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RESEARCH ARTICLE

Temporal trends in exposure to parabens, benzophenones, triclosan, and triclocarban in adult females in Kyoto, Japan, from 1993 to 2016

Nao Yoshida[1] · Zhaoqing Lyu[1] · Sungmin Kim[2] · Nayoun Park[2] · Toshiaki Hitomi[3] · Yukiko Fujii[4] · Younglim Kho[2] · Kyungho Choi[5] · Kouji H. Harada[1]

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Abstract

Products used in daily life can contain chemicals such as parabens, benzophenones, triclosan, and triclocarban that have potential endocrine-disrupting effects. Little is known about the temporal trends of exposure levels to some of these chemicals in Japan. Our study assessed the intake and risk associated with exposure to commonly used chemicals. We measured the concentrations of five parabens, four benzophenones, and triclosan and triclocarban in 133 single spot urine samples. The urine samples were collected in 1993, 2000, 2003, 2009, 2011, and 2016 from healthy female residents in Kyoto, Japan. With the exception of methylparaben, ethylparaben, and butylparaben, there were no significant fluctuations in the concentrations of target chemicals over the study period; however, methylparaben, ethylparaben, and butylparaben showed temporal changes in concentrations. Methylparaben concentrations peaked in 2003 with a median value of 309 μg/g creatinine, ethylparaben concentrations peaked in 1993 with a median value of 17.3 μg/g creatinine, and butylparaben showed a decline, with the median values becoming non-detectable in 2009 and 2016. We calculated estimated daily intakes and hazard quotients for each chemical. In the analysis of total samples, 2.3% (3 samples) for butylparaben and 0.8% (1 sample) for propylparaben were found to surpass a hazard quotient of 1. Overall, 3% ($n=4$) of the study participants exceeded a hazard index of 1. The potential health risks associated with exposure to butylparaben and propylparaben emphasize the need for further monitoring and research.

Keywords Parabens · Benzophenones · Triclosan · Human biomonitoring · Temporal trend · Risk assessment · Japan

Introduction

Industrialization has advanced rapidly in recent decades, leading to increased exposure to industrial chemicals and by-products from the environment in daily life (Ambade et al. 2020, 2023; Patidar et al. 2023; Sankar et al. 2023; Sethi, et al. 2023). Parabens as preservatives, benzophenones as UV filters, and triclosan and triclocarban as antimicrobial agents are all chemicals that have been widely utilized in everyday products for an extended period. Consequently, people can easily come into contact with these substances through the use of such products. It has been suggested that these chemicals may have endocrine-disrupting effects (Wei et al. 2021; Mao et al. 2022; Gavrila et al. 2023; Milanović et al. 2023). Exogenous chemicals with endocrine-acting properties may mimic, block, or interfere with hormone action and exposure to them can cause hazards to human health (Yilmaz et al. 2020). These chemicals are ubiquitously present in both environmental settings and biological

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Nao Yoshida and Zhaoqing Lyu are contributed equally.

✉ Kouji H. Harada
kharada-hes@umin.ac.jp

[1] Department of Health and Environmental Sciences, Kyoto University Graduate School of Medicine, Yoshida Konoe, Sakyo, Kyoto 606-8501, Japan

[2] Department of Health, Environment & Safety, Eulji University, Seongnam 13135, Korea

[3] Department of Preventive Medicine, St. Marianna University School of Medicine, Kawasaki 216-8511, Japan

[4] Department of Pharmaceutical Sciences, Daiichi University of Pharmacy, Fukuoka 815-8511, Japan

[5] Department of Environmental Health Sciences, School of Public Health, Seoul National University, Seoul 08826, Korea

samples due to their extensive use as additives. They have been identified in various matrices, including environmental samples like indoor dust and surface water, as well as in human fluids such as urine, placenta, and breast milk (Wei et al. 2021; Gavrila et al. 2023; Milanović et al. 2023). Given the widespread occurrence of these potential endocrine-disrupting chemicals, it is crucial to conduct surveillance measures, including monitoring exposure levels and performing risk assessments, to prevent the potential hazards that may arise from exposure.

