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ScienceDirect
Environmental Research 107 (2008) 320–331
Environmental Research
www.elsevier.com/locate/envres

Concentration and profile of 22 urinary polycyclic aromatic hydrocarbon metabolites in the US population

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Received 25 September 2007; received in revised form 6 December 2007; accepted 16 January 2008
Available online 3 March 2008

Abstract

Urinary monohydroxy polycyclic aromatic hydrocarbons (OH-PAHs) are a class of PAH metabolites used as biomarkers for assessing human exposure to PAHs. The Centers for Disease Control and Prevention's National Health and Nutrition Examination Survey (NHANES) uses OH-PAHs to establish reference range concentrations for the US population, and to set benchmarks for future epidemiologic and biomonitoring studies. For the years 2001 and 2002, 22 OH-PAH metabolites were measured in urine specimens from 2748 NHANES participants. Percentages of samples with detectable levels ranged from nearly 100% for metabolites of naphthalene, fluorene, phenanthrene, and pyrene, to less than 5% for metabolites from parent compounds with higher molecular weight such as chrysene, benzo[*c*]phenanthrene, and benz[*a*]anthracene. The geometric mean for 1-hydroxypyrene (1-PYR)—the most commonly used biomarker for PAH exposure—was 49.6 ng/L urine, or 46.4 ng/g creatinine. Children (ages 6–11) generally had higher levels than did adolescents (ages 12–19) or adults (ages 20 and older). Model-adjusted, least-square geometric means for 1-PYR were 87, 53 and 43 ng/L for children, adolescents (ages 12–19) and adults (ages 20 years and older), respectively. Log-transformed concentrations for major detectable OH-PAHs were significantly correlated with each other. The correlation coefficients between 1-PYR and other metabolites ranging from 0.17 to 0.63 support the use of 1-PYR as a useful surrogate representing PAH exposure.

Keywords: PAH; 1-Hydroxypyrene; Reference range; NHANES; Biomarker

1. Introduction

Polycyclic aromatic hydrocarbons (PAHs) are a group of environmental carcinogens widely distributed in the ambient air, in food, in soil, and in many occupational environments. Because PAHs form during incomplete combustion of organic materials, they are found in vehicle exhaust, in wood smoke, in cigarette smoke, and are also found at high concentrations in grilled and flame-broiled food (ATSDR, 1995; Bostrom et al., 2002; Guillen et al., 1997; IARC, 1983). Some PAHs have been show to be causative agents of lung, esophageal, gastric, colorectal, bladder, skin, prostate, and cervical cancers in humans and animal models (ATSDR, 1995). Given their carcinogenic and mutagenic potential and their wide distribution that results in exposure in the general population, PAHs have, from a toxicological standpoint, generated considerable interest (Armstrong et al., 2004; ATSDR, 1995; IARC, 1983). Several PAHs, including benzo[*a*]pyrene, benz[*a*]anthracene, and chrysene, have been classified as probable human and animal carcinogens. Furthermore, in humans and laboratory animals, PAHs have been reported to possess reproductive, developmental, hemato-, cardio-, neuro-, and immuno-toxicities (ATSDR, 1995). Due to

Abbreviations: GC/IDHRMS, gas chromatography/isotope dilution high-resolution mass spectrometry; MA, Mexican Americans; NHANES, National Heath and Nutrition Examination Survey; NHB, non-Hispanic blacks; NHW, non-Hispanic whites; OH-PAH, monohydroxylated polycyclic aromatic hydrocarbon; PAH, polycyclic aromatic hydrocarbon; SPE, solid phase extraction.

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0013-9351/$ - see front matter © 2008 Elsevier Inc. All rights reserved.
doi:10.1016/j.envres.2008.01.013

PAHs' well-characterized potential for human exposure and documented toxicity, 16 PAHs have been included in US EPA's list of 188 hazardous air pollutants.

Humans are exposed to PAHs through multiple routes, including inhalation of polluted air or cigarette smoke, ingestion of food containing PAHs or incidental ingestion of soil containing PAHs, as well as dermal absorption from soil or other PAH-containing materials such as creosote or coal tar. The two dominant routes of exposure are ingestion and inhalation for the general population (ATSDR, 1995; Bostrom et al., 2002; Ramesh et al., 2004), while in certain occupational settings such as coke oven plants, dermal absorption can become the primary route of PAH exposure (ATSDR, 1995). After entering the human body, PAHs undergo a series of biotransformation processes. During Phase I metabolism, PAHs are oxidized by the cytochrome P450 enzymes to form highly reactive epoxide intermediates, which are then reduced or hydrolyzed by the epoxide hydroxylase enzyme to hydroxylated metabolites. PAH parent compounds can also be directly hydroxylated without the formation of the epoxide intermediate. In Phase II metabolism, the hydroxy-PAH metabolites are conjugated with glucuronic acid or sulfate to facilitate detoxification and excretion through urine or feces (Estabrook et al., 1980; Grover, 1986; Pelkonen and Nebert, 1982). Several metabolites can be identified from this process, including epoxides, DNA-adducts, dihydrodiols, and conjugated monohydroxy PAHs (OH-PAHs). Generally, metabolites of smaller PAHs with two to three rings are excreted preferentially in the urine, mostly as glucuronic acid conjugates (Li et al., 2006), whereas PAHs with higher molecular weight are excreted primarily in the feces (Ramesh et al., 2004).

