out

with 3 mL of methanol (after the first three extractions) to confirm that extraction of BPA from paper samples was complete. BPA was detected in the fourth extraction, at concentrations ranging from 12.5 to 23.3 ng/mL, in thermal receipt samples. In comparison with the extremely high concentrations of BPA detected in thermal receipt samples (on the order of milligram-per-gram), the residual BPA found in the fourth extraction was only 0.03 to 0.07% of the total concentration in the thermal receipt samples. For other paper types, BPA was not detected in the fourth extraction. Instrumental drift in sensitivity was checked by duplicate injection of samples and by analyzing a continuing calibration check standard after every ten samples. The calibration of BPA standard injected at concentrations ranging from 0.05 to 100 ng/mL showed good linearity (r > 0.99, n = 10). The limit of quantitation (LOQ) was 1 ng/g. Quantification was made using the isotope-dilution method. Prior to the analysis of samples, recovery and reproducibility of the method were verified by spiking known concentrations of BPA into selected paper samples. Because thermal receipt papers contained high concentrations of BPA, these samples were stored and analyzed in separate batches from other paper types.

Estimation of Daily Intake. Skin uptake/dermal absorption from handling of paper products (especially thermal paper receipts) can be a pathway of human exposure to BPA. In thermal papers, BPA exists as a free monomer that is mobile and transferable to objects with which it comes in contact.[29,35] The extent of human exposure to BPA through handling of paper products remains unknown.[29,35,39,40] Biedermann et al. [29] tested the transfer of BPA from thermal receipt paper to human skin and reported that holding a thermal paper with 15.2 g BPA/kg (mean value) for 5 s resulted in the transfer of 1636 ng BPA to the surface of the hand. On the basis of this information, we calculated a paper-to-skin transfer rate of BPA as k = 1636 ng/(15.2 g/kg·5s) = 21 522 ng/s. It has been reported that 27% of BPA found on skin surface penetrates and reaches the bloodstream within 2 h.[29]

We estimated human exposure to BPA based on the measured concentrations and frequency of handling of paper products. We assumed that the general population handles thermal receipts twice a day. The frequency of use and handling time are probably different for various paper types. Some paper types, including magazines, newspapers, napkins, paper towels (or kitchen roll), and toilet papers may be handled more frequently. We assumed that the general population handles these five paper types ten times a day and the remaining paper types five times a day. Individuals who work at cash registers (e.g., cashiers, bank tellers), however, can handle receipts more frequently on a daily basis. For occupational exposures, we assumed that individuals handle thermal receipts 150 times a day, and handle other paper types at rates similar to the general population. Based on the geometric mean, median, fifth and 95th percentile concentrations of BPA measured in our paper samples, we estimated the daily intake (EDI; ng/day) of BPA as shown in eq 1:

$$\mathrm{EDI} = k \times C \times \mathrm{HF} \times \mathrm{HT} \times \mathrm{AF}/10^6 \quad (1)$$

where k is paper-to-skin transfer coefficient of BPA (calculated as 21522.4 ng/s); C is the concentration of BPA in paper samples (μg/g); HF is handling frequency (times/day; for thermal receipt paper, 2 and 150 times/day for the general population and occupationally exposed individuals, respectively; for other paper types, 5 times/day for flyer, ticket, mailing envelope, food contact paper, food carton, airplane boarding pass, airplane luggage tag, printing paper, and business card, and 10 times/day for magazine, newspapers, napkin, paper towel, and toilet paper for both the general population and occupationally exposed individuals); HT is handling time of paper and is assumed to be 5 s for each handling; and AF is the absorption fraction of BPA by skin, which is 27%.[29] For example, if the median BPA concentration in thermal receipt is 0.299 mg/g (= 299 μg/g), the estimated median daily intakes of BPA, from handling of thermal receipts, by the occupationally exposed individual can be calculated as follows:

$$\begin{aligned}\mathrm{EDI} &= 21522.4\mathrm{ng/s} \times 299\mu\mathrm{g/g} \times 150\mathrm{times/day} \times 5\mathrm{s/time} \times 27\%/10^6 \\ &= 21.5224\mathrm{ng/s} \times 0.299 \times 150\mathrm{times/day} \times 5\mathrm{s/time} \times 27\% \\ &= 1303\mathrm{ng/day}\end{aligned}$$

Statistical Analysis. Geometric mean (GM), median, and concentration ranges were used to describe the results. Concentrations below the LOQ were substituted with a value equal to the LOQ divided by the square root of 2 for the calculation of GM. Differences between groups were tested by a one-way ANOVA with the Tukey test.