Parabens are used as preservatives and antiseptics in personal care products, pharmaceuticals, and food products since the 1920s (Soni et al. 2005; Hong et al. 2021). Their broad application has let to environmental detection and human exposure through dermal and oral routes (Wei et al. 2021). Increased use of lotions, sunscreens, and cosmetics correlates with higher urinary paraben levels (Dodson et al. 2020). Past studies have reported that some parabens exhibit estrogenic and antiandrogenic effects, potentially impacting sperm quality and testosterone levels in animal models (Fisher et al. 1999; Oishi 2001; Oishi 2002; Guerra et al. 2017; Pollock et al. 2017; Nowak et al. 2018). Epidemiological studies linked paraben exposure to metabolic diseases (Li et al. 2018; Kim and Chevrier 2020; Wei et al. 2021). In 2014, the European Union limited the use of propylparaben (PrP) and butylparaben (BuP) in cosmetics to 0.14% (EC 2014a). It also banned iso-PrP, iso-BuP, pentylparaben, and benzylparaben (BzP) in cosmetics (EC 2014b).

Benzophenones are a group of organic compounds, used as a UV filter in sunscreens and cosmetics. They can strongly absorb UV radiation, especially UV-A (320–400 nm) and UV-B (290–320 nm) radiation (Song et al. 2020; Mao et al. 2022). They are also used to coat the surface of plastic products to prevent photodegradation of polymers, such as food packaging materials. The primary route of exposure to benzophenones is by sunscreens and other consumer products on the skin. Among benzophenones, present studies indicate that benzophenone-1 (BP-1) and benzophenone-3 (BP-3) are the most likely to be detected in human biological samples (Mao et al. 2022). BP-1 is also the major metabolite of BP-3 in humans (Wang and Kannan 2013; Kim and Choi 2014). Some benzophenones have been found to have potential estrogenic and antiandrogenic effects in vitro and in vivo (Wang et al. 2016; Mao et al. 2022; Yao et al. 2024). Moreover, epidemiological studies correlated higher BP-3 exposure to lower thyroid hormone levels (Mustieles, et al. 2023). Currently in Japan, the use of benzophenone in products is regulated by the Ministry of Health, Labour, and Welfare of Japan, which allows up to 5% BP-3 for cosmetic use (Ministry of Health of Japan 2000). The U.S. Food and Drug Administration (FDA) allows up to 6% BP-3 in commercial sunscreen products (FDA 2017).

Triclosan and triclocarban have been used in soaps and detergents as antimicrobial agents. Triclosan and triclocarban have also recently been called into question for their endocrine-disrupting effects (Yueh and Tukey 2016; Zhang and Lu 2023). For instance, triclosan and triclocarban has been reported to be estrogenic, and can cause decrease in thyroid hormones in vitro and in vivo (Dodson et al. 2020; Iacopetta et al. 2021). Epidemiological studies also linked triclosan and triclocarban with various adverse outcomes in human, such as reproductive and developmental defects (Weatherly and Gosse 2017; Zhang and Lu 2023). In 2016, the FDA announced that selling antibacterial soaps containing triclosan and triclocarban must stop within a year, on the grounds that their effectiveness and safety were not guaranteed (FDA 2016). In Japan, the Ministry of Health, Labour and Welfare and a coalition of companies promoted a switch to products that do not contain these ingredients (Ministry of Health, Labour and Welfare of Japan 2016).

Despite that research has provided evidence on the potential toxicity, safety data on long-term exposure to some of these chemicals regarding human health remain limited (Zhang and Lu 2023; Yao et al. 2024). Consequently, continuous biomonitoring and health risk assessment on the exposure level to these chemicals is necessary. Several studies have observed long-term temporal changes in the exposure level to parabens, BP-3, and triclosan over the last decades in Europe, the United States and Canada (Han et al. 2016; Moos et al. 2017; Jiang et al. 2023). However, those targeting the East Asian region are rare.

This study aimed to assess trends in the intake of the abovementioned chemicals, parabens, benzophenone, triclosan and triclocarban, and the risks associated with exposure to them, using urine samples collected between 1993 and 2016.

Materials and methods

Study subjects

A study protocol was reviewed and approved by the Kyoto University Graduate School and Faculty of Medicine, Ethics Committee (approval number R1478, last approved date: May 31, 2022). Informed consents were given either verbally (before 2000) or in writing before participation of the participants.

