UDC 612.461:[547.6:66-05]
DOI: 10.21668/health.risk/2022.3.08.eng

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Research article

IDENTIFICATION AND CHARACTERIZATION OF 1-HYDROXYPYRENE CONTENTS IN URINE AS A MARKER OF EXPOSURE TO PAH IN WORKERS OF ELECTROLYSIS WORKSHOPS AT ALUMINUM PRODUCTION

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Potential harmful effects produced by highly toxic aromatic hydrocarbons (PAH) on health of workers employed at aluminum production make it necessary to identify biomarkers of exposure to the toxicants and to assess health risks.

Our research goal was to identify and assess contents of 1-hydroxypytene (1-OHPyr) as a biomarker of exposure to PAH. The chemical was identified in urine of workers from electrolysis workshops where either conventional or updated aluminum production technologies were employed. We comparatively examined contents of the marker metabolite 1-OHPyr in urine of 142 workers with basic occupations employed at electrolysis workshops with different aluminum production technologies (the test group) and 14 people who were included in the reference group. The chemical was identified with the authors' high-sensitivity gas chromatography-mass spectrometry method for 1-OHPyr identification in urine with the lower limit of detection being equal to 0.1 μg/l and total error not exceeding 15 %.

The research results revealed high 1-OHPyr contents in urine of workers employed at electrolysis workshops. These contents were by 2–30 times higher than the permissible value of the biological exposure index (BEI) and were associated with exposure to PAH components, an aluminum production technology applied in a given workshop and a worker's occupation. The highest PAH burdens as per 1-OHPyr contents in urine and associated health risks were determined for workers who handled anodes of electrolyzers and crane operators in workshops that employed a conventional technology with self-baking anodes. The lowest ones were established for electrolysis operators and anode frame operators in workshops that employed an updated technology with prebake anodes. It is noteworthy that 1-OHPyr contents were by 2.7–4.7 times higher than permissible BEI value in urine of EOT (bridge) crane operators since these cranes were located in the upper zone of the analyzed electrolysis workshops.

Our research results allow us to recommend the inclusion of biological monitoring of 1-OHPyr contents in urine of workers employed at electrolysis workshops of aluminum productions into periodical medical examinations. This is necessary for developing activities aimed at primary and secondary prevention of occupational and work-related diseases.

Keywords: *aluminum production, polycyclic aromatic hydrocarbons, biomarker of exposure, 1-hydroxypyrene, workers, gas chromatography-mass spectrometry, biological monitoring, biological media.*

Polycyclic aromatic hydrocarbons (PAH) are among priority and the most hazardous persistent organic pollutants. They are highly toxic and produce strong mutagenic and carcinogenic effects. Their influence on the human body is a serious threat to health and a risk factor of oncologic diseases. All this calls for monitoring of biomarkers of exposure to toxicants belonging to the PAH group [1–3]. Exposure to technogenic PAH occurs due to functioning of various metallurgical, petrochemical and coal-processing industries (aluminum, cast iron and steel smelting; coke, bitumen and asphalt production, etc.) [4, 5].

In aluminum production, PAH occur due to anode mass smelting in electrolyzers where aluminum is manufactured using the Soderberg technology with either self-baking or prebake

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charcoal electrodes. Coal-tar pitch sublimes (tarry matter) account for a big share of PAH that are emitted in workplace air. More than 12 PAH with different carcinogenic potential are determined in these emissions including benz(a)pyrene, chrysene, dibenz(a,i)pyrene, benzo(k)fluoranthene, phenanthrene, pyrene, anthracene and others [6–8].

In Russia and in most other countries effects produced by PAH are assessed and their contents are standardized as per benz(a)pyrene since it is the most hazardous and the most profoundly studied chemical in this group. At the same time, to assess an actual chemical burden and associated health risks, not only PAH contents are controlled in workplace air, but also biomonitoring is performed with its aim to identify contents of the actual substances or their metabolites in substrates in the human body. Biomonitoring results allow quantifying contents of toxicants that have actually entered the body and affect it [9, 10].

