Human urine contamination with environmental pollutants: simultaneous determination using UPLC-MS/MS
Asma Beltifa, Monia Machreki, Asma Ghorbel, Afifa Belaid, Emna Smaoui, Feriele Messadi Akrout, Giuseppa Di Bella, Nezar H. Khdary, Tim Reynolds, Hedi Ben Mansour and Joris Van Loco

ABSTRACT
Paraben derivatives are widely used as an antifungal, antimicrobial preservative in cosmetic products, pharmaceuticals, and food. These molecules are called endocrine disruptors (EDCs). The exposure of the human body to paraben derivatives needs further study and for this purpose 200 urine samples were collected from Tunisian men and women aged between 5 and 90 years to determine three paraben derivatives: methylparaben (MP), ethylparaben (EP) and propylparaben (PP) using ultra performance liquid chromatography–tandem mass spectrometer (UPLC-MS/MS). The three major parabens were found in 95 urine samples. The obtained results indicate that MP, EP, and PP were detected in 57%, 46%, and 40% of all samples, respectively. Urinary concentration for the three parabens was in the range of 0.88–84.46 ng/mL, 0.52–29.2 ng/mL, and 0.51–28.17 ng/mL of PP, MP, and EP, respectively. In addition, the concentrations of the paraben derivatives in women were higher than those of men. These findings indicate that the exposure occurs from common products (foods, cosmetics, and pharmaceuticals). The Tunisian authorities should control the composition of packaging of these common products in order to protect humans against EDCs.

Key words | biomonitoring, endocrine disruptors, environmental contamination, paraben derivatives, UPLC-MS/MS

INTRODUCTION
Parabens are esters of para-hydroxybenzoic acid. The most commonly used parabens are methylparaben (MP), ethylparaben (EP), propylparaben (PP), and butylparaben (BP) in combination or alone (Son et al. 2005). Their widespread use has led to their prevalent distribution in the environment. In fact, they have been detected in wastewater, sewage sludge, and other environmental samples (Tohidi & Cai 2015; Camino-Sánchez et al. 2016). Otherwise, they are known to be used as anti-microbial preservatives in a range of consumer products, especially in cosmetics,
pharmaceuticals, and food products (Elder 1984; Soni et al. 2005; Tillett 2012). Consequently, humans are exposed to these derivatives by dermal (cosmetic products), oral (food, medicines), and inhalation routes. Then, they are absorbed in the intestine, metabolized in the liver, and excreted through urine as parabens in free form or in the form of two biomarkers: p-hydroxybenzoic acid (PHBA) and p-hydroxyhippuric acid (PHHA) (Kiwada et al. 1980; Soni et al. 2005; Ye et al. 2006a, 2006b; Boberg et al. 2010). Urine is the most suitable matrix used for the diagnosis and the assessment of paraben exposure (Boberg et al. 2010). Thus, urinary levels of parent parabens can be considered as biomarkers of recent human monitoring (Ye et al. 2006a, 2006b; Calafat et al. 2010; Ma et al. 2013; Wang et al. 2013). Indeed, the total consumption of parabens from foods, cosmetics, and pharmaceuticals has been estimated to be 0.017, 0.833, and 0.417 mg/kg BW/day, respectively (Soni et al. 2005).

Several in vitro studies (Routledge et al. 1998; Nishihara et al. 2000) and in vivo studies (Oishi 2001; Lemini et al. 2005) have indicated the estrogenic activity of parabens and demonstrated many adverse effects of endocrine disruption (Ji et al. 2015), reproductive toxicity (Laing et al. 2016), and genotoxicity (Lee et al. 2013a, 2013b), leading to obesity, type 2 diabetes (Kuo et al. 2013), breast cancer (Deb et al. 2016), and other diseases (Zhou et al. 2017). Meeker et al. (2011) also found an association between urinary levels of parabens and sperm DNA damage. In that regard, the joint Food and Agricultural Organization/World Health Organization Expert Committee on Food Additives (JECFA/WHO) in 1974 showed that the acceptable daily intake (ADI) of parabens for the sum of MP, EP, and PP is lower than 10 mg/kg/day (JECFA 1974).