The samples analyzed were collected from healthy female study participants living in and around Kyoto City, Japan. They were recruited during their participation in a cross-sectional healthcare checkup program in the years 1993, 2000, 2003, 2009, 2011, and 2016. The sampling years corresponded to the specific years the program was implemented. Due to the availability of participants, the individuals in the study were not the same across each sampling year, and the sample exclusively included women. Each participant was required to collect their first morning urine sample in a paper

cup, then transfer a sample to a polypropylene tube and store in a home refrigerator until the sample was transported to the health checkup facilities. The samples were kept at − 30 °C in the Kyoto University Human Specimen Bank (Koizumi et al. 2009).

Determination of target analytes in urine samples

A total of 11 compounds were assessed in the study, including methylparaben (MeP), ethylparaben (EtP), BuP, PrP, benzylparaben (BzP), BP-1, benzophenone-2, -4 and -8 (BP-2, BP-4, and BP-8), triclosan, and triclocarban. These compounds were acquired from the Cambridge Isotope Laboratory in Andover, MA, U.S..

The method used for measuring the target analytes is briefly summarized in the supplementary material. Detailed procedures have been previously described (Mok et al. 2021; Lyu et al. 2023). The LODs and results of method validation are shown in Table S2.

Calculation of daily intake

In analyzing the data, the urinary concentrations of target analytes were corrected with urinary creatinine concentrations to account for the urine dilution effect of single spot samples. The estimated value of creatinine excretion per day (PRCr) was calculated by the following equation (Tanaka et al. 2002):

$$PRCr(mg/day) = -2.04 \times age + 14.89 \times weight(kg) + 16.14 \times height(cm) - 2244.45$$

Since the values of body weight and height were unknown for the subjects in 2000 and 2003, the average values of women from the same age group in the national nutrition survey of the same year were used in the calculations (Ministry of Health, Labour and Welfare of Japan 2001, 2005).

The daily excretion of each compound was calculated by the following equation:

$$Ev(\mu g/day) = CR(\mu g/gcreatinine) \times PRCr(g/day)$$

The creatinine ratio (CR) of a target analyte was determined by dividing the urinary concentration (μg/L) by the urinary creatinine concentration (g/L).

The daily intake (DI) of each compound was estimated based on the calculated daily excretion using the following equation (EPA 1986):

$$DI(\mu g/kgbw/day) = \frac{Ev(\mu g/day)}{F_{ue} \times weight(kg)}$$

F_{ue} is the urinary excretion factor. The F_{ue} for each compound and the references are presented in Table S3.

Risk assessment

The hazard quotient (HQ) was calculated by dividing DI by a dose of no concern [e.g., the reference dose (RfD) or acceptable daily intake (ADI)]. Hazard index (HI) is defined as the sum of HQs (Moos et al. 2017). HIs were calculated for benzophenones (BP-1 and BP-2), parabens (MeP, EtP, PrP, and BuP), and the sum of triclosan and triclocarban. HQ or HI values greater than 1 indicates that the exposure exceeds an acceptable amount. Reference values of no concern used for determining HQ are presented in Table S3.

Data analysis

For urinary concentration, the non-detected values were set to 1/2 of the LODs. The urinary concentrations were adjusted using creatinine concentrations to reduce the effects of variation of analyte concentrations in single spot urine samples. Data were log-transformed in the analysis. JMP Pro 16 was used for statistical analyses. One-way analysis of variance (ANOVA) and Tukey's honest significant differences test were used to investigate the differences in means of concentrations between each sampling year. Partial correlation coefficients were calculated to examine the changes in urinary concentrations of the chemicals across the years, in which age was set as a control variable. Pearson correlation coefficients were calculated between the chemicals. Two-tailed p-values less than 0.05 were considered statistically significant. A principal component analysis (PCA) was employed to identify potential variances in target compounds through a correlation matrix approach. For the analysis, eigenvectors were utilized when eigenvalues exceeded 1. Additionally, varimax rotation was applied to these eigenvectors to enhance interpretability.

Results and discussion

This study used a total of 133 urine samples collected from different participants each year: $n = 10$ in 1993; $n = 25$ in 2000 and 2003; $n = 26$ in 2009; $n = 22$ in 2011; and $n = 25$ in 2016. Table 1 shows demographic data for the subjects. The number of subjects in each year and participants characteristics are presented in Table 1.