In world practice, biomonitoring of PAH is usually accomplished by identifying 1-hydroxyperen (1-OHPyr), a conventionally accepted marker metabolite, in urine. This is due to pyrene being the basic component in PAH mixtures and contents of its metabolite correlating with total PAH contents in ambient air and damage to DNA in people exposed to benz(a)pyrene [11–15]. The American Conference of Governmental Industrial Hygienists (ACGIH) established the maximum permissible value of the biological exposure index (BEI) for 1-OHPyr contents in urine, which equals 2.5 μg/dm^3 [1]. Biomonitoring studies that were accomplished at aluminum productions abroad established high 1-OHPyr contents in urine of workers who dealt with electrolyzer maintenance and made charcoal anodes [11, 12, 16, 17]. In Russia, similar studies have not been performed so far. There are also no available data on comparative assessment of 1-OHPyr contents in workers with basic occupations from workshops where different aluminum production technologies are applied.

Measuring of 1-OHPyr contents in urine is a significant stage in biomonitoring studies. Gas chromatography-mass spectrometry (GC-MS) is a promising and reliable method for identifying 1-OHPyr in urine. It is highly effective, employs selectivity in separation of components on a column and gives a possibility to use the deuterated internal standard 1-OHPyr-d9. Moreover, we tested and implemented our own high-sensitivity GC-MS method for determining 1-OHPyr in urine. The method was developed based on available foreign GC-MS procedures [12, 18, 19] and metrologically certified in the RF [20]. The use of it will allow performing authentic assessment of exposure to PAH and its effects on the human body within biomedical monitoring.

Our research goal was to identify and assess contents of 1-hydroxypytene (1-OHPyr) as a biomarker of exposure to PAH in urine of workers employed at electrolysis workshops with either conventional or updated aluminum production technologies.

Materials and methods. Our study was accomplished at a large aluminum production enterprise located in the Eastern Siberia. The enterprise employed both a conventional aluminum production technology with self-baking anodes and an updated one with pre-bake anodes.

We estimated contents of coal-tar pitch sublimes and benz(a)pyrene in workplace air inside electrolysis workshops at the analyzed aluminum production enterprise. The assessment was performed by analyzing the results obtained by our own examinations and measurements accomplished by a sanitary-industrial laboratory of the enterprise [21] as well as data available in Russian and foreign research works [22, 23].

A chemical analytical examination of PAH metabolite 1-hydroxypyrene contents in urine consisted of two stages. The first one involved collecting urine samples and preparing them; at the second stage, the metabolite

[1] 2020 TLVs and BEIs: Based on the documentation of the threshold limit values for chemical substances and physical agents and biological exposure indices. Cincinnati, ACGIH, 2020, 292 p.

was analyzed by using GC-MS and the obtained results were assessed.

1-OHPyr was identified and quantified in urine on Agilent 7890A gas chromatographer with Agilent 5975 mass selective detector, HP-5MS capillary column (30×0.25×0.25 μm), and Agilent 7693 automatic liquid sampler according to the suggested procedure [20]. Sample preparation was performed by optimized enzymatic hydrolysis of a conjugated metabolite with β-glucuronidaze at 55 °C for 60 minutes, liquid-liquid analyte extraction with hexane with evaporation in an inert gas, derivatization with a silylating solution of N, O-bis trifluoroacetamide (BSTFA) into trimethylsilyl ether under the room temperature, and gas chromatography operating in the selected ion monitoring (SIM) mode with m/z 290, 275, 299, 284 [24]. 1-OHPyr quantification in urine was performed with the isotope-labeled internal standard 1-OHPyr-d9. Chromatograms of individual 1-OHPyr identification in workers' urine are shown in Figure 1.

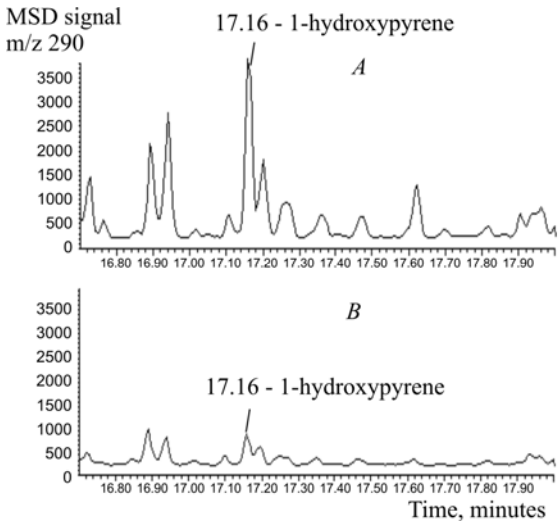

Figure 1. Chromatograms of urine samples from the test and reference groups: *A* is a production worker, concentration is 1.98 μg/l; *B* is a reference sample, concentration is 0.28 μg/l