RESULTS AND DISCUSSION

Thermal Receipt Papers. BPA was detected in 94% of thermal receipt paper samples (n = 103) at concentrations ranging from below LOQ to 13.9 mg/g with a GM of 0.211 mg/g (Table 1). Of the 103 receipt samples analyzed, 73 (71%) were collected from Albany, New York. BPA concentrations in receipts from Albany were in the range of 0.005 to 9.38 mg/g with a GM of 0.341 mg/g (Figure 1). These values are slightly lower than those found in samples collected from other cities in the USA, including New York City, Buffalo, Boston, Chicago, Weston, and Charlotte (GM: 0.496 mg/g; one-way ANOVA, p > 0.05), but significantly lower than the concentrations found in samples from Incheon, Korea (GM: 1.56 mg/g; p < 0.01) and Hanoi, Vietnam (GM: 6.32 mg/g; p < 0.05). No significant difference was found in the concentrations of BPA in thermal receipt papers collected between Korea and Vietnam (Figure 1). Interestingly, BPA was not detected in any of the six thermal receipt paper samples collected from several stores in Matsuyama and Tokyo, Japan (Table 1). This is attributed to a phase-out of BPA usage in thermal receipt papers in Japan in 2001.[41] Although BPA was reported to have been replaced with Bisphenol S by a major manufacturer of thermal receipt papers in the USA, BPA is still widely present in thermal receipt papers from the USA in 2010−2011. Some receipt papers claimed to be "BPA-free" (specifically printed on the receipt papers), but all of these receipt papers contained hundreds of μg/g levels of BPA (GM: 217 μg/g).

A few earlier studies have reported BPA concentrations in thermal receipt papers.[28,29] Eight of 10 blank (unprinted) thermal receipt papers collected from retail stores in Wilmington, Massachusetts, USA, contained BPA at concentrations ranging from <LOQ (26 μg/g) to 0.17 mg/g (GM: 0.072 mg/g; Figure 1);[28] the reported concentrations were lower than the values found in our study (GM: 0.211 mg/g, range: <LOQ to 13.9 mg/g; p < 0.05). BPA was detected in 11 of 13 thermal receipt papers (GM: 2.47 mg/g; LOQ = 0.5 μg/g) from Zurich, Switzerland.[29] The GM concentration of BPA found in our study (0.211 mg/g) was 1 order of magnitude lower than what was

Table 1. BPA Concentrations in Thermal Receipt Papers (mg/g) From the USA, Japan, Korea, and Vietnam and in Other Types of Papers (μg/g) from Albany, New York, USA

BPA concentration in thermal receipt papers (mg/g)							
site	n^a	GM[b]	fifth percentile	median	95th percentile	range	detection ratio (%)
Albany, USA	73	0.341	0.0069	0.269	8.46	0.0048−9.38	100
other cities, USA	10	0.496	0.0144	3.26	12.3	0.0131−13.9	100
Japan[c]	6	0.0000007	0.0000007	0.0000007	0.0000007	<LOQ[d]	0
Korea	11	1.56	0.0166	5.89	9.79	0.0163−9.88	100
Vietnam	3	6.32	6.17	6.29	6.51	6.15−6.53	100
all thermal receipt papers	103	0.211	0.0005	0.299	9.31	<LOQ-13.9	94
BPA concentration in several papers and paper products (μg/g)							
paper type	*n*	GM	fifth percentile	median	95th percentile	range	detection ratio (%)
flyers	24	0.0230	0.0007	0.0226	0.346	<LOQ−0.598	88
magazines	5	0.0193	0.0083	0.0167	0.0520	0.0083−0.055	100
tickets	4	0.676	0.134	0.388	12.3	0.118−14.4	100
mailing envelopes	5	0.0015	0.0007	0.0007	0.0130	<LOQ-0.0159	40
newspapers	8	0.151	0.0315	0.277	0.656	0.0307−0.658	100
food contact papers	12	0.0038	0.0007	0.0014	0.248	<LOQ-0.264	50
food cartons	7	0.0134	0.0007	0.0471	0.0547	<LOQ-0.0549	71
airplane boarding passes	4	0.0510	0.0132	0.0451	0.364	0.0124−0.415	100
airplane luggage tags	4	0.0031	0.0007	0.0007	0.212	<LOQ-0.249[e]	25
printing paper	3	0.0197	0.0181	0.0203	0.0211	0.0178−0.0212	100
business cards	6	0.0238	0.0080	0.0279	0.0859	0.0075−0.100	100
napkins	8	0.0110	0.0009	0.0034	2.38	<LOQ-3.34	88
kitchen rolls (paper towels)	3	0.0014	0.0008	0.0018	0.0022	<LOQ-0.0022	67
toilet paper	6	0.0092	0.0019	0.0028	0.164	0.0018−0.180	100
all papers	99	0.0160	0.0007	0.0178	0.600	<LOQ-14.4	81