Table 1 Demographic characteristics of participants

Years	1993	2000	2003	2009	2011	2016
N	10	25	25	26	22	25
Age (years old)	52.7 (4.0)	49.4 (9.4)	65.7 (4.9)	59.0 (14.4)	65.5 (12.5)	60.2 (12.7)
Height (cm)	154.5 (5.1)	154.3 (2.2)	150.0 (1.6)	153.3 (8.1)	153.6 (4.0)	155.9 (5.4)
Weight (kg)	54.6 (6.2)	54.0 (0.6)	53.1 (1.0)	50.0 (7.2)	52.5 (8.7)	53.4 (8.0)
Body mass index	22.9 (2.7)	22.7 (0.7)	23.6 (0.4)	21.4 (3.9)	22.2 (3.6)	22.0 (3.0)
Urinary creatinine (g/L)	0.8 (0.5)	0.8 (0.4)	0.7 (0.4)	0.8 (0.6)	1.1 (0.8)	0.9 (0.6)

Values are the mean and standard deviation in parenthesis

Only MeP had a detection frequency of 100%; the detection frequencies of BP-4, BP-8, and BzP were extremely low (< 10% in each year). Tables S4 and S5 summarize the urinary concentrations of chemicals examined and the creatinine-corrected values. Table S4 also shows the detection frequency of each chemical substance for each year. BP-4, BP-8, and BzP were excluded from the following data analysis because of the low detection frequencies.

Temporal trends of exposure of target analytes in this study

The distributions of urinary concentrations of all analytes are shown in Tables S4 and S5. Except for MeP, EtP, and BuP, there were no significant differences in the concentration of target chemicals from year to year (Table S5). Figure 1 shows the temporal trends in creatinine-adjusted urinary concentrations of MeP, EtP, and BuP. The exposure levels of MeP and EtP both demonstrated a minimal descending trend over the study period, with correlation coefficients of r = -0.235 and -0.225 and p-values of 0.007 and 0.009, respectively (Table S5). The urinary concentrations of MeP were highest in 2003 (median 309 μg/g), while median levels ranged from 73.2 to 189 μg/g in other years. The median MeP concentration declined 3.7-fold between 2003 and 2016, resulting in the overall downward trend observed ($p = 0.040$, Table S6). For EtP, the exposure levels showed a fluctuation during the study period. The urinary concentrations were lowest in 2009 (median 2.76 μg/g) and highest in 1993 (median 17.3 μg/g), with a significant difference observed between these two years ($p = 0.023$, Table S6). Median EtP levels in other years remained relatively consistent, ranging from 6.06 to 11.3 μg/g. BuP concentrations were lowest in 2016, with significant differences noted when compared to 1993, 2000, 2003, and 2011 ($p = 0.001$, 0.008, 0.003, and 0.009, respectively, Table S6). Median BuP concentrations ranged from 3.49 to 8.93 μg/g during 1993–2003 and were measured at 2.52 μg/g in 2011. However, the medians were "not detectable" in 2009 and 2016, indicating a slight decrease in BuP exposure levels over the study period (r = -0.395, $p < 0.001$, Table S5). Exposure levels of the three parabens all fluctuated during the study period. Given that parabens' short biological half-lives, exposure level fluctuations could stem from factors such as variations in participants' product use status around the time of sampling.

Temporal trends of exposure reported in other countries

Previous studies have investigated temporal changes in these chemicals worldwide, yielding varied results.

For parabens, a German study by Moos et al. (2015) examined 24 h urine samples (total 660) over a period of 17 years (1995–2012). They found that mean urinary paraben concentrations remained unchanged except for MeP, whose median concentration in 2012 was 80.1 μg/g creatinine, more than twice the median of 34.0 μg/g creatinine in 1995. In Boston, MA, U.S., Jiang et al. (2023) investigated 1815 participants, and observed an overall decreasing trend in urinary concentrations of MeP, BuP, and PrP during 2000–2017 (percent change per year − 5.37%, − 14.2%, and − 10.2% for MeP, BuP, and PrP, respectively), with increases during 2000–2007 followed by declines from 2007 to 2017. Additionally, urinary concentrations of EtP showed an 11.8% decrease per year during 2010–2017 in their study. Similarly, in a high-familial risk autism spectrum disorder cohort in California, U.S., the least squares geometric means (LSGMs) decreased during 2007–2014 (percent change per year − 13.0%, − 5.5%, and − 13.3% for MeP, EtP, and PrP, respectively) among pregnant women (Kim et al. 2021). However, given the specific study population, the researchers speculated that this decrease may be attributed to intentional changes in consumer product choices. Similarly, based on biomonitoring data from the Canadian Health Measures Survey, Pollock et al. (2021) observed significant decreasing trends for a 32% decline for MeP and a 36% decline for PrP between the 2012 − 2013 research cycle and the 2016–2017 research cycle.