Despite the health concerns about the possible toxic effects of parabens, particularly as endocrine disruptors (EDCs) in recent years, no data devoted to human exposure, distribution, and excretion of parabens in the Tunisian population are available.

The objective of this study is to evaluate the extent of the Tunisian population exposure to different parabens (ME, EP, PP). Urine samples were collected from subjects living in three separate regions in Tunisia (Mahdia, Sfax, and Gafsa) in order to elucidate geographic trends in exposure to parabens. Measurements were performed with a sensitive and specific method using liquid chromatography–tandem mass spectrometry (LC-MS/MS).

**EXPERIMENTAL WORKS**

**Chemicals**

All parabens, methyl, ethyl, n-butyl, and benzylparabens and their internal standards were purchased from Sigma-Aldrich (Bornem, Belgium). β-Glucuronidase-sulfatase (Helix pomatia) was obtained from Sigma-Aldrich (Bornem, Belgium). Acetonitrile, methanol, and ammonia (HPLC-grade) were purchased from Merck (Darmstadt, Germany). Ultra-pure water was obtained using MilliQ quality (Millipore Corp., Bedford MA, USA). The stock solution of parabens (1 mg/mL) was prepared in MeOH and stored at –20 °C. Working solutions were prepared by diluting the appropriate amount of the stock solution in MeOH. The whole solutions were brought to an ambient temperature just before use.

**Study participants, sample collection, and storage**

The study was conducted on a group of women and men aged between 5 and 90 years, randomly selected from three regions of Tunisia, who participated at University Hospital Mahdia Taher Sfar, Regional Hospital Gafsa Houcine Bouzine, and University Hospital Sfax. In total, 200 samples of human urine were collected for this study. The urine collection of men was done in the following steps: (i) wash the hands thoroughly, (ii) retract completely the foreskin and clean the tip of the penis, (iii) remove the pot, the bottle and then the bottle lid, (iv) begin to urinate to fill half of the pot, then remove the bottle from the pot, and close the lid on the bottle when the bottle is full. Finally, write the name, date of birth, and date/time of collection on the urine label. The samples were collected in amber glass bottles and stored at –80 °C. All participants completed the questionnaire about age, weight, education, medical status, diet, and smoking habits. The research protocol was accepted by the ethics committee of Sfax, Mahdia, and Gafsa hospitals.
Sample preparation

Urine samples (500 μL each) were added into 2 mL glass vials, fortified with 100 μL ammonium acetate (1 M) and vortex mixed for 10 s. Ten μL of enzyme solution (sulfatase and β-glucuronidase) was added, then the glass vials were incubated overnight at 37 °C. Thereafter, 25 μL of the internal standard of parabens and 365 μL of mobile phase were placed in the already prepared solution. All solutions were vortex agitated and centrifuged at 10,000 rpm for 5 min (10 °C). A 10 μL aliquot was injected into the UPLC-MS/MS (Lee et al. 2013a, 2013b).

Instrumental method

Paraben was analyzed by UPLC-MS/MS. The UPLC analysis was performed using an Acquity® sample and solvent manager from Waters (Milford, MA, USA). Chromatographic separation was achieved using an Acquity UPLC® BEH C18 column (2.1 mm i.d., 1.7 μm) from Waters. The autosampler and the column were kept at 8 and 40 °C, respectively. Mobile phases consisted of 0.1% ammonia in water and in acetonitrile. A gradient program was run to analyze the samples within 10 min. The column effluent was analyzed by a XEVO TQ MS® triple quad mass spectrometer (Waters) operating in the negative electrospray ionization (ESI-) MS/MS mode. The limit of detection (LOD) of MP, EP, and PP in urine was 0.5 ng/mL, which was calculated as 3 S0, where S0 was the standard deviation as the concentration approaches zero (Taylor 1987).