[a] *n*: number of samples. [b] GM: geometric mean. [c] not detectable. [d] LOQ: 1 ng/g. [e] 1 out of 4 samples was detectable.

reported from Switzerland (Figure 1; $p < 0.001$). Further, 100% of the thermal receipt papers collected from the USA contained BPA. It should be noted that our LOQ (1 ng/g) was two to 4 orders of magnitude lower than the LOQs reported in the two earlier studies (26 μg/g and 0.5 μg/g). The earlier studies reported the occurrence of BPA in 80−85% of the thermal receipt papers collected from grocery stores.[28,29]

The concentration/distribution of BPA in several portions of thermal receipt papers was compared. Six thermal receipt samples were randomly selected, and five 19 mm circular spots were taken from each receipt: upper left corner (denoted as ULC), lower left corner (LLC), middle (M), upper right corner (URC), and lower right corner (LRC). No remarkable difference in the concentrations of BPA was found among the five spots taken within each receipt paper (Figure S1; Supporting Information).

BPA has been used for the elastification of phenolic resins that are used as binding agents in printing inks. Thus, printing ink is considered a potential source of BPA in papers.[32] To examine potential sources of BPA on receipts, we determined BPA concentrations in two blank (unprinted) receipt-paper rolls, purchased from an office products supply store in Albany, New York. Of the two receipt-paper rolls, one was thermal and the other was regular ink-printing paper. The blank (unprinted) thermal receipt paper was analyzed in triplicate in two batches, and the concentration of BPA was found to be 8.88 ± 1.39 mg/g (mean ± SD), which was greater than the mean concentration of BPA (3.06 ± 3.65 mg/g) found for all printed thermal receipt samples combined. The regular (i.e., non-thermal) ink-paper receipt was also analyzed in triplicate, and the concentration of BPA was found to be 0.050 ± 0.005 μg/g, which was lower than the concentration of BPA (0.26 ± 1.48 μg/g) found in non-thermal papers analyzed in this study. Our results suggest that BPA contamination in thermal receipt papers originates mainly from the use/coating of BPA on the thermal paper as a color developer rather than from printing ink.[28]

Paper and Paper Products. Because BPA in thermal receipt paper is not chemically bound, it can easily be transferred from thermal paper to other objects, including various types of papers.[28,29] BPA contamination in paper products can arise from recycling of thermal receipt paper, along with other papers, and from the use of BPA for the elastification of phenolic resins in printing inks.[28,29] Recycled paper is used in the production of a wide range of paper products, from toilet papers, paper towels, newspapers to cartons for snack foods and cardboard boxes.[32,34,37,38] Recycling of thermal papers along with other papers can increase the risk of human exposure to BPA via cross-contamination of foods stored in recycled paper products. BPA has been found in recycled paper towels and other food-contact papers at higher levels than is found in virgin papers.[32] In this study, 14 types of paper and paper products contained BPA, in 81% of the samples analyzed. The overall BPA concentrations in the 99 paper samples ranged from < LOQ to 14.4 μg/g (GM: 0.016 μg/g). BPA concentrations were similar among the 13