For triclosan and triclocarban, consistent with our study results, the study by Kim et al. (2021), mentioned above, did not observe any temporal trends in the urinary concentrations of triclosan and triclocarban among cohort participants

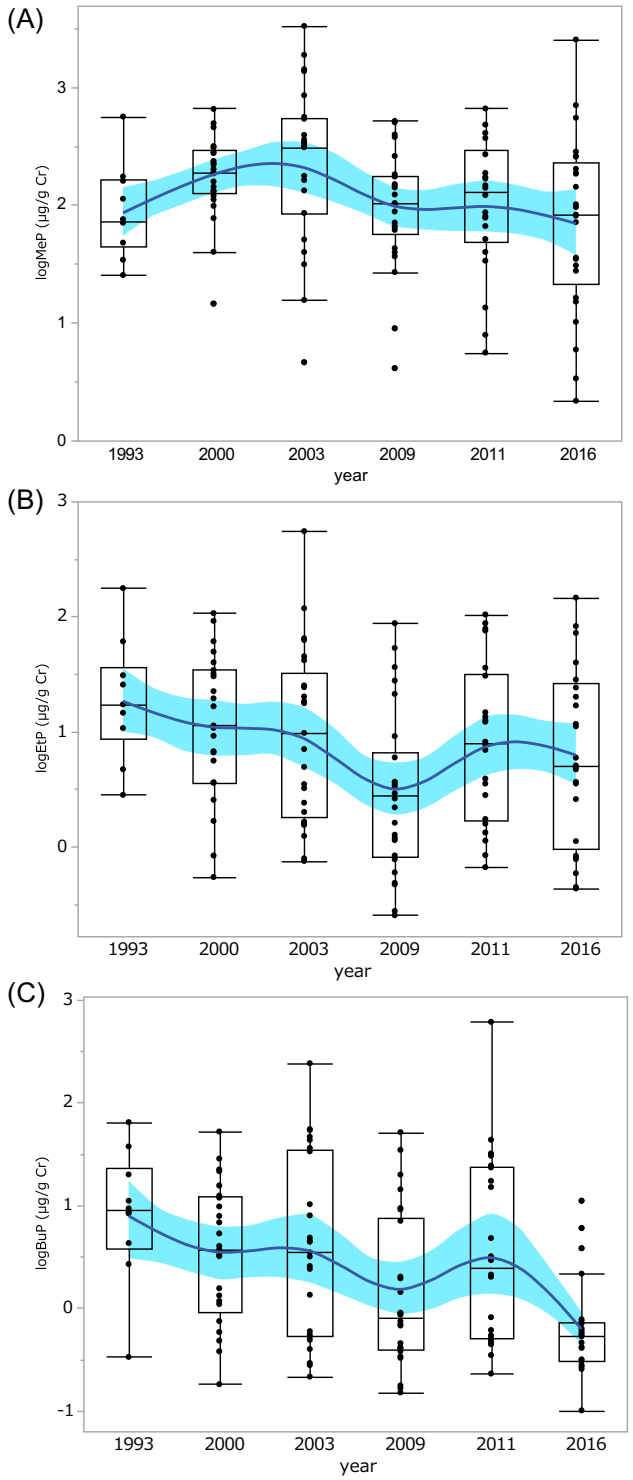

Fig. 1 Urinary concentrations of methylparaben (**A**), ethylparaben (**B**), and butylparaben (**C**) (µg/g creatinine). Values are $\log_{10}$-transformed. The boxes and whiskers indicate the median and interquartile ranges, and the 5th and 95th percentiles, respectively. The smoothing splines (blue curves) are fitted (lambda = 0.1) with 95% confidence intervals

during 2007–2014 in California. However, other studies presented different results.

