

Exposure assessment of *para*-hydroxybenzoic acid esters (parabens) using their urinary metabolites as biomarkers

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Parabens are alkyl esters of *para*-hydroxybenzoic acid used as antimicrobial preservatives in cosmetics, pharmaceuticals, food and beverage. They are widely used because of their low toxicity and low cost. However, *in vitro* studies suggest that parabens had weak estrogenic activity. *In vivo* studies suggest increased uterine weight in immature mice after exposure of butyl and benzyl parabens, and decreased excretion of testosterone in male rodents after propyl paraben exposure. Thus, further human health risk assessment of parabens is in need. Human exposure of parabens, however, has poorly been characterized because of their ubiquitous exposure pathways. In this study, exposure assessment of parabens was conducted for 43 young Japanese using urinary metabolites as biomarkers. Urinary samples were collected from volunteers and they were incubated with glucuronidase and sulfatase. Then the samples were passed through solid phase extraction cartridge (Sep-Pak tC18) and deconjugated parabens were eluted with ethanol. The eluates were concentrated under gentle stream of nitrogen gas and dissolved in methanol. The parabens in the methanol solution were quantified by LC-MS/MS. The median and 90 percentile concentrations were 59 and 353 for methyl, 2.9 and 55 for ethyl, 0.3 and 12 for *iso*-propyl and 1.8 and 8.7 for *n*-propyl, ND and 0.3 for *iso*-butyl, 0.1 and 1.1 ng/mL for *n*-butyl paraben, respectively. These levels were not much different from those reported for Americans by CDC (Xiaoyun et al., 2006). Significantly higher levels of methyl and *n*-propyl parabens were observed for female than for males ($p < 0.01$). Moreover, methyl and *n*-propyl paraben concentrations were correlated with number of cosmetics the examinees used. The median amounts of methyl, ethyl, propyl, and butyl paraben exposure estimated by reconstruction method were 46.0, 1.55, 1.34, and 0.44 $\mu\text{g}/\text{kg}$ bw/day, respectively.