Aromatic DNA Adducts in Human White Blood Cells and Skin after Dermal Application of Coal Tar


Department of Health Risk Analysis and Toxicology, University of Maastricht, 6200 MD Maastricht (R. W. L. G., E. J. C. M., J. C. S. K., F. J. v. S.), and Department of Dermatology, Academic Hospital Maastricht, 6200 MD Maastricht (J. U. O., H. A. M. N.), the Netherlands.

Abstract

A group of eczema patients topically treated with coal tar (CT) ointments was used as a model population to examine the applicability of DNA adducts in WBC subpopulations as a measure of dermal exposure to polycyclic aromatic hydrocarbons (PAHs). Aromatic DNA adducts were examined by 32P-postlabeling in exposed skin and WBC subsets, and urinary excretion of PAH metabolites was determined to assess the whole-body burden. The median urinary excretion of 1-hydroxypyrene and 3-hydroxybenzo(a)pyrene was 0.39 (range, 0.12–1.57 μmol/mol creatinine) and 0.01 μmol/mol creatinine (range, <0.01–0.04 μmol/mol creatinine), respectively, before the dermal application of CT ointments. After treatment for 1 week, these levels increased to 139.7 (range, 26.0–510.5 μmol/mol creatinine) and 1.18 μmol/mol creatinine (range, <0.01–2.14 μmol/mol creatinine), respectively, indicating that considerable amounts of PAHs were absorbed. Median aromatic DNA adduct levels were significantly increased in skin from 2.9 adducts/108 nucleotides (nt; range, 0.7–10.0 adducts/108 nt) before treatment to 63.3 adducts/108 nt (range, 10.9–276.2 adducts/108 nt) after treatment with CT, in monocytes from 0.28 (range, 0.25–0.81 adducts/108 nt) to 0.86 adducts/108 nt (range, 0.56–1.90 adducts/108 nt), in lymphocytes from 0.33 (range, 0.25–0.89 adducts/108 nt) to 0.89 adducts/108 nt (range, 0.25–3.01 adducts/108 nt), and in granulocytes from 0.28 (range, 0.25–0.67 adducts/108 nt) to 0.54 adducts/108 nt (range, 0.25–1.58 adducts/108 nt). A week after stopping the CT treatment, the DNA adduct levels in monocytes and granulocytes were reduced to 0.38 (range, 0.25–0.71 adducts/108 nt) and 0.38 adducts/108 nt (range, 0.25–1.01 adducts/108 nt), respectively, whereas the adduct levels in lymphocytes remained enhanced (1.59 adducts/108 nt (range, 0.25–2.40 adducts/108 nt)). Although the adduct profiles in skin and WBC subsets were not identical, the adduct levels in WBCs were significantly lower as compared with those in skin, the total DNA adduct levels in skin correlated significantly with the adduct levels in monocytes and lymphocytes, but not with those in granulocytes. Excretion of urinary metabolites during the first week of treatment was correlated with the percentage of the skin surface treated with CT ointment and decreased to background levels within a week after the cessation of treatment. 3-Hydroxybenzo(a)pyrene excretion, but not that of 1-hydroxypyrene, correlated significantly with the levels of DNA adducts in skin that comigrated with benzo(a)pyrene-diol-epoxide-DNA. This study indicates that the DNA adduct levels in mononuclear WBCs can possibly be used as a surrogate for skin DNA after dermal exposure to PAHs.

Introduction

CT2 is a complex chemical mixture containing high concentrations of PAHs, some of which have been found to be carcinogenic in laboratory animals and are suspected to be carcinogenic for man (1). Excesses of cancer in the skin and scrotum were found in groups of workers handling pitch, tar, and oils, and these cohorts were mainly exposed to PAHs via dermal absorption (2). Nonoccupational dermal exposure to PAHs predominantly occurs via CT-based shampoo or cosmetics and in the treatment of skin diseases. For example, psoriasis or eczema patients are often treated by dermal application of CT ointments. Because exposures to PAHs may involve health risks, interest has risen in the development of biological markers to assess PAH exposure in human populations. A well-known example is measuring the excretion profiles of PAH metabolites in urine, especially that of 1-OH-pyrene (3). However, the levels of urinary PAH metabolites give no direct information about the dose that actually interacts with DNA. The formation of these DNA adducts is thought to play a crucial role in the development of cancer and other degenerative diseases (4). Nowadays, the 32P-postlabeling procedure has emerged as a sensitive tool to assess aromatic DNA adduct levels in small quantities of DNA, which makes this assay suitable for human studies when limited material is available, e.g., biopsy samples. In tissues of laboratory rodents topically treated with PAH-containing complex mixtures, high concentrations of aromatic DNA adducts determined by 32P-postlabeling were found in skin and internal organs (e.g., lung and heart), whereas the adduct levels in WBCs were low as compared with the tissue levels (5). PAH-DNA adducts were also detectable by 32P-postlabeling.