Han et al. (2016) studied 10,232 participants from the U.S. National Health and Nutritional Examination Survey (NHANES) during 2003–2012, and observed a decreasing trend of the LSGM of urinary triclosan concentrations since the 2005–2006 research cycle (Han et al. 2016). In particular, the authors noticed a significant decrease in urinary triclosan levels in males in 2011–2012 compared with 2003–2004, while in females, a significant increase in triclosan levels was found in 2005–2010 compared with 2003–2004, with no significant change in 2011–2012. Nevertheless, they found no statistically significant changes in the concentration of urinary triclosan over the entire study period. In contrast, Li et al. (2023) found a reduction in HQ values for triclosan over the 2005–2016 period in U.S. children and adolescents aged 6–19 years participating in NHANES, with an annual percent change in LSGM HQ for triclosan of − 9.2% (Li et al. 2023). Similarly, Jiang et al. (2023) reported triclosan showing a large decreasing trend with a –18.8% change per year during 2010–2017 in Boston, MA, U.S.; Pollock et al. (2021) found a 31% decline for triclosan between the 2009–2011 cycle and the 2014–2015 cycle according to biomonitoring data in Canada.

Correlations of target analytes

Pearson correlations among the analytes in urine samples are shown in Table S7. The values of BP-1 and BP-2 were positively correlated ($r = 0.20$, $p = 0.022$). The urinary concentrations of triclosan and triclocarban have a slight positive correlation ($r = 0.32$, $p < 0.001$). The paraben concentrations were positively correlated with each other. Among them MeP and PrP were most significantly associated ($r = 0.54$, $p < 0.001$). Chemicals from each group were not associated with those from other groups. A PCA was applied to more thoroughly investigate the different sources of exposure. The results revealed three significant factors that contributed 27.8%, 16.5%, and 13.4% to the total variance, respectively, each with an eigenvalue greater than 1.0 (Table S8). These factors corresponded primarily to the three groups of target compounds: parabens, triclosan and triclocarban, and benzophenones, except for EtP (Fig. 2). This result suggested that the exposure of the population to triclosan and triclocarban originated from different sources or through distinct exposure pathways from parabens and benzophenones. However, given that parabens and benzophenones are both used in cosmetics and other personal care products (Wei et al. 2021; Mao et al. 2022), there may be some overlap in the exposure sources or pathways.

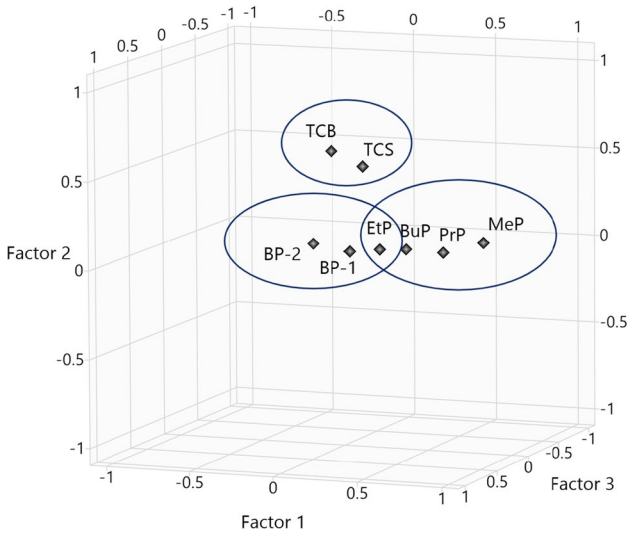

Fig. 2 Principal component analysis among target compounds through a correlation matrix approach. Dara was based on log-transformed urinary concentrations of each analyte. Eigenvectors were utilized when eigenvalues exceeded 1. Varimax rotation was applied to these eigenvectors

Similarly to our results, numerous studies found strong correlations between parabens (Ma et al. 2013; Asimakopoulos et al. 2014; Moos et al. 2015; Zhang et al. 2020; Wang et al. 2021; Wei et al. 2022). Associations between MeP and PrP concentrations have been detected in personal care products (Guo et al. 2014) and indoor dust (Wang et al. 2021), suggesting a possible co-exposure to both of these chemicals. Furthermore, several studies have found significant correlations among other parabens, such as between MeP and EtP (Shirai et al. 2013; Kang et al. 2016; Wei et al. 2022).