Statistical analysis and estimated daily intake

The paraben concentrations were expressed as minimum or maximum and selected percentile values were calculated to describe the distribution of paraben levels. Statistical analysis of the results was performed using SPSS standard version 13.0 software. Urinary metabolite concentration was calculated in ng/mL. The estimated daily intake (EDI) of parabens was calculated using the equation described by Ma et al. (2013), as shown in Equation (1):

\[ EDI = 50 \times Ci \times V / BW \]  

where EDI (μg/kg BW/day) is the estimated daily intake of individual parabens, Ci (μg/L) is the measured urinary concentration of individual parent parabens, V (L/day) is the daily urine excretion rate (a value of 1.7 L was used in this study) (Perucca et al. 2007), and BW (kg) is body weight (62.7 kg for males and 54.8 kg for females were applied in this study) (Yang et al. 2005). Factor 50 was applied to account for metabolites (p-HB) whose proportions were 50 times higher than that of the parent paraben.

RESULTS

Urine samples of both young and old Tunisian population were analyzed by using UPLC-MS/MS, as shown in Figure 1, in order to determine paraben rate.

The geographic characteristics of the Tunisian population are detailed in Table 1. Participants were aged between 5 years and 90 years. Focusing on the urinary paraben levels according to sex, age, and other geographic factors (evenly distributed), participant rate did not significantly differ.

MP, EP, and PP were detected in all samples (n = 95). MP, EP, and PP were detected in 57%, 46%, and 40% of adults examined, respectively (Table 2). The geometric means and medians of urinary concentration in all samples were detected at concentrations 6.38 ng/mL with median 5.35 ng/mL, 2.78 ng/mL with median 2.54 ng/mL, and 1.88 ng/mL with median 1.59 ng/mL for PP, MP, and EP, respectively. The three parabens were detected in urine at concentrations ranging from 0.88 to 84.46 ng/mL for PP, from 0.52 to 29.2 ng/mL for MP, and from 0.51 to 28.17 ng/mL for EP.

In addition, MP, EP, and PP were detected in 40%, 35%, and 28% of women, respectively. The geometric mean levels and selected percentile (95%) concentrations of PP, MP, and EP found in the women's group (n = 67) were respectively 5.82 ng/mL (47.87 ng/mL), 2.91 ng/mL (18.07 ng/mL), and 1.91 ng/mL (8.05 ng/mL). However, MP, EP, and PP were positively detected in 16%, 12%, and 12% of the men's group (n = 28), respectively. In fact, the geometric mean levels and selected percentile (95%) concentrations of parabens in men were 7.89 ng/mL (65.08 ng/mL), 2.74 ng/mL (12.13 ng/mL), and 1.56 ng/mL (5.86 ng/mL)
of PP, MP, and EP, respectively, as shown in Table 3. In the same way, the level of parabens in the women’s urinary concentrations was significantly higher than in men (Figure 2).

The average concentration, geometric means, and 95th percentile of urinary parabens based on the regions of Tunisia are illustrated in Table 4. EP, MP, and PP levels were lower in the Mahdia women’s group compared to the Sfax and Gafsa women’s groups. The highest geometric means of parabens were found in women from Gafsa region with 6.50 ng/mL, 4.05 ng/mL, and 1.98 ng/mL for PP, MP, and EP, respectively. The 95th percentile in this study showed that concentrations of PP in women from the Gafsa region was 68.40 ng/mL, 23.61 ng/mL of MP, and 8.85 ng/mL of EP.

We noticed a significant difference in MP between the Sfax women’s group and that of Mahdia (Figure 2(b)). The human urinary concentrations of PP, MP, and EP are presented in Figure 3(a)–3(c), respectively. EDCs were revealed at high concentrations in the urine collected from all study regions (Sfax, Mahdia, and Gafsa cities).

### DISCUSSION

In our study, PP, EP, and MP were the important parabens detected in the urine samples from the Tunisian population in comparison with other studies carried out in Korea and the USA (Kang et al. 2016). PP was the highest paraben then MP and EP. The reason for this high paraben concentration in human urine is due to the greater use of products containing personal care products (Soni et al. 2005). According to the results, they found that personal care products are the major source of parabens. The detection limits of MP,
EP, and PP found in urine samples ranged from 0.5 ng/mL and the limit of quantification was 0.5 μg/mL.