2 The abbreviations used are: CT, coal tar; PAH, polycyclic aromatic hydrocarbons; 1-OH-pyrene, 1-hydroxypyrene; 3-OH-B(a)P, 3-hydroxybenzo(a)pyrene; nt, nucleotide(s); r, Spearman’s rank correlation coefficient; HPLC, high-performance liquid chromatography; PEl, poly(ethyleneimine); BPDE, trans-7,8-dihydroxy-anti-9,10-epoxy-7,8,9,10-tetrahydrobenzo(a)pyrene; NP1, nuclease P1; DRZ, diagonal radioactive zone.

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1 To whom requests for reprints should be addressed, at Department of Health Risk Analysis and Toxicology, University of Maastricht, P.O. Box 616, 6200 MD Maastricht, the Netherlands.
postlabeling and by immunological assays in human skin treated with CT-based ointments (6–8). In humans, however, internal organs are not readily accessible; therefore, WBCs are often used as a surrogate source of DNA. WBC subpopulations (monocytes, lymphocytes, and granulocytes) vary in metabolic and repair capacity, life span, and relative quantities among one another and as compared with other cells/organisms. Therefore, it is still controversial whether WBCs or specific WBC subsets reflect the binding of aromatic compounds to the DNA of tissues in which tumors will eventually be induced. Although reports that investigated a possible link between the therapeutic use of CT and increased cancer rates are not conclusive (9), CT-treated patients form a proper study population to investigate the relationship between the target and surrogate source of DNA, because the potential target tissue (i.e., skin) can easily be obtained by biopsy. Other studies focused on the DNA adduct levels in WBCs and predominantly lung tissue from smokers. Overall, in studies that used total WBC DNA, no significant correlations were observed (10, 11), whereas the DNA adduct levels in mononuclear blood cells seemed to indicate the biologically effective dose in lung tissue more reliably (12). Hence, understanding the possibilities and limitations of DNA adduct analysis in WBC subpopulations may increase their applicability as a measurement for exposure to PAHs and to estimate adduct levels in nonavailable organs. Therefore, we investigated the aromatic DNA adduct levels in WBC subpopulations (monocytes, granulocytes, and lymphocytes) and skin biopsies of 10 eczema patients before and after treatment with CT ointments covering 20–86% of their body surface. Furthermore, urinary excretion of 1-OH-pyrene and 3-OH-B(a)P was assessed as an indicator of the whole-body dose.

Materials and Methods

Sample Collection of Patients Treated with CT-based Ointments. Three male and seven female patients diagnosed with atopic eczema (age, 34 ± 5 years; range, 18–52 years) were treated with CT ointments for 21 ± 9 days (range, 7–33 days), covering 20–86% of their body surface. Treatment started twice a day with 3% pix lanhistrantracis in petrolatum or in 10% zinc oxide plus 90% petrolatum during the first 2–3 days. In all cases, this treatment was well tolerated and intensified by applying 5% pix lanhistrantracis in petrolatum/zinc oxide-petrolatum twice a day for another 2–3 days. Subsequently, 10% CT ointment was applied until the patient was discharged from the hospital. After informed consent, punch biopsies (4 mm) from treated areas were obtained under local anesthesia before treatment (t = 0) and after 1 week of continuous application of CT ointments (t = 7). Biopsy samples were stored at −20°C until DNA isolation. Ten ml of peripheral blood were obtained by venapuncture at several time points: (a) before treatment (t = 0); (b) at 7 days of continuous treatment (t = 7); and (c) 7 days after the end of treatment (t = 7x). Polymorphonuclear cells (granulocytes) were separated from mononuclear WBCs (i.e., monocytes plus lymphocytes) by gradient centrifugation on lymphoprep according to BÖyum (13). Both fractions were washed with PBS. The granulocyte fraction was treated with lysis buffer (155 mm NaCl, 10 mm KHCO3, and 10 mm EDTA (pH 7.4)) to lyse the erythrocytes and subsequently washed with PBS. Monocytes and lymphocytes were resuspended in medium (RPMI 1640 supplemented with 10% FCS, 2 mm l-glutamine, 10 IU/ml penicillin, and 10 μg/ml streptomycin) at a concentration of approximately 1 × 106 cells/ml and separated by the adherence of monocytes to plastic T.C. flasks for 40 min at 37°C. Cells were stored at −20°C until DNA isolation. Morning urine was obtained at t = 0, 1, 7, and 7x and stored at −20°C for analysis of the urinary metabolites 1-OH-pyrene and 3-OH-B(a)P.

