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Benzonphenone-type UV filters in urine of Chinese young adults: Concentration, source and exposure

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ABSTRACT

Benzophenone (BP)-type UV filters are commonly used in our daily life. 2-hydroxy-4-methoxy benzophenone (BP-3), 4-hydroxy benzophenone (4-HBP), 2,4-dihydroxy benzophenone (BP-1), 2,2′,4,4′-tetrahydroxy benzophenone (BP-2) and 2,2′-dihydroxy-4-methoxy benzophenone (BP-8) were measured in urine samples from Chinese young adults. The results indicated that Chinese young adults were widely exposed to BP-3, BP-1, and 4-HBP, with the median concentrations of 0.55, 0.21, and 0.08 ng/mL, respectively. No significant difference was found between males and females, between urban and rural population. The correlations between urinary concentrations provided important indications for sources and metabolic pathways of target compounds. The estimated daily excretion doses of BP-3, 4-HBP, BP-1, BP-2 and BP-8 were 27.2, 2.24, 5.86, 0.76 and 0.30 ng/kg-bw/day, respectively. The ratio of exposure to excretion must be considered for the exposure assessment with chemicals based on urine measurement. This is the first nationwide study on BP-derivatives with young adults in China.

1. Introduction

Ultraviolet (UV) light filters are a group of chemicals that have the ability to absorb and/or reflect UV irradiation. Benzophenone (BP)-type UV filters are commonly used in our daily life. For the protection of skin and hair from solar radiation, 2-hydroxy-4-methoxy benzophenone (BP-3) is commonly used as UV filter in sunscreen as well as in a variety of cosmetic products such as moisturizing creams, lipsticks, makeup formulations, after-shave lotions and hair-care products (Chisvert et al., 2012). BP-3 can be metabolized into 4-hydroxy benzophenone (4-HBP), 2,4-dihydroxy benzophenone (BP-1), 2,2′,4,4′-tetrahydroxy benzophenone (BP-2) and 2,2′-dihydroxy-4-methoxy benzophenone (BP-8) in human body (Okereke et al., 1994, 1993). A previous study showed that BP-1 were also directly used in some sunscreen lotions (Kunisue et al., 2010). In addition, BP-1 and BP-2 are used as UV stabilizers in plastic surface coatings on food packaging to prevent polymer degradation and quality loss of food (Shaath, 1987; Suzuki et al., 2005). Furthermore, human exposure to UV filters can occur through food or dermal absorption of these chemicals present in cosmetic products, textiles, painting and building materials. Therefore, BP-derivatives, such as BP-3, 4-HBP, BP-1, BP-2 and BP-8, were reported to occur in human specimens, such as urine, breast milk and semen (Felix et al., 1998b; Hagedorn-Leweke and Lippold, 1995; Hayden et al., 1997; Jiang et al., 1999).

BP-derivatives have been reported to associate with endocrine-disrupting activities, such as estrogenic, androgenic and anti-androgenic activities (Schreurs et al., 2005). For example, BP-3, BP-2, BP-8, and 4-HBP showed anti-androgenic activity (Fent et al., 2008). Earlier studies have shown that some BP-derivatives possess more endocrine-disrupting activities than BP-3 in wildlife and humans (Kawamura et al., 2003; Nakagawa and Suzuki, 2002; Suzuki et al., 2005; Takatori et al., 2003). For instance, BP-1, BP-2,

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and 4-HBP possesses greater estrogenic activities than BP-3 (Kawamura et al., 2005, 2003; Nakagawa and Suzuki, 2002; Suzuki et al., 2005; Takatori et al., 2003). Previous studies pointed out that BP-derivatives were widespread in human biological fluids and tissues such as urine, breast milk and semen (Zhang et al., 2013). The 2003–2004 National Health and Nutrition Examination Survey (NHANES) conducted by the U.S. Centers for Disease Control and Prevention (CDC) found that BP-3 was found in over 97% of urine samples from the U.S. general population (Calafat et al., 2008). A study on Danish children and adolescents also showed that BP-3 was detected in 98.4% of the urine samples (Frederiksen et al., 2013a). In France, 80.5% of 191 urine from pregnant women had BP-3 exposure (Philippat et al., 2012). Thus, measurement of BP-derivatives in urine samples could provide a new insight into the understanding of the exposure levels, profiles, and pollution characteristics of BP-derivatives for general population. However, little information is available on the exposure of BP-derivatives for Chinese general population, especially for the national scale.