The high concentrations of PP and MP found in these results were indicated as being present in human urine samples from China, Denmark, Spain, and the USA (Ye et al. 2006a, 2006b; Casas et al. 2011; Frederiksen et al. 2011; Ma et al. 2013). However, the median concentration of parabens in urine samples from Tunisia vacillated compared with other countries, for example, the USA with 191 ng/mL for MP (Calafat et al. 2010) and China (Ma et al. 2013) with 6.50 ng/mL. High PP, MP, and EP concentrations were measured in all samples from the different regions of Tunisia for female and male subjects. Table 5 compares urinary paraben concentrations of this study with those reported in other studies (Ye et al. 2006a, 2006b; Shirai et al. 2013); we found that the geometric means and average urinary concentrations were lower than those in the previous studies. According to the USA, the urinary paraben concentrations detected in all 100 sample subjects (women and men) ranged between 43.9 ng/mL for MP and 9.1 ng/mL for PP (Ye et al. 2006a, 2006b) which are higher than those found in our study. The remarkable difference in urinary concentrations of parabens between Tunisia and other developed countries might hinge on the lower consumption rate of cosmetics and personal care products in Tunisia.

Indeed, the results of increased concentrations of MP and EP found in the women’s groups were in agreement with a previous study (Moos et al. 2014). The United States National Health and Nutrition Examination Survey (NHANES) reported comparable gender-specific differences as in this study. In the NHANES study, women had three-fold higher adjusted geometric mean levels of MP and seven-times higher adjusted geometric mean levels of PP compared to men (Calafat et al. 2010). A significant difference in urinary concentration of the three parabens between males and females was also observed in several other studies (Smith et al. 2012; Engel et al. 2014; Kang et al. 2016). MeP and n-PrP are frequently used parabens and are often used in combination in personal care products (Soni et al. 2005; Guo & Kannan 2013). The major reason for the detection of these compound parabens MP, E, P and PP is that they

<table>
<thead>
<tr>
<th>Compounds</th>
<th>GM</th>
<th>5th</th>
<th>25th</th>
<th>Median</th>
<th>75th</th>
<th>95th</th>
<th>Average</th>
<th>Range</th>
<th>DR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (n = 95)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>PP</td>
<td>6.38</td>
<td>1.36</td>
<td>2.72</td>
<td>5.35</td>
<td>13.62</td>
<td>54.44</td>
<td>13.85</td>
<td>0.88–84.46</td>
<td>40</td>
</tr>
<tr>
<td>EP</td>
<td>1.88</td>
<td>0.64</td>
<td>0.93</td>
<td>1.59</td>
<td>3.85</td>
<td>8.31</td>
<td>3.04</td>
<td>0.51–28.17</td>
<td>46</td>
</tr>
<tr>
<td>MP</td>
<td>2.78</td>
<td>0.58</td>
<td>1.46</td>
<td>2.54</td>
<td>4.68</td>
<td>18.03</td>
<td>4.75</td>
<td>0.52–29.2</td>
<td>57</td>
</tr>
</tbody>
</table>

Table 2 | Concentration (ng/mL) of parabens in urine samples (n = 95) from Tunisian adults

<table>
<thead>
<tr>
<th>Compounds</th>
<th>GM</th>
<th>5th</th>
<th>25th</th>
<th>Median</th>
<th>75th</th>
<th>95th</th>
<th>Average</th>
<th>Range</th>
<th>DR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men (n = 28)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>PP</td>
<td>7.89</td>
<td>1.64</td>
<td>2.02</td>
<td>9.61</td>
<td>17.39</td>
<td>65.08</td>
<td>18.35</td>
<td>1.62–84.1</td>
<td>12</td>
</tr>
<tr>
<td>EP</td>
<td>1.56</td>
<td>0.84</td>
<td>0.97</td>
<td>1.17</td>
<td>2.05</td>
<td>5.86</td>
<td>2.15</td>
<td>0.84–8.67</td>
<td>12</td>
</tr>
<tr>
<td>MP</td>
<td>2.74</td>
<td>1.07</td>
<td>1.43</td>
<td>2.02</td>
<td>5.09</td>
<td>12.13</td>
<td>4.32</td>
<td>0.58–18.09</td>
<td>16</td>
</tr>
<tr>
<td>Women (n = 67)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PP</td>
<td>5.82</td>
<td>1.36</td>
<td>2.98</td>
<td>4.97</td>
<td>8.71</td>
<td>47.87</td>
<td>11.92</td>
<td>0.88–84.46</td>
<td>28</td>
</tr>
<tr>
<td>EP</td>
<td>1.91</td>
<td>0.52</td>
<td>0.87</td>
<td>1.82</td>
<td>3.94</td>
<td>8.05</td>
<td>3.27</td>
<td>0.35–28.17</td>
<td>35</td>
</tr>
<tr>
<td>MP</td>
<td>2.91</td>
<td>0.67</td>
<td>1.68</td>
<td>2.60</td>
<td>4.49</td>
<td>18.07</td>
<td>5.02</td>
<td>0.52–29.2</td>
<td>40</td>
</tr>
</tbody>
</table>