We tested the suggested GC-MS method for determining 1-OHPyr contents in urine and revealed the following methodical peculiarities. First, we established optimal conditions and parameters for sample preparation that facilitated a significant decrease in its duration. This was achieved due to a shorter time required for enzymatic hydrolysis with β-glucuronidaze and derivatization of 1-OHPyr with BSTFA silylating reagent. Second, we managed to make the analysis highly precise due to using the isotope-labeled internal standard 1-OHPyr-d9 and noted higher sensitivity of determination due to greater extraction of analyte from a biomaterial by liquid-liquid extraction with hexane. The limit of detection and the limit of quantification for 1-OHPyr equaled 0.02 and 0.1 mg/ml accordingly and this is significantly lower than the limit of detection established by foreign procedures for measuring this metabolite in urine (0.1–0.5 mg/ml) [12, 18].

We identified and analyzed contents of 1-OHPyr in urine of 142 workers employed at electrolysis workshops and 14 people who did not work at the analyzed production. They were divided into three groups: workers who had occupational contacts with PAH depending on an occupation and employed technology for aluminum electrolysis (two test groups) and the reference group. The first test group was made of 112 workers with basic occupations in workshops where self-baking anodes were used: electrolysis operators, anode handlers and crane operators (their average age was 37.5 ± 0.8 years and their average work records, 9.0 ± 0.5 years). The second group included 30 workers from workshops where prebake anodes were used: operators of automated production responsible for handling new high-performance electrolyzers (electrolysis operators), anode frame operators responsible for its maintenance and EOT (bridge) crane operators. Average age of workers in this group was 37.4 ± 1.2 years; average work records, 6.7 ± 0.7 years. The third or reference group was made up of 14 people who were not employed at the analyzed enterprise and did not have any occupational contacts with PAH.

To assess 1-OHPyr contents objectively, urine samples were taken during a periodical medical examination provided for workers at the enterprise polyclinic. All the samples were taken in the morning before the next morning shift started. The results of 1-OHPyr measur-

ing in worker's urine were compared with the median level detected in the reference group (0.17 μg/l) and the maximum permissible BEI value in urine (ACGIH) that equaled 2.5 μg/l [1].

All the results were statistically analyzed in Jamovi statistical software package (version 2.3.2) with the non-parametric Kruscal – Wallis test and Mann – Whitney test with the Bonferroni correction and without it. The results are given as the median value (*Me*), interquartile range (Q_{25}–Q_{75}) and a range of concentrations, μg/l.

Results and discussion. We established that contents of volatile components typical for coal-tar pitch sublimes and benz(a)pyrene were 0.2–0.36 mg/m^3 and 0.21–3.9 μg/m^3 accordingly in workplace air inside the analyzed electrolysis workshops where safe-baking anodes were used. This was higher than permissible levels (0.2 mg/m^3 and 0.15 μg/m^3 accordingly) on average by 1.8 and 26 times accordingly. The highest average shift concentrations of tarry matter and benz(a)pyrene that exceeded MPC by up to 1.8 and 26 times accordingly were detected at workplaces of anode handlers and electrolysis operators. At the same time, average concentrations of coal-tar pitch sublimes were within their permissible ranges (0.2 mg/m^3) in workshops where prebake anodes were used; benz(a)-pyrene concentrations varied from 0.5 to 1.4 MPC in those workshops [21, 22]. According to some foreign authors, contents of benz(a)-pyrene varied from 0.19 to 2.8 μg/m^3 in workplace air inside electrolysis workshops at European aluminum-producing enterprises. They could reach 48 μg/m^3 at a workplace of an anode handler in close proximity to Soderberg self-baking anodes [17, 23]. Therefore, if we want to optimize working conditions in electrolysis workshops to make them conform to hygienic standards, obviously, we have to update production equipment and replace a conventional technology with updated one that employs prebake anodes.

We analyzed 1-OHPyr contents in urine of workers employed at workshops with either conventional or updated aluminum production technology by using GC-MS. The results are provided in the Table and Figure 2.