PAH Content of CT (pix lithantracis)-based Ointments. To determine the PAH levels of the CT ointments with which the patients were treated, extracts of the ointments were analyzed for the 16 EPA-listed PAHs. First, 0.2 g of ointment was extracted five times with 3 ml of hexane. Fractions were pooled, and hexane was added to obtain a final volume of 50 ml. Subsequently, 200–500 μl were cleaned up using a 0.5-g silica column (Ø 5 mm). After evaporation of the eluate, the residue was dissolved in acetonitrile, and concentrations of the EPA-listed PAHs were measured by reverse-phase HPLC with fluorescence detection using excitation and emission wavelengths of 250 and >350 nm, respectively, as described by Van Maanen et al. (14). The individual PAH congeners were identified and quantified by comparing retention times and peak areas with those of selected standards. Because all ointments were based on pix lanhistrantracis, similar PAH profiles were found for the different ointments (3, 5, and 10%). The relative distribution of PAH concentration per percentage of pix lanhistrantracis (in milligrams/kilogram) was as follows: naphthalene, 375 ± 23; acenaphthylene, not detected; acenaphthene, 120 ± 9; fluorene, 15 ± 21; phenanthrene, 63 ± 4; anthracene, 17 ± 10; fluoranthene, 80 ± 6; pyrene, 60 ± 4; benzo[a]anthracene, 43 ± 3; chrysene, 55 ± 4; benzo[b]fluoranthene, 53 ± 5; benzo[k]fluoranthene, 23 ± 1; benzo(a)pyrene, 52 ± 3; dibenzo[a,h]anthracene, 74 ± 8; benzo[g,h,i]perylene, 51 ± 3; and indeno[1,2,3-c,d]pyrene, 24 ± 22.

DNA Isolation. Biopsy samples were cut into small pieces and lysed overnight with 2.5 ml of 1% SDS, followed by treatment with RNase A (100 μg/ml) and T1 (50 units/ml) for 30 min, and then proteinase K was added to obtain a final concentration of 1 mg/ml and incubated at 37°C for 4 h. WBC subpopulations were lysed with 2.5 ml of SDS/NEP (75 mm NaCl, 25 mm EDTA, 50 μg/ml proteinase K, and 1% SDS) and incubated for 4 h at 37°C. Samples were extracted with phenol-chloroform:isoamyl alcohol (25:24:1, v/v/v) and chloroform:isoamyl alcohol (24:1, v/v), respectively. DNA was precipitated with 2 volumes of cold ethanol after the addition of one-thirtieth volume of 3 m sodium acetate (pH 5.3) and washed with 70% ethanol. Subsequently, DNA was dissolved in 2 ml Tris (pH 7.4). Concentration and purity were determined spectrophotometrically by the absorbance at 230, 260, and 280 nm. The final volume was adjusted to achieve a DNA concentration of 2 mg/ml.

32P-Postlabeling. The 32P-postlabeling assay was performed as described by Reddy and Randerath (15) with some modifications. DNA (10 μg) was digested using micrococcal endonuclease (0.4 unit) and spleen phosphodiesterase (2.8 μg) for 3 h at 37°C. Subsequently, half of the digest was treated with NPI (6.3 μg) for 40 min at 37°C. The modified nt were labeled with [γ-32P]ATP (50 μCi/sample) by incubation with T4-polynucleotide kinase (5.0 units) for 30 min at 37°C. [γ-32P]ATP was synthesized in the laboratory using carrier-free 32P (DuPont, Brussels, Belgium). NPI efficiency and ATP excess were checked with an aliquot of the NPI-treated fraction by one-dimensional chromatography on PEI-cellulose sheets from Merck (Germany; solvent, 0.12 m NaH2PO4 (pH 6.8)). Radiolabeled adduct nt biphosphates were separated by chromatography on PEI-cellulose sheets from Machery Nagel (Germany). The following solvent systems were used: (a) D1, 1 m NaH2PO4 (pH 6.5); (b) D2, 8.5 m urea and 5.3 m lithium...
Fig. 1. DNA adduct profiles obtained by ³²P-postlabeling in WBC subpopulations and skin DNA at \( t = 0 \) (before treatment), \( t = 7 \) (after 1 week of treatment), and \( t = 7x \) (1 week after the cessation of treatment). Origins are located at the lower left corner of each panel and were excised before analysis. The panel at the lower right corner represents a [³H]BPDE-DNA adduct standard with a modification level of 1 adduct/10⁷ nt.