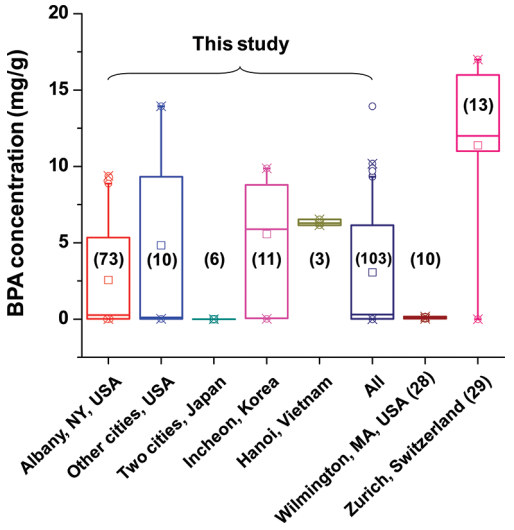

Figure 1. Comparison of BPA concentrations in thermal receipt papers from different countries. The box plot shows fifth (lower whisker), 25th (bottom edge of the box), 75th (top edge of the box), and 95th (upper whisker) percentiles. The lower and upper stars represent 1st and 99th percentiles, respectively. The arithmetic mean and median concentrations are given as the open square and the line within the box, respectively. The dots are outliers. The number in parentheses is the sample number for each group. In *x*-axis, "other cities, USA" includes New York City and Buffalo in New York, Boston in Massachusetts, Chicago in Illinois, Weston in Vermont, and Charlotte in North Carolina; "two cities, Japan" includes Matsuyama and Tokyo. The two plots on the right were based on published values, and the number within parentheses adjacent to *x*-axis is the reference number.

paper types, except for tickets, which contained elevated concentrations ($p < 0.05$). Usually, people place tickets aside thermal receipts in their wallets and tickets can be contaminated by BPA via contacting with thermal receipts. One outlier value was also found in a ticket sample (14.4 μg/g, Figure S2, Supporting Information), which elevated the overall mean concentration of BPA in tickets. BPA concentrations in paper products were three to 4 orders of magnitude lower than the concentrations found in thermal receipt papers (Figure S2, Supporting Information). BPA was detected in 100% of magazine papers, tickets, newspapers, airplane boarding passes, printing paper, business cards, and toilet papers (Table 1). Most of these products were made from recycled paper.[32,34,37,38]

Our results indicate that exposure of humans to BPA via paper products is ubiquitous because these papers are frequently used on a daily basis. The highest concentration of BPA was found in tickets (GM: 0.676 μg/g; Table 1), followed by newspapers (0.151 μg/g) and flyers (0.023 μg/g). BPA concentrations in ticket samples were 2 orders of magnitude higher than the concentrations found in mailing envelopes (0.0015 μg/g) and kitchen rolls (i.e., paper towels) (0.0014 μg/g). It is likely that paper products made from recycled papers contain BPA due to contamination arising from the recycling process, as explained above.

Few studies have reported the occurrence of BPA in paper and paper products.[32,34,37,38] Vinggaard et al. [32] collected 20 brands of paper towels, nine of which were made from recycled paper and the remainder from virgin pulp, from retail stores in Copenhagen, Denmark. BPA was detected at concentrations of 0.6 to 24.1 μg/g (GM: 3.9 μg/g) in recycled paper products, and the concentrations in virgin papers were below 0.04 μg/g, with the exception of one sample that contained 0.1 μg BPA/g. The concentrations of BPA reported for paper towels from Denmark were two to 3 orders of magnitude higher than the concentrations found in our paper towels (range: < LOQ to 0.0022; GM: 0.0014 μg/g) and toilet paper (range: 0.0018 to 0.180; GM: 0.0092 μg/g; Table 1). Gehring et al. [34] collected three kinds of toilet papers made from 100% recycled paper and municipal waste paper (including flyers, magazines, and newspapers) from local supermarkets in Dresden, Germany. BPA was found in all types of paper samples, at concentrations ranging from 3.2 to 46.1 μg/g (GM: 18.9 μg/g) for toilet paper and from 0.09 to 5.1 μg/g (1.24 μg/g) for other waste paper types. Ozaki et al.[37] collected 28 paper and cardboard products in Osaka, Japan, which have been used as food containers (e.g., cereal boxes), 12 of which were made from recycled paper and the remainder from virgin pulp. BPA was present in both virgin and recycled paper samples (67%), at a concentration range of <LOQ to 0.36 μg/g (GM: 0.044 μg/g) and <LOQ to 26 μg/g (GM: 0.255 μg/g), respectively.