Estimated daily intakes and associated risks

The estimated DIs of each target chemical are shown in Table S9. The prior research, which presented estimated Daily Intakes (DIs) based on urinary concentrations, was summarized in the supplementary tables by each group of target chemicals (Tables S10, S11, and S12). However, these estimates are challenging to compare directly because of the variability in urinary excretion factors, as well as other parameters employed in calculations across different studies. The current study has presented the urinary excretion factors used in previous studies, selecting factors that we believe have the most significant impact on the estimated results (Tables S10, S11 and S12).

The calculated HQs and cumulative HIs for BPs, parabens, and the sum of triclosan and triclocarban are depicted in Table S13. The HQs for BPs, the sum of triclosan and triclocarban, and the sum of MeP and EtP were considerably below 1 in all sampling years. The maximum HQ for the sum of MeP and EtP was 0.031 in 2003. However, unlike the MeP and EtP HQ values, the calculated HQ values for BuP exceeded 1 in 2.3% of the total samples. The highest HQ value for BuP was 7.8 from one sample in 2011. For PrP, only one sample, collected in 2003, had an HQ value higher than 1 among all years.

The HIs for BPs, parabens, and the sum of triclosan and triclocarban in each sampling year are presented in Fig. 3. For the HI, BPs had a median value of 0.002 and maximum of 0.09, and the sum of triclosan and triclocarban had a median of 0.004 and maximum of 0.18. The HI of parabens was a median value of 0.06 and 90th percentile of 0.64, but the maximum value was 7.8 from one participant in 2011, who generated the highest HQ value for BuP. Overall, 3% ($n=4$) of the 133 samples from participants in our study exceeded the HI of 1. The percentages of HQs and HIs that exceeded 1 for parabens are shown in Table 2.

Several studies have also calculated HQ and HI for the abovementioned chemicals. Yu et al. (2019) reported 15 workers (2.7%, $n=562$) with an HQ greater than 1 for PrP between 2013 and 2015 in South China, using the same RfD [0.1 mg/kg body weight (bw)/day] as our study (Yu et al. 2019). Moos et al. (2017) found that 5.2% of study participants ($n=660$) had HQs for n-PrP greater than 1 during the period 1995–2012, based on a lower RfD of 0.02 mg/kg bw/day (Moos et al. 2017). It is noteworthy that this dose is five times lower than the RfD of 0.1 mg/kg bw/day used in the current study. Varghese et al. (2022) reported a margin of exposure of PrP less than 10000 (based on 6.5 mg/kg bw/day as the no-observed-adverse-effect level value) in Indian pregnant women ($n=28$), suggesting potential health risks (Varghese et al. 2022). None of the abovementioned studies

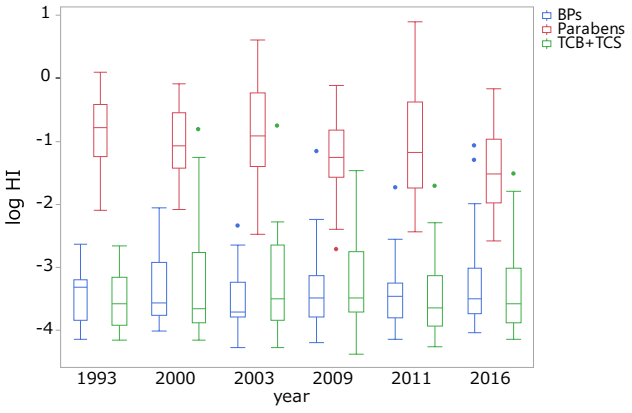

Fig. 3 Boxplots of hazard index (after $\log_{10}$-transformation, log HI) of benzophenones (BPs), parabens, and the sum of triclocarban and triclosan (TCB + TCS). The boxes depict the interquartile ranges and whiskers depict the 5th and 95th percentiles

Table 2 The percentages (%) of hazard quotients and hazard indexes that exceeded 1 for parabens