According to the research results, 1-OHPyr was detected in urine of all the examined workers employed at electrolysis workshops as well as people from the reference group who did not have any occupational contacts with PAH. The metabolite contents varied within quite a wide range, from 0.17 to 267.0 μg/l and from 0.08 to 0.9 μg/l accordingly.

We established significant differences in 1-OHPyr contents in urine of workers employed at electrolysis workshops. The differences were established both between basic occupational groups and between the test groups and the reference one as well as the maximum permissible BEI value recommended by the ACGIH. Thus, median 1-OHPyr concentrations

Table

Concentrations of 1-hydroxypyrene in urine of workers with basic occupations in electrolysis workshops where aluminum is produced

An employed technology, occupation	*n*	*Me* (Q_{25}–Q_{75}), μg/l	Min–Max, μg/l
Self-baking anodes. All occupations	112	11.0 (2.4–39.3)*	0.17–267.0
Electrolysis operator	49	3.6 (1.5–13.3)▲	0.17–98.0
Anode handler	26	75.2 (16.5–138.5)▲, ■, ♦	0.87–267.0
Crane operator	37	11.8 (2.7–30.0)■	0.18–57.7
Prebake anodes. All occupations	30	3.5 (1.4–7.3)*	0.61–14.7
Electrolysis operator	16	3.5 (1.3–7.7)	0.61–14.7
Anode frame operator	6	2.2 (1.6–3.4)♦	1.1–7.3
EOT (bridge) crane operator	8	6.8 (2.4–7.8)	0.81–10.9
The reference group	14	0.17 (0.10 – 0.30)	0.08–0.9

Note: *, ♦, ▲, ■ mean there are differences in compared indicators between the groups; the statistical significance is taken as $p < 0.05$.

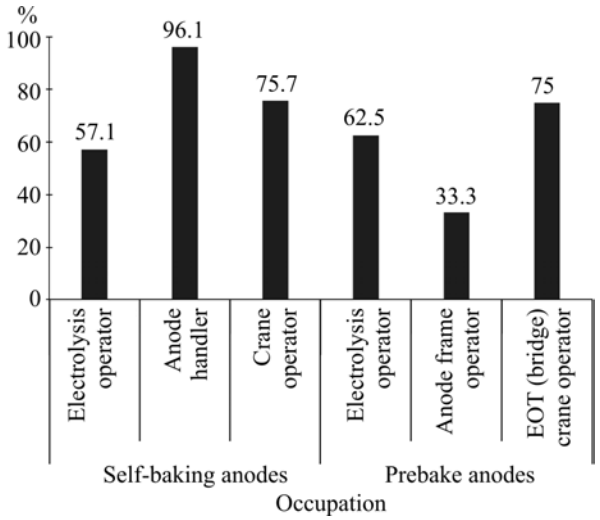

Figure 2. A share of samples (%) with 1-OHPyr contents in urine higher than the maximum permissible BEI value in basic occupational groups in workshops where either self-baking or prebake anodes are applied

in urine of workers employed at workshops (all there occupational groups) where self-baking anodes were used were higher than the same indicator in the reference group as well as the BEI value by 21–442 and 1.4–30 times accordingly ($p < 0.05$). The highest shares of samples with 1-OHPyr contents being higher than the recommended BEI value were detected among anode handlers and crane operators, 96.1 and 75.7 % accordingly, whereas this share was only 57.1 % among electrolysis operators. Anode handlers who maintained and replaced self-baking charcoal anodes in electrolyzers had the highest 1-OHPyr contents in urine, on average by 30 times higher than the recommended BEI value. 1-OHPyr contents in urine were by 20 times higher than this value in electrolysis operators and by 6.3 in crane operators ($p < 0.05$). This indicates that exposure to PAH was predominantly work-related at workplaces of anode handlers and that these workers had high health risks due to it.

Median 1-OHPyr contents in urine varied within the 2.2–6.8 μg/l range in workers with basic occupations in workshops where the updated aluminum production technology (with prebake anodes) was applied. This was on average by 1.4–2.7 times higher than the maximum permissible BEI value and was detected predominantly in electrolysis operators and EOT (bridge) crane operators ($p < 0.05$). The lowest 1-OHPyr concentrations in urine, which were within the permissible BEI range, were detected in anode frame operators (2.2 μg/l) who had to replace anodes in frames and to repair anode installation units in electrolyzers. A share of samples with 1-OHPyr contents being higher than the maximum permissible BEI value was also higher among electrolysis operators (62.5 %) and EOT (bridge) crane operators (75.0 %) against anode frame operators (33.3 %).