BPA concentrations in various paper products (in the three studies cited above), regardless of the origin (i.e., virgin pulp or recycled paper), were similar. A recent study from Spain reported the occurrence of BPA in 48% of paper and cardboard boxes that are used for take-out fast food (GM: 0.0024 μg/g).[38] To our knowledge, our study is the first to report BPA concentrations in a wide range of paper products collected from the USA. The overall BPA concentrations (range: < LOQ to 14.4; GM: 0.016 μg/g) in paper products analyzed in our study were similar to the concentrations reported from Japan and Spain but were one to 2 orders of magnitude lower than those reported from Denmark and Germany. BPA is being replaced with alternatives in thermal receipt papers in many countries. The largest U.S. manufacturer of thermal receipt paper has reported replacement of BPA with Bisphenol S in thermal receipt papers since 2006.[42,43]

Sources of BPA in Papers. In addition to its use as a register receipt, thermal paper is also used in the production of other products, including shipping labels, luggage tags, lottery tickets, and fax paper.[33] It has been reported that approximately 30% of thermal papers enter recycling streams of municipal wastepaper.[33] Recycling of thermal paper can introduce BPA into the cycle of paper production,[34] and BPA has been reported to occur in the effluents of eight wastepaper recycling plants, in Shizuoka, Japan, at concentrations of 8 to 370 μg/L (GM: 79.2 μg/L).[44] In 2002, a report from the largest U.S. manufacturer of thermal paper indicated that the consumption of thermal paper in the USA and Canada was >160 000 tons per year.[45] On the basis of the median and 95th percentile concentrations of BPA found in thermal receipt papers (0.299 and 9.31 mg/g) analyzed in our study (Table 1), and the estimation that 30% of the thermal paper enters recycling processes of municipal wastepaper (i.e., 70% of the thermal paper is released into the environment),[33] we calculated that from 33.5 (based on median) to 1040 (based on 95th percentile) tons of BPA are released into the environment in the USA and Canada through the disposal of thermal receipt papers. This is an underestimate because it does not take into account the production estimates for thermal papers from other manufactures and imports from other countries.

Many paper products, such as paper towels, facial tissue, advertisement brochures (flyers), magazines, and newspapers, are made from recycled paper. The occurrence of BPA in various paper products can depend on the proportion of wastepaper introduced into the production process.[32,34,37] Many types of

Table 2. Estimated Daily Intake (ng/day) of BPA, via Handling of Papers, by the General Population and Occupationally Exposed Individuals

	general population				occupational exposure			
paper type	GM	fifth percentile	median	95th percentile	GM	fifth percentile	median	95th percentile
thermal receipts	12.3	0.0279	17.4	541	921	2.09	1303	40590
flyers	0.0033	0.0001	0.0033	0.0503	0.0033	0.0001	0.0033	0.0503
magazines	0.0056	0.0024	0.0048	0.0151	0.0056	0.0024	0.0048	0.0151
tickets	0.0982	0.0194	0.0564	1.79	0.0982	0.0194	0.0564	1.79
mailing envelopes	0.0002	0.0001	0.0001	0.0019	0.0002	0.0001	0.0001	0.0019
newspapers	0.0438	0.0091	0.0803	0.1906	0.0438	0.0091	0.0803	0.1906
food contact papers	0.0006	0.0001	0.0002	0.0360	0.0006	0.0001	0.0002	0.0360
food cartons	0.0019	0.0001	0.0068	0.0080	0.0019	0.0001	0.0068	0.0080
airplane boarding passes	0.0074	0.0019	0.0065	0.0528	0.0074	0.0019	0.0065	0.0528
airplane luggage tags	0.0004	0.0001	0.0001	0.0308	0.0004	0.0001	0.0001	0.0308
printing paper	0.0029	0.0026	0.0029	0.0031	0.0029	0.0026	0.0029	0.0031
business cards	0.0035	0.0012	0.0041	0.0125	0.0035	0.0012	0.0041	0.0125
napkins	0.0032	0.0003	0.0010	0.693	0.0032	0.0003	0.0010	0.693
kitchen rolls (paper towels)	0.0004	0.0002	0.0005	0.0006	0.0004	0.0002	0.0005	0.0006
toilet paper	0.0027	0.0005	0.0008	0.0477	0.0027	0.0005	0.0008	0.0477
total exposure (ΣEDI)[a]	12.5	0.066	17.5	544	921	2.13	1303	40593
exposure percentage from receipt (%)	98.6	42.2	99.0	99.5	100.0	98.2	100.0	100.0

[a] Rounded values.

paper and paper products are widely used as food packaging cartons and cardboard boxes, which are in direct contact with foodstuffs and can contribute to contamination of foods. When the food is heated (e.g., microwaved) with the paper product, this may accelerate the migration of BPA to the food.[32] Considering that paper products are placed in indoor environments, indoor dust [15,23,46] can be an additional source of BPA contamination in paper products and vice versa.

