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Human biomonitoring after chemical incidents and during short-term maintenance work as a tool for exposure analysis and assessment

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HIGHLIGHTS

- Human biomonitoring (HBM) investigations were carried out for *p*-chloroaniline after a spill incident, and for benzene during regular turnarounds in three different chemical plants.
- *p*-Chloroaniline above background levels was detected mostly in urine samples of firefighters responding to the pyrolysis of pyraclostrobin, contaminated clothes being the most likely source of exposure.
- Three urinary biomarkers of benzene (ttMA, SPMA, unmetabolized benzene) were monitored throughout turnaround campaigns between 1993 and 2012.
- The correlations between the biomarkers of benzene in urine were significant: 25 μg SPMA/g creatinine correspond to 0.5 mg ttMA/g creatinine, and to 4.5 μg benzene/L, respectively.
- Human biomonitoring is a valuable tool for exposure analysis and assessment after incidental or short-term exposure to hazardous chemicals.

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ABSTRACT

Human biomonitoring (HBM) is frequently used for the analysis and assessment of exposure to chemicals under routine working conditions. In recent years, HBM has also been applied to monitor the exposure of the general population, and of emergency responders in the aftermath of chemical incidents. Two examples of targeted HBM programs in the chemical industry are described and discussed in this paper: (1) analysis and assessment of the exposure of firefighters and chemical workers after the spill of *p*-chloroaniline from a burning chemical barrel, and (2) biomonitoring of maintenance workers potentially exposed to benzene during regular turnarounds. The results of these investigations underline that human biomonitoring contributes substantially to comprehensive exposure analyses, human health risk assessments and communication. In addition, regular HBM surveillance and feedback can assist in the continuous improvement of workplace safety measures and exposure control. In conclusion, data on accidental or short-term exposure to hazardous chemicals are an important source of information for the further development of limit and assessment values, the validation of biomarkers and of targeted HBM programs for both routine monitoring and disaster management.

1. Introduction

The quantitative analysis and the toxicological as well as medical assessment of human exposure to hazardous chemicals is a central issue not only in case of regular exposure at work, but in particular during unscheduled peak exposures, e.g., during maintenance work or chemical incidents. In this respect, different approaches are applied to estimate the exposure and the uptake of chemicals as well as the corresponding health risk. The most widely used procedures comprise ambient air monitoring and the analysis of environmental media such as groundwater or dust samples. Also, models for the estimation of the spatial and temporal dispersion of chemicals are applied if exposure data are missing. While these methods may assist in identifying possible routes of exposure, they can not provide data on individual exposure and health risk. As a consequence, human exposure could be overestimated as well as

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underestimated, leading to inappropriate conclusions and actions. Also, dermal absorption may contribute significantly to the overall uptake of a chemical and should be considered. To account for these issues, human biomonitoring (HBM) is increasingly proposed and applied for exposure analysis and assessment (HBM-UBA, 2006; Manno et al., 2010; Scheepers et al., 2011; Hahn et al., 2012; Bader et al., 2012a; Decker et al., 2013). Its main advantages comprise the generation of individual data as a basis for health risk estimation and communication, the inclusion of all potential routes of exposure, and not at least, the benefit of an already existing broad knowledge on the toxicology and health effects of most compounds. These aspects have turned HBM into a valuable tool for the surveillance and interpretation of an exposure to chemicals in occupational and environmental medicine.

However, HBM can also be applied to monitor workers or populations after short-term exposure and after chemical incidents. In particular, the exposure of emergency responders such as firefighters, paramedics, remediation service staff, or residents in the vicinity of chemical incidents has been increasingly investigated and reported in recent years (for review, see Scheepers et al., 2011 incl. supplement). However, HBM in connection with chemical incidents is a relatively novel tool that needs some expertise in the application, and it has not yet become a standard procedure in disaster response and management plans. Some new and comprehensive approaches have recently been suggested and published to tackle this issue (HBM-UBA, 2006; Scheepers et al., 2011; Müller and Schmiechen, 2012; Decker et al., 2013), focussing on the applicability and feasibility of HBM (selection of biomarkers, biological half-lives and time of sampling, transport and storage conditions, etc.). These recommendations are consistent in their opinion that HBM programs need to rely on suitable and validated analytical methods, established biomarkers, and toxicologically derived assessment values. However, if one or more of these prerequisites are missing, it may be still an option to collect biological material, and only afterwards start working on the development of methods and assessment criteria. This way, accidental exposures may trigger the further development of biological monitoring, and enable at least a delayed assessment of an incident.