We measured 1-OHPyr excretion with urine in exposed workers depending on an aluminum production technology applied in a given workshop and compared the results. We established that median concentrations of the metabolite in urine were authentically lower among anode frame operators as well as the whole group of workers with basic occupations in workshops with the updated technology (prebake anodes) than among the same occupational groups in workshops where the conventional technology (self-baking anodes) was employed (by 34.2 and 3.1 times accordingly). This might be associated with a substantial decrease in volumes in which PAH components occur and enter workplace air due to prebake anodes used in up-to-date electrolyzers as confirmed by monitoring data on contents of tarry matter and benz(a)pyrene in workplace air [21, 22].

We should note that in general the research results are in line with data obtained in foreign studies and fully reflect occupational peculiarities of 1-OHPyr excretion with urine in workers who deal with electrolyzer maintenance [12, 17, 24]. It is especially noteworthy that elevated 1-OHPyr contents in urine were established in anode handlers in workshops with self-baking anodes as well as EOT (bridge) crane operators. The latter worked on cranes located in the upper zone of electrolysis workshops where hazardous dust and gas mixtures were brought to by ascending airflows. Several researchers revealed that exposure to

PAH at a level when 1-OHPyr contents in urine is 4.4 μg/l can correspond to a relative risk of lung cancer being equal to approximately 1.3; the metabolite contents in urine that exceeds 7.7 μg/l can already be considered the highest risk of lung carcinoma for workers [25, 26]. Therefore, high 1-OHPyr contents in urine that we have established in workers from basic occupational groups employed in aluminum production can indicate there are serious threats for their health since these contents are substantially higher than the maximum permissible BEI value. The GC-MS method, which we have applied to identify and quantify contents of 1-OHPyr as a marker PAH metabolite in urine of exposed workers, allows performing objective assessment of effects produced by exposure to PAH on the body within biomonitoring studies. The most effective and radical way to prevent occupational and work-related incidence (oncologic one included) among workers is to implement new technologies of aluminum electrolysis. Such technologies should employ prebake charcoal and inert anodes and up-to-date pressurized electrolyzers; dust collection should be fully automated and modernized since in this case it removes toxic and carcinogenic substances from the occupational environment much more effectively.

Conclusions. Therefore, the results obtained by the accomplished biomonitoring study indicate that workers employed in electrolysis workshops at the analyzed aluminum production enterprise have high contents of 1-OHPyr, a marker PAH metabolite, in their urine. These contents depend on a level of exposure to PAH components, a technology applied in a given workshop and a worker's occupation. The highest PAH burdens as per 1-OHPyr contents in urine and associated health risks were determined for anode handlers and crane operators in workshops that employed the conventional technology with self-baking anodes. The lowest ones were established for electrolyzer operators and anode frame operators in workshops that employed the updated technology with prebake anodes. In this study, we tested the GC-MS method for identifying the PAH metabolite 1-OHPyr in urine as a biomarker. This method is quite adequate for assessing occupational exposure to PAH compounds, benz(a)pyrene included. Our research results allow us to recommend the inclusion of biological monitoring of 1-OHPyr contents in urine of workers employed in electrolysis workshops at aluminum productions into profound periodical medical examinations. This is necessary for developing activities aimed at primary and secondary prevention of occupational and work-related diseases.

Funding. The research was accomplished due to funding granted to the East-Siberian Institute of Medical and Ecological Research for accomplishing the state task.

Competing interests. The authors declare no competing interests.

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Shayakhmetov S.F., Alekseenko A.N., Merinov A.V., Zhurba O.M. Identification and characterization of 1-hydroxypyrene contents in urine as a marker of exposure to PAH in workers of electrolysis workshops at aluminum production. Health Risk Analysis, 2022, no. 3, pp. 90–97. DOI: 10.21668/health.risk/2022.3.08.eng

Received: 20.05.2022
Approved: 11.08.2022
Accepted for publication: 21.09.2022