	HQ			HI
	methylparaben and ethylparaben	butylparaben	propylparaben	
RfD	10 mg/kg bw/day	0.02 mg/kg bw/day	0.1 mg/kg bw/day	
1993	0	10 ($n=1$)	0	10 ($n=1$)
2000	0	0	0	0
2003	0	4 ($n=1$)	4 ($n=1$)	8 ($n=2$)
2009	0	0	0	0
2011	0	4.5 ($n=1$)	0	4.5 ($n=1$)
2016	0	0	0	0
All years	0	2.3 ($n=3$)	0.8 ($n=1$)	3 ($n=4$)

RfD: reference dose; HQ: hazard quotients; HI: hazard index

reported HQ values for the sum of MeP and EtP greater than 1 (ADI was 10 mg/kg bw/day) (EFSA 2004).

Contrary to our findings, Moos et al. (2017) did not find any participants with an HQ greater than 1 for BuP (Moos et al. 2017). Certain studies reported that HQ and HI values of parabens (Li et al. 2021; Wei et al. 2022; Xu et al. 2022), triclosan (Li et al. 2021; Wei et al. 2022; Xu et al. 2022), and BPs (Wei et al. 2022; Xu et al. 2022) did not exceed 1 among Chinese general populations in 2018 and 2020, even though two of these three studies (Li et al. 2021; Xu et al. 2022) used RfDs similar to the present study.

Regarding triclosan alone, Jin et al. (2020) reported HQ values lower than 1 among pregnant women in China in 2010 and 2013, using an RfD of 0.047 mg/kg bw/day (Jin et al. 2020). Li et al. (2023) calculated HQs lower than 1 for triclosan in US children and adolescents from 2005–2016 using a tolerable DI of 50 mg/kg bw/day as an RfD. They also noted a descending trend in the LGSM HQ values, as we have discussed in the previous section regarding temporal trends (Li et al. 2023).

Limitations

This study had several limitations. First, the study population consisted exclusively of women living in the same geographic area until 2016, with a maximum of 26 participants in each sampling year. The sample size was particularly limited in 1993, attributable to participant availability and challenges associated with long-term sample storage. Due to the restricted study location, the findings cannot be generalized to other locations. Second, the current study used single spot urine samples for chemical analysis, and the concentration of target chemicals may include large variabilities. Additionally, although both BP-1 and BP-3 were reported to be the most ubiquitous benzophenones in human biological samples (Mao et al. 2022), we only investigated urinary concentrations of BP-1, BP-2, BP-4, and BP-8.

Conclusion

Our research investigated urinary concentrations of multiple endocrine-disrupting chemicals among a female population in Japan from 1993 to 2016. Our findings indicated that exposure to these chemicals within this population remained relatively steady over this two-decade span. The HQs for PrP and BuP, as well as the HI values for parabens, suggest potential health risks associated with paraben exposure among Japanese women. As far as we know, this study is the first in Japan to investigate prolonged temporal variations in exposure to multiple groups of endocrine-disrupting chemicals, along with associated risk assessments. Therefore, continued monitoring and further evaluations are needed, particularly focusing on parabens, due to their potential health implications.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11356-024-33627-w.

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Authors contributions Kouji H. Harada, Younglim Kho and Kyungho Choi contributed to the study conception and design and supervised the study. Material collection was performed by Zhaoqing Lyu, Toshiaki Hitomi, and Yukiko Fujii. Sample preparation and chemical analyses were performed by Sungmin Kim, Nayoun Park, and Younglim Kho. Statistical analysis was performed by Nao Yoshida, and Zhaoqing Lyu. The first draft of the manuscript was written by Nao Yoshida, and Zhaoqing Lyu. All authors reviewed and commented on the first draft. All authors read and approved the final manuscript.

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Data availability The data that support the findings of this study are available from the corresponding author upon reasonable request under the ethical guidelines for medical and biological research involving human subjects in Japan..

Declarations

Ethical approval A study protocol was reviewed and approved by the Kyoto University Graduate School and Faculty of Medicine, Ethics Committee (approval number R1478, last approved date: May 31, 2022). Informed consents were given either verbally (before 2000) or in writing before participation of the participants.

Consent to publish Not applicable to this study.

Consent to participate Informed consents were given either verbally (before 2000) or in writing before participation of the participants.

Competing interests The authors have no relevant financial or non-financial interests to disclose.

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