Table 3 | Urinary concentration (ng/mL) of parabens (geometric means and 95th percentile) in the Tunisian population according to sex

PP, propylparaben; EP, ethylparaben; MP, methylparaben; GM, geometric mean; DR, detection rate (%); percentile (5th, 25th, 75th and 95th); range (min–max).
are used as personal care products, especially cosmetic products (Andersen et al. 2009). The second major reason is that they are used in food packaging. Both oral and dermal administrations are more likely to lead to hydrolysis of parabens (Soni et al. 2008; Ye et al. 2008a, 2008b). Thus, the levels of parabens we measured in human urine presumably reflect

treatments are more likely to lead to hydrolysis of parabens and are used in food packaging. Both oral and dermal administrations are more likely to lead to hydrolysis of parabens (Andersen et al. 2009). The second major reason is that they are used in food packaging. Both oral and dermal administrations are more likely to lead to hydrolysis of parabens (Soni et al. 2008; Ye et al. 2008a, 2008b). Thus, the levels of parabens we measured in human urine presumably reflect

Table 4 | Concentration (ng/mL) of parabens in urine samples (n = 95) of three regions of Tunisia

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Mahdia region</th>
<th>Sfax region</th>
<th>Gafsa region</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Women (n = 11)</td>
<td>Men (n = 13)</td>
<td>Women (n = 38)</td>
</tr>
<tr>
<td>PP</td>
<td>2.39</td>
<td>5.23</td>
<td>1.28</td>
</tr>
<tr>
<td>EP</td>
<td>2.22</td>
<td>4.16</td>
<td>1.62</td>
</tr>
<tr>
<td>MP</td>
<td>1.38</td>
<td>7.61</td>
<td>1.62</td>
</tr>
<tr>
<td>GM</td>
<td>Average</td>
<td>2.92</td>
<td>2.61</td>
</tr>
<tr>
<td></td>
<td>95th</td>
<td>5.23</td>
<td>4.16</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>2.92</td>
<td>2.61</td>
</tr>
<tr>
<td></td>
<td>Men</td>
<td>4.16</td>
<td>1.62</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>2.92</td>
<td>2.61</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>4.16</td>
<td>1.62</td>
</tr>
<tr>
<td></td>
<td>95th</td>
<td>5.23</td>
<td>4.16</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>2.92</td>
<td>2.61</td>
</tr>
<tr>
<td></td>
<td>Men</td>
<td>4.16</td>
<td>1.62</td>
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<tr>
<td></td>
<td>Female</td>
<td>2.92</td>
<td>2.61</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>4.16</td>
<td>1.62</td>
</tr>
</tbody>
</table>

PP, propylparaben; EP, ethylparaben; MP, methylparaben; GM, geometric mean.
only a fraction of human paraben exposure. The fraction of
the parent compound of paraben excretion in urine may
depend on the route of exposure. Uptake of parabens
through the skin may result in more parent compound
avoiding degradation in the liver before urinary excretion
compared with oral uptake. Considering that parabens are
rapidly metabolized into non-specific metabolites, the
higher urinary excretion of parent parabens seen in some
urine specimens could also be explained by a less continu-
ous exposure to parabens.

In this study, the total concentration of parabens is
higher in adults than in children. CDC (2015) showed the
opposite relationship in the USA, where adults had a
higher concentration of parabens than children, suggesting
that the observed age trend in the US population is most
likely due to child-specific exposure sources such as baby
products (wipes, lotions, etc.). This may be the result of be-
havioral or physiological differences between children and
adults, such as chewing behaviors (Tulve et al. 2002; Xue
et al. 2007) or a larger surface area-to-body weight ratio
that may increase the potential for exposure via dermal
absorption (WHO 2011).