In our previous study, we reported BP-3, 4-HBP, BP-1, BP-2, and BP-8 in urine samples collected from children, adults and pregnant women in Tianjin, Shanghai, and Qiqihar, China (Kunisue et al., 2010). In this study, BP-3, 4-HBP, BP-1, BP-2, and BP-8 were analyzed in 109 urine samples from Chinese young adults in most of the provinces and municipalities of China. The aims of this study were: to establish a baseline database on the concentrations and profiles of BP-derivatives in Chinese young adults on the national scale, to investigate the differences in concentrations and profiles of BP-derivatives between genders and between urban and rural groups, and to estimate daily excretion doses of BP-derivatives for Chinese young adults.

2. Materials and methods

2.1. Chemicals and reagents

BP-3 (98%), 4-HBP (98%), BP-1 (99%), BP-2 (97%), BP-8 (98%), β-glucuronidase/sulfatase (made from *Helix pomatia*; 145,700 U/mL β-glucuronidase and 887 U/mL sulfatase), and creatinine (99%) were purchased from Sigma–Aldrich (St. Louis, MO). The detail information of all the BP-derivatives is presented in Table 1. HPLC grade methanol, acetonitrile, and ACS grade ammonium acetate were purchased from J.T. Baker (Phillipsburg, NJ). $^{13}C_{12}$-2-OH-4-MeO-BP ($^{13}C_{12}$-BP-3) (99%) was purchased from Cambridge Isotope Laboratories (Andover, MA), and D_3-creatinine (99%) was purchased from CDN Isotopes (Quebec, Canada). Milli-Q water was purified by a water purification system (Barnstead International, Dubuque, IA).

2.2. Study group, sample collection and preparation

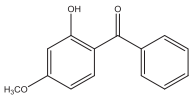
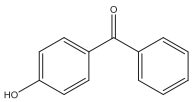
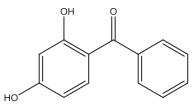
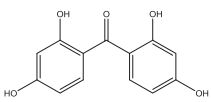
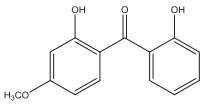
A total of 109 urine samples were collected from Chinese young adults aged 18–22 years in September 2010 (males/females: 68/41, urban/rural: 59/50). All adults were from throughout China except for Qinghai Province, the Tibet Autonomous Region, Ningxia Hui Autonomous Region, Hong Kong and Taiwan. The spatial distribution of donors of urine samples on the national scale can be found in our previous study (Ma et al., 2013). First morning-void urine samples were collected into polypropylene (PP) tubes and stored at −20 °C until further analysis. All the urine samples were collected with the same standard operating procedure in order to decrease variability introduced by sampling.

The details of sample preparation methods including enzymatic deconjugation and solid phase extraction were described in our previous study (Guo et al., 2011; Wang and Kannan, 2013). In brief, 0.5 mL of urine sample was spiked with 20 ng of $^{13}C_{12}$-BP-3 and buffered with 200 μL of 1 M ammonium acetate (pH = 4.5). Then, 50 μL of β-glucuronidase/sulfatase (2 μL/mL) and 0.5 mL of Milli-Q water were added into urine samples. Urine samples were incubated at 37 °C overnight for deconjugation. Subsequently, an ABS ELUT-Nexus SPE cartridge (60 mg/3 mL; Varian, Walnut Creek, CA) and a Rapid Trace Workstation (Caliper Life Science, Hopkinton, MA, USA) were applied for extraction and purification procedures. The extract was concentrated under a gentle stream of nitrogen to near dryness and then resolved in 0.5 mL acetonitrile: Milli-Q water (1:9, V:V) for analysis.

2.3. Instrumental analysis

An Agilent 1100 Series HPLC system (Agilent Technologies, Santa Clara, CA) equipped with an ABSciex API 5500 electrospray triple

Table 1
Information of all BP-derivatives analyzed in the present study.

Commercial name	Chemical name	Chemical abbreviations	Structures	Molecular weight	CAS no.
BP-3	2-hydroxy-4-methoxy benzophenone	2-OH-4MeO-BP		228.24	131-57-7
4-HBP	4-hydroxy benzophenone	4-OH-BP		198.22	1137-42-4
BP-1	2,4-dihydroxy benzophenone	2,4-diOH-BP		214.22	131-56-6
BP-2	2,2′,4,4′-tetrahydroxy benzophenone	2,2′,4,4′-tetraOH-BP		246.22	131-55-5
BP-8	2,2′-dihydroxy-4-methoxy benzophenone	2,2′-diOH-4-MeO-BP		244.24	131-53-3