Excretion of 1-OH-pyrene and 3-OH-B(a)P in Urine. Detection of 1-OH-pyrene and 3-OH-B(a)P in urine was performed as described previously by Jongeneelen et al. (3). The method consisted of enzymatic hydrolysis with \( \beta \)-glucuronidase and arylsulfatase, solid-phase extraction on a Sep-pak C-18 cartridge, and elution with methanol. Reverse-phase HPLC (Kratos solvent delivery system; column, Hypersil 5 ODS) and fluorescence detection (Perkin-Elmer LS-30) were used, using excitation and emission wavelengths of 253 and 423 nm for 3-OH-B(a)P and 232 and 384 nm for 1-OH-pyrene, respectively. Peak area was used for quantification. Concentrations were corrected for creatinine excretion, which was measured using a diagnostic kit of Sigma (No. 555-A). The detection limit was 200 ng of 3-OH-B(a)P and 80 ng of 1-OH-pyrene per liter of urine, using a signal:background ratio of 3. Day-to-day variation and intra-assay variation were 14 and 6%, respectively.

Statistics. Results are presented as the median and range. Overall, due to the relatively small number of observations (n = 10), nonparametric tests for paired samples were applied. Spearman rank correlations were used to assess the relationships between the DNA adduct levels in blood cells, skin biopsy samples, and urinary excretion of 1-OH-pyrene and 3-OH-B(a)P. \( P < 0.05 \) was considered significant.
Results

Adduct Profiles and Levels in Skin Biopsies and WBCs. After 1 week of treatment with CT ointments, aromatic DNA adducts were readily detectable by 32P-postlabeling in skin DNA as well as in DNA obtained from WBC subpopulations. Adduct profiles in skin and WBCs, however, were not completely identical. As shown in Fig. 1, in both skin and WBC DNA, an adduct was found that comigrated with the [3H]-BPDE-DNA adduct standard. Furthermore, in skin, a DRZ was detected with high levels of radioactivity close to the origin, whereas in WBCs, no clear DRZs were seen, but distinct adducts also other than the putative BPDE-DNA were seen at the upper right corner of the TLC plates (Fig. 1). No adduct spots or DRZs could be detected in WBC subpopulations before treatment with CT ointments, except for one individual who smoked 10 cigarettes/day. On the other hand, in all skin samples before treatment, an adduct spot was detectable (Fig. 1). Quantitatively, the median DNA adduct levels in skin increased approximately 20-fold due to treatment for 1 week [median DNA adduct levels were 2.89 (range, 0.66–10.04 adducts/10⁸ nt) before treatment and 63.3 adducts/10⁸ nt (range, 10.9–276.2 adducts/10⁸ nt) after treatment with CT, respectively; $P = 0.005$]. Furthermore, the DNA adduct levels were increased in monocytes [0.28 (range, 0.25–0.81 adducts/10⁸ nt) versus 0.86 adducts/10⁸ nt (range, 0.56–1.90 adducts/10⁸ nt); $P = 0.04$], lymphocytes [0.33 (range, 0.25–0.89 adducts/10⁸ nt) versus 0.89 adducts/10⁸ nt (range, 0.25–3.01 adducts/10⁸ nt; $P = 0.04$), and granulocytes [0.28 (range, 0.25–0.67 adducts/10⁸ nt) versus 0.54 adducts/10⁸ nt (range, 0.7–1.90 adducts/10⁸ nt); $P = 0.05$]. Cessation of CT treatment for 1 week resulted in a significant reduction of the DNA adduct levels in monocytes [0.38 adducts/10⁸ nt (range, 0.25–0.71 adducts/10⁸ nt)] and granulocytes [0.38 adducts/10⁸ nt (range, 0.25–1.01 adducts/10⁸ nt), but adduct levels in lymphocytes were still elevated [1.18 (<0.01–2.14) adducts/10⁸ nt; Table 1; Fig. 2].