High urinary concentrations of parabens in Tunisian
women have been found in the city of Gafsa, and weak con-
centrations were detected in Mahdia city; a signifi-
cant difference was observed in particular for MP. The reason
for this high concentration in women from Gafsa was greater
use of cosmetic products, especially solar creams and lotions.
The EDI values of parabens measured from the urinary
concentrations in Tunisian adults are shown in Table 5. The
EDI for MP, PP, and EP in males was 3.71, 10.69, and
2.11 μg/kg BW/day, respectively. Compared to Tunisian
women, for MP, PP, and EP, identical EDI values were

<table>
<thead>
<tr>
<th>Sex</th>
<th>Compounds</th>
<th>MP (μg/kg bw/day)</th>
<th>PP (μg/kg bw/day)</th>
<th>EP (μg/kg bw/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Tunisian adults</td>
<td>GM</td>
<td>3.71</td>
<td>10.69</td>
<td>2.11</td>
</tr>
<tr>
<td>5th percentile</td>
<td></td>
<td>1.45</td>
<td>2.22</td>
<td>1.13</td>
</tr>
<tr>
<td>Median</td>
<td></td>
<td>0.02</td>
<td>13.02</td>
<td>1.58</td>
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<tr>
<td>95th percentile</td>
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<td>16.67</td>
<td>88.22</td>
<td>7.94</td>
</tr>
<tr>
<td>Female Tunisian adults</td>
<td>GM</td>
<td>4.51</td>
<td>9.02</td>
<td>2.96</td>
</tr>
<tr>
<td>5th percentile</td>
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<td>1.03</td>
<td>2.10</td>
<td>0.80</td>
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<tr>
<td>Median</td>
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<td>4.03</td>
<td>7.70</td>
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<tr>
<td>95th Percentile</td>
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<td>74.25</td>
<td>12.48</td>
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<tr>
<td>Chinese male adults</td>
<td>GM</td>
<td>6.69</td>
<td>2.50</td>
<td>3.63</td>
</tr>
<tr>
<td>5th percentile</td>
<td></td>
<td>0.73</td>
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<td>0.35</td>
</tr>
<tr>
<td>Median</td>
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<td>5.20</td>
<td>1.83</td>
<td>2.96</td>
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<td>95th percentile</td>
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<td>154</td>
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<tr>
<td>Chinese female adults</td>
<td>GM</td>
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<td>3.06</td>
<td>8.94</td>
</tr>
<tr>
<td>5th percentile</td>
<td></td>
<td>2.60</td>
<td>0.26</td>
<td>0.65</td>
</tr>
<tr>
<td>Median</td>
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<td>15.5</td>
<td>2.50</td>
<td>10.7</td>
</tr>
<tr>
<td>95th percentile</td>
<td></td>
<td>242</td>
<td>74.9</td>
<td>125</td>
</tr>
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</table>

PP, propylparaben; EP, ethylparaben; MP, methylparaben; GM, geometric mean; percentile (95th).
found in male Tunisians (4.51, 9.02, 2.96 μg/kg BW/day and 3.71, 10.69, 2.11 μg/kg BW/day, respectively). The EDI values of parabens for young Tunisian adults were lower than the ADI (10 mg/kg/day).

CONCLUSION

In this study, we have determined the levels of parabens in the urine of young and elderly Tunisians. Studies on human exposure to parabens in Third World countries are still rare. The present study revealed that most Tunisians had detectable levels of parabens in their urine, thus indicating ubiquitous exposure to these compounds in Tunisia. Furthermore, 200 urine samples were collected from various geographic regions. The results showed that the urinary concentration of parabens MP, PP, and EP differed according to age, sex, and demographic factors in the Tunisian population. Dietary and dermal exposure data for parabens in the Tunisian population are still limited. The presence of parent compounds in the urine indicates that paraben uptake results in the exposure of human tissues to the potentially harmful parent compounds. In this way, further research is necessary to assess whether the paraben concentrations to which the Tunisian population is exposed are high enough to cause a threat to human health.

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