Exposure of Humans to BPA via Handling of Papers. The estimated fifth percentile, median, and 95th percentile daily intakes of BPA through dermal absorption, from handling of thermal receipt papers, by the general population were 0.028, 17.4, and 541 ng/day, respectively; the corresponding values for occupationally exposed individuals were 2.09, 1303 and 40 590 ng/day (Table 2). Among the other paper types, the highest daily BPA intakes (calculated from fifth percentile, median and 95th percentile concentrations in papers) by the general population and occupationally exposed individuals were from the handling of tickets (0.019, 0.056, and 1.79 ng/day) and newspapers (0.009, 0.080, and 0.191 ng/day). The estimated median and 95th percentile values for the total daily intakes of BPA (ΣEDI) from all 15 types of paper products analyzed in this study were 17.5 and 544 ng/day for the general population, and 1303 and 40 593 ng/day for occupationally exposed individuals, respectively (Table 2). It should be noted that the EDI values for BPA via handling of 14 types of papers (except for thermal receipt paper) by the general population and occupationally exposed individuals were same in our exposure assessments. The EDI values for BPA from the handling of paper products were 10-fold higher than those (8.44 and 43.5 ng/day) reported from dust ingestion in the USA.[15] Despite the high concentrations of BPA found in several types of paper products (e.g., tickets, newspapers, napkins), thermal receipt paper contributed to the preponderance of the daily BPA exposures (>98%; Table 2), with an exception of the fifth percentile value for the general population (42%; Table 2). This is mainly because thermal receipt papers contain extremely high concentration of BPA (Figure 1).

For the calculation of intakes adjusted for body weight (bw), the values were divided by a nominal body weight of 80 kg for adults. The estimated median daily intake values of BPA were 0.219 and 16.3 ng/kg bw/day for the general population and occupationally exposed individuals, respectively. Several previous studies have estimated BPA exposures in the range of 0.008 to 5 μg/kg bw/day for adults in the USA.[3,21,22] Assuming a total BPA intake value of 1 μg/kg bw/day, the dermal contact with paper contributes 1.6% (based on median) to 51% (based on the 95th percentile) of the total intake for occupationally exposed individuals. The EDI values calculated for BPA from paper products were several orders of magnitude lower than the RfD of 50 μg/kg bw/day (based on oral toxicity) established by the USEPA and the EFSA.[7,8]

There are several uncertainties in our estimate of BPA exposures from paper products. A dose−response relationship for the transfer coefficient of BPA from paper products to skin has not yet been established. The EDI can be higher when paper products are handled with wet or greasy fingers or by hand-to-mouth contact.[29] The duration and frequency of exposures can be much higher than what was used in our calculations. Inhalation during the handling of papers can be an important source of BPA exposures, and this was not estimated. Transfer of BPA from food-cartons to foods can be another source of human exposure. A recent study indicated that human exposure to BPA from unknown sources is much higher than what was previously assumed because many sources have still not been identified or characterized.[24] Studies have also reported that BPA at doses as low as tens to hundreds of ng/kg bw/day can cause adverse endocrine disruptive effects,[9,27] suggesting the significance of identifying all potential sources of human exposures. Our study fills an important knowledge gap by identifying paper products as a source of BPA exposure in the general population.

In summary, BPA was detected in most thermal receipt paper samples at very high concentrations. BPA concentrations in thermal receipt papers from the USA were lower than the concentrations found in samples from Korea and Vietnam. BPA was not found in thermal receipt papers from Japan. On the basis of the annual consumption of thermal paper in the USA and Canada, and median concentrations of BPA measured in thermal receipt papers (0.299 mg/g), we estimated that approximately 33.5 tons of BPA are released into the environment through discharge of thermal paper in the USA and Canada every year. BPA was found in other types of paper and paper products (such as newspapers, toilet paper, napkins, paper towels) that are frequently used on a daily basis. The estimated median daily intake values of BPA through dermal absorption from touching of paper products were 0.219 and 16.3 ng/kg bw/day for the general population and occupationally exposed individuals, respectively. The transfer of BPA from paper products into air and food, and subsequent human exposures, need to be examined in future studies.

■ ASSOCIATED CONTENT

Supporting Information. Details of the analytical method and a figure showing comparison of BPA in different portions of thermal receipt papers and a figure showing distribution of BPA in paper products. This material is available free of charge via the Internet at http://pubs.acs.org.

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