Relationship between Different Parameters. Although the number of volunteers was low ($n = 10$), a clear effect of gender on the aromatic DNA adduct levels in skin DNA after treatment with CT ointments was found; in males, the median adduct levels [13.6 adducts/10⁸ nt (range, 10.9–47.1 adducts/10⁸ nt); $n = 3$; 70 ± 21% of the skin surface was treated] were approximately eight times lower as compared with those of female volunteers [106.7 adducts/10⁸ nt (range, 23.1–276.2 adducts/10⁸ nt); $n = 7$; 65 ± 24% of the skin surface was treated]. Analysis of the relationship between skin and WBCs showed that the total DNA adduct levels in skin were related to the adduct levels in lymphocytes ($r = 0.65; P < 0.001$) and monocytes ($r = 0.74; P = 0.005$) but not to those of granulocytes ($r = 0.44; P = 0.07$; Fig. 3). The absence of a relationship with granulocyte DNA can be explained by the observation that the adduct levels in granulocytes were only increased above the background level in individuals that were treated with CT ointment for >70% of their body surface (6 of 10 patients), whereas adducts in skin were increased in all individuals, irrespective of the percentage of treated body sur-
creatinine) and 0.45 mmol/mol creatinine (range, <0.01-1.59 mmol/mol creatinine). Urinary excretion of 1-OH-pyrene and 3-OH-B(a)P at the time of biopsy correlated significantly with the level of adducts in skin that comigrated with the BPDE-DNA adduct spot (r_s = 0.75; P = 0.025; Fig. 4).

**Discussion**

In the present study, dermal application of CT-based ointments significantly increased aromatic DNA adduct levels in human skin and WBC subpopulations. Although aromatic DNA adduct levels in WBC subpopulations were lower as compared with the DNA adduct levels in skin, significant correlations were observed between adduct levels in peripheral blood lymphocytes or monocytes and skin DNA. Furthermore, the DNA adducts in monocytes and granulocytes were less persistent as compared with adducts in the lymphocyte fraction. Urinary excretion of monohydroxylated PAH metabolites indicated that large amounts of PAHs were absorbed, and the levels of 3-OH-B(a)P excretion correlated with the level of the putative BPDE-DNA adduct in skin DNA.

After topical application of CT for 1 week, DRZs were observed in skin DNA, indicating a broad spectrum of different aromatic DNA adducts. Also, an adduct spot that comigrated with the [3H]BPDE-DNA standard was found. Although chromatography on TLC is unable to identify adducts formed by complex mixtures, 32P HPLC analysis of mouse skin DNA demonstrated that the retention time of the major CT-induced adduct closely resembled that of the adduct formed by B(a)P (16). Quantitatively, aromatic DNA adduct levels were 10-fold higher than the levels previously reported in the skin of CT-treated psoriasis patients (6, 7). Although differences in exposure cannot be excluded, these adduct levels might be underestimated, because in the study of Zhang et al. (6), additional immunofluorescence techniques indicated that the adduct levels could be higher than 1 adduct/10^8 nt. Aromatic DNA adduct levels were higher in female patients as compared with male patients. Similarly, enhanced adduct levels were reported in the lung (17, 18) and cells obtained by bronchoalveolar lavage (19) of female smokers as compared with those of male smokers. In the B(a)P-treated skin of C3H mice, the decay curves of anti-BPDE-related DNA adducts were steeper in male rodents as compared with female rodents (20). Thus, human as well as rodent studies suggest that women are at a greater risk of PAH-induced malignancies, which is confirmed by epidemiological studies on smoking individuals (21, 22).
DNA Adducts after Dermal Exposure to CT

Although CT-treated patients have high dermal exposures to PAHs, Pavanello and Levis (23) and Santella et al. (24) were unable to find significantly increased aromatic DNA adduct levels in lymphocytes and total WBCs, respectively, from CT-treated psoriasis patients. On the contrary, in the present study, the DNA adducts were readily detectable in WBC subpopulations of eczema patients after 1 week of continuous application of CT ointments. After cessation of CT treatment, a quick decrease in aromatic DNA adduct levels was found in monocytes and granulocytes, which is in line with the half-lives of these cell types in peripheral blood (hours-days). In lymphocyte DNA, aromatic DNA adduct levels were still elevated after 1 week. Unfortunately, this period is too short to calculate the persistence of DNA adducts in lymphocytes. The results of Pavanello and Levis (23) and Paleologo et al. (25), using ELISA for adduct quantitation, showed a significant reduction over a period of 2–5 months after the end of CT therapy. Similarly, Mooney et al. (26) estimated the half-life of tobacco smoke-related DNA adducts in lymphocytes to be between 9 and 13 weeks after smoking cessation.