Urinary OH-PAHs have been used as biomarkers or surrogates to assess human exposure to environmental PAHs (Gunier et al., 2006; Jacob and Seidel, 2002; Scherer et al., 2000), with 1-hydroxypyrene (1-PYR) as the most commonly used indicator. A number of toxicological studies have investigated the kinetics for urinary OH-PAH excretions from different exposure routes. The half-life for urinary 1-PYR in humans was reported to be 9.8 h (Brzeznicki et al., 1997) and 6–35 h (Jongeneelen et al., 1990) after inhalation exposure, 4.4 h (Buckley and Lioy, 1992) and 12 h (Viau et al., 1995a) after oral ingestion, and 11.5–15 h for PAH exposure through dermal absorption (Viau and Vyskocil, 1995). Due to the short half-lives of PAHs, biomonitoring of urinary OH-PAHs provides information on a subject's recent exposure to PAHs.

Since the 1980s, a number of studies have assessed occupational PAH exposure by evaluating levels of urinary OH-PAHs, or specifically 1-PYR, in various occupational populations, including coke oven workers (Grimmer et al., 1993; Jongeneelen et al., 1990; Levin et al., 1995; Qiu et al., 2007), aluminum smelter workers (Levin et al., 1995), graphite-electrode plant workers (Angerer et al., 1997), road pavers (Levin et al., 1995; Vaananen et al., 2003), coal-tar distillation workers (Preuss et al., 2005), bus-garage and waste-collection workers (Kuusimaki et al., 2004), and traffic police officers (Merlo et al., 1998). From the mid-1990s, biomonitoring studies have focused on low-level, non-occupational exposure to environmental PAHs, especially children's exposure. Levels of urinary 1-PYR and other OH-PAHs were measured in general populations, in reference groups, or in children from a number of countries, such as Canada (Viau et al., 1995b), Germany (Goen et al., 1995; Gundel et al., 1996; Heudorf and Angerer, 2001; Scherer et al., 2000), The Netherlands (van Wijnen et al., 1996), Poland (Siwinska et al., 1998), Ukraine (Mucha et al., 2006), Korea (Kang et al., 2002; Kim et al., 2001), Denmark (Hansen et al., 2005), and the United States (Grainger et al., 2006).

The most extensive PAH biomonitoring study to date is through the National Health and Nutrition Examination Survey (NHANES) conducted by the Centers for Disease Control and Prevention (CDC). This survey takes a statistically representative sample of the US population, assesses the health and nutritional status of that population, and evaluates its exposure to a wide range of chemicals, including PAHs. The OH-PAHs were first measured in the NHANES survey during the years 1999 and 2000. Fourteen OH-PAHs were measured in urine samples from approximately 2300 study participants (Grainger et al., 2006). We report here the results from the NHANES 2001–2002 survey on levels of 22 OH-PAHs formed from seven parent compounds (Table 1). In this study, urine samples from over 2700 subjects ages 6 years and older were analyzed for OH-PAHs using a newly developed, automated laboratory method (Romanoff et al., 2006). In addition, we have investigated the influence of age, sex, and race/ethnicity on the levels of these PAH metabolites. In order to evaluate the potential of using a single biomarker (e.g., 1-PYR) as an indicator for assessing PAH exposure in the general population, we have studied the concentration profile of OH-PAHs excreted in urine, as well as correlations among different OH-PAH analytes.

2. Materials and methods

2.1. Survey description and sample collection

The CDC's National Center for Health Statistics (NCHS) designed and conducted NHANES to assess the health and nutritional status of the civilian, non-institutionalized population in the United States (NCHS, 2005). Currently, the survey is conducted on a 2-year cycle using a stratified, multi-stage probability sample. It examines a nationally representative sample of approximately 10,000 civilians from 30 sites every 2 years. Certain demographic groups, such as the economically underserved, adolescents (ages 12–19), older adults ($\geqslant$60 years), African Americans and Mexican Americans, are over-sampled to produce reliable statistics for these populations. The NHANES data collection process includes a household interview, followed by a standardized physical examination in a mobile examination center. The detailed home interviews collect demographic and socioeconomic information, as well as dietary and health-related information. The health examination component consists of physiological measurements, medical and dental examinations, biological sampling, and laboratory tests. Spot urine specimens are collected from participants 6 years of age and older, and blood samples are