At present, human biomonitoring is an established tool and best practice, if not a legal requirement, for exposure analysis and assessment in the workplace. The use of HBM after chemical incidents or short-term work with potential higher exposures such as maintenance jobs is a promising approach to extend its applicability (e.g., Boogaard and Rocchi, 1999; Bader et al., 2012b; Leng et al., 2013). In this paper, two examples of HBM after accidental contact or short-term exposures to chemicals are reported and discussed. The original rationale for these studies was to obtain exposure data for a differentiation between exposed and non-exposed persons after accidental exposure, and for checking the efficacy of safety measures during turnaround campaigns.

2. Materials and methods

2.1. HBM after exposure to p-chloroaniline from a burning chemical barrel

2.1.1. Background and study group

In October 2005, a transport barrel containing the crop protection agent pyraclostrobin (methyl [2-[1-(4-chlorophenyl) pyrazol-3-yloxymethyl]phenyl]-*N*-methoxycarbamate, CAS No. 175013-18-0, Fig. 1) overheated in a chemical laboratory and an unknown amount of carbonized material was spilled and further distributed by thermal convection and fire extinguishing water into the vicinity of the accident site. Soon after the fire was put out, it was observed that *p*-chloroaniline (*p*CA), a degradation product of pyraclostrobin, had contaminated the clothes of firefighters

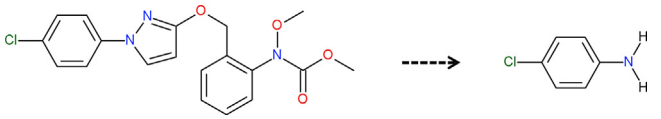

Fig. 1. Chemical structures of pyraclostrobin and its breakdown product *p*-chloroaniline.

and the fire extinguishing water. *p*-Chloroaniline is a potential carcinogen (group 2B, according to IARC (1993)), and an HBM program was initiated for 145 persons who were working close to the accident site, or were involved in firefighting and site remediation. The study group comprised 39 firefighters from three local and one company fire brigades, 84 company employees and contractor workers (plant staff), 4 paramedics, 7 employees of the company's site security, and 11 employees of an industrial remediation service. Biomonitoring was part of the occupational medical care program offered, and the participation in this HBM program was voluntary.

2.1.2. Sample collection

For an initial biomonitoring, spot urine samples were collected post-shift in polyethylene containers on the day of the accident (firefighters) and one day (plant staff, paramedics, remediation staff) or two days (site security) later. A second sampling was offered 5–7 days after the accident if the initial *p*CA concentrations were above the company internal action value of 20 μg/g creatinine, or if a person was specifically interested in a second sampling. The urine specimens were immediately picked up by an internal transport service from the laboratory and kept frozen prior to analysis at −27 °C. Altogether 190 valid urine samples were collected (creatinine concentration >0.3 g/L and <3.0 g/L).

2.1.3. Biomarker analysis

Urinary *p*-chloroaniline (*p*CA) was analyzed according to a validated method for arylamines in urine based on alkaline hydrolysis of the amine conjugates and subsequent HPLC determination with electrochemical detection (ECD), modified from a procedure described by Lewalter et al. (1994). 10 mL of urine were incubated with 2 mL of sodium hydroxide solution (32%) and 100 μL internal standard (3,5-dimethylaniline, $c = 53$ mg/L) for 2 h at 95 °C. Afterwards, the samples were extracted with 30 mL diethylether. The aqueous layer was removed and the organic layer was washed with 10 mL 0.1 M sodium hydroxide solution. The organic layer was then transferred to a 100 mL round-bottom flask. After addition of 1 mL potassium hydrogen buffer (0.02 M, pH 5.1), the diethylether was stripped off in a rotary evaporator. The residual buffer sample was then transferred into an HPLC sample vial and analyzed subsequently. The HPLC system comprised an Agilent 1100 series binary pump, column oven, autosampler (Agilent Technologies, Santa Clara, CA, USA) and a Waters 2465 electrochemical detector (Waters Corporation, Milford, MA, USA). The column used was an Agilent Eclipse Plus C18 (4.6 × 250 mm, 5 μm particle size). The flow was adjusted to 1.2 mL/min. The solvent gradient started with 85% KH_2PO_4 and 15% methanol, and was continually changed to a ratio of 45/55 until 28.5 min (total runtime: 33 min). The ECD was set to 0.8 V. The limit of quantification of this procedure is 5 μg/L (limit of detection: 2 μg/L), the imprecision between series is less than 5% at a concentration of 50 μg/L ($n = 6$ samples), and the recovery from spiked urine samples is 98% ± 6% ($n = 10$ different samples, $c = 50$ μg/L). All chemicals were of at least p.a. grade and purchased from Sigma–Aldrich (Taufkirchen, Germany) or from Merck (Darmstadt, Germany). No external quality assessment program is available for urinary *p*CA, but the same analytical method was successfully tested and certified for the analysis of other amines in urine, e.g., methylene dianiline, in the round robin tests of the