The applicability of DNA adducts in WBCs to assess exposure to carcinogens or as a measure of the biologically effective dose in relevant tissues is still a matter of debate. Most studies that tried to validate carcinogen DNA adduct levels in WBCs as a measure of adduct levels in potential target tissues focused on smoking individuals (10–12, 27). In the present study, CT-exposed eczema patients were used as a model population, and aromatic DNA adduct levels in monocytes and lymphocytes, but not in granulocytes, were found to be significantly correlated with adduct levels in skin DNA. Aromatic DNA adducts in granulocytes and monocytes disappeared quickly after cessation of exposure. Therefore, for biomonitoring purposes, it might be important to use lymphocytes as a surrogate source of DNA with more persistent adduct levels. In all WBC subpopulations, lower adduct levels were found as compared with adduct levels in skin DNA, which indicates that DNA adducts in WBCs will probably result in an underestimation of the biologically relevant dose after dermal exposure to PAH mixtures. Nonetheless, the results of the present study indicate that peripheral blood lymphocytes are probably a valid surrogate for estimating the levels of aromatic DNA adducts in skin. However, the influences of different exposure routes on adduct formation in target as well as surrogate DNA should be further investigated. Furthermore, no clear dose-response relationship was observed; adduct levels in monocytes and lymphocytes were increased in individuals with the lowest exposure (approximately 20% of their body surface was covered with CT ointment), but they did not increase further if higher exposures (>70%) were applied. A possible explanation is that at low/moderate exposure levels, adduct formation is proportional to dose, but at higher levels, saturation may occur, as recently demonstrated in environmentally (28) and occupationally exposed subjects (28, 19) and smokers (19).

The excretion of 1-OH-pyrene is considered to be a well-established indicator for total exposure to PAHs (3). As expected, urinary excretion of 1-OH-pyrene and 3-OH-B(a)P was increased after 1 day and 1 week of treatment. Although B(α)P and pyrene were administered in nearly equal levels, the urinary levels of 1-OH-pyrene were more than 150 times greater than the levels of 3-OH-B(α)P. During the first week of exposure, the level of excretion was correlated with the surface area that was treated with CT ointment, but after the exclusion of the pretreatment measurements (τ = 0) from the analysis, these relationships were lost. However, no corrections were made for differences between anatomical sites that may influence the total uptake of PAHs and, consequently, the concentrations of PAH metabolites in urine (29). Furthermore, urinary concentrations of PAH metabolites may eventually decrease during the continuation of CT treatment (30). The levels of 1-OH-pyrene excretion were higher in patients of the present study as compared with individuals that were occupationally exposed to PAH mixtures (31–33). Overall, the excretion of 1-OH-pyrene was correlated with the excretion of 3-OH-B(α)P, but individuals with the highest levels of 1-OH-pyrene excretion did not necessarily have high 3-OH-B(α)P excretion. Grimmer et al. (34) suggested that invariant interindividual differences in PAH metabolite profiles could possibly form a suitable tool to estimate the individual cancer risks at PAH-exposed work places. An invariant PAH metabolite profile may indicate an individual and invariant set of PAH-metabolizing enzymes, producing a certain ratio of carcinogenic and noncarcinogenic PAH metabolites. Carcinogenic PAH may covalently interact with DNA, whereas noncarcinogenic metabolites are excreted in the urine or feces. Therefore, a correlation between distinct urinary metabolites and DNA adduct formation can be expected. Indeed, in the present study, the excretion profile of 1-OH-pyrene versus 3-OH-B(α)P concentrations showed significant interindividual variation, but low intraindividual variations. Moreover, 3-OH-B(α)P excretion significantly correlated with the level of the putative BPDE-DNA adduct in skin DNA. Thus, it can be suggested that urinary profiles of monohydroxylated metabolites may reflect exposure to PAHs and the binding of reactive metabolites to DNA and may therefore play a role in cancer risk assessments. However, further confirmation is needed.

In conclusion, monitoring PAH-DNA adduct levels in mononuclear WBCs by 32P-postlabeling can be a useful molecular index for the quantitative estimation of the biologically effective dose in relevant tissues. However, the sensitivity of DNA adducts in WBC subpopulations as a measure of exposure is limited. For that purpose, measurements of urinary PAH metabolites seem to be more sensitive.

References


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R W Godschalk, J U Ostertag, E J Moonen, et al.


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