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TECHNICAL NOTE: RESIDUES OF GASEOUS AIR POLLUTANTS IN RABBIT (*ORYCTOLAGUS CUNICULUS*) TISSUES

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Abstract: The modern consumer is concerned not only for meat quality, but also about animal welfare and the environment. Studies were conducted to determine the concentration of gaseous residues in the tissues of rabbits. For this purpose, gaseous air pollutants were measured at the height of rabbit cages. Immediately after slaughter, samples were taken for analysis to determine the level of residual pollutants in the tissues (blood, perirenal fat and lung). Headspace gas chromatography was performed on the tissue samples to test for volatile toxic substances. Gas residues of 11 compounds were determined in the samples of blood, perirenal fat and lungs. The same chemicals were present in the air of the farm and the animal tissues, which may indicate their capacity for bioaccumulation. We recommend that the results should be used to develop guidelines regarding the welfare of meat rabbits and requirements for laboratory rabbits.

Key Words: gaseous air pollutant, residual pollutant, tissue, farm, *Oryctolagus cuniculus*, rabbit.

INTRODUCTION

World production of rabbit meat is estimated at over a million tonnes, a large share of which comes from Italy and France, with the highest consumption of rabbit meat. Around 25000 tonnes of rabbit meat is produced in Poland, most of which is exported. As consumers pay more attention to a healthy lifestyle, in recent years the demand for meat with high nutritional value has risen. Due to the dietary benefits associated with its low fat content and high proportion of linolenic acid, rabbit meat is enjoying growing popularity among consumers. Among the many factors contributing to the nutritional value of rabbit meat, the most important include a balanced diet for rabbits and the microclimate of the farm environment.

Gaseous pollutants, which can have a significant adverse effect on the gas composition of the air on farms, are inextricably associated with animal production. The most common gaseous impurities include ammonia, methane, carbon dioxide and nitrogen oxides, among many others (EPA, 2010; Belenguer *et al.,* 2011). The specific manner in which rabbits are fed and housed is conducive to the formation of gaseous pollutants. During rearing of rabbits, about 60% of the nitrogen taken in with feed is excreted in the form of urine and faeces, and some of it is released as ammonia (Calvet *et al.,* 2008).

During gas exchange, gaseous pollutants can penetrate the cellular membranes of the alveoli into the blood and can then be distributed with it and accumulate in tissues. The capacity of gaseous pollutant to accumulate in tissues is determined by its concentration, the type of pollutant, the chemical form it occurs in, and the overall condition of the body. The distribution of pollutants in the body and their bioaccumulation largely depend on their affinity for water and fats (solubility). Fat tissue, which is poorly supplied with blood, absorbs substances introduced into the body

more slowly, but they are stored in it. The distribution of substances and their metabolites in organs also depends on their capacity to bind xenobiotics and remove them from the body. It is difficult to estimate the effect of mixtures of pollutants introduced with air. Their biotransformation in the body as well as the resulting metabolites may be atypical (Viau, 2002; Nowakowicz-Dębek *et al.,* 2007).

The increasing level of environmental contamination and its permanent character necessitates the search for bioindicators of pollution. Numerous studies have been conducted on the bioaccumulation of heavy metals in animal tissues, especially those of wild animals, as markers of anthropogenic pollution (Caussy *et al.,* 2003). There are no studies, however, on the occurrence of gas residues in the tissues of farm animals and the risks entailed by their inclusion in the human food chain. Therefore, a study was undertaken to determine the concentrations of residues of gaseous pollutants in the tissues of rabbits.

MATERIAL AND METHODS

Gaseous air pollutants were measured three times at 10 measuring points at the height of the rabbit cages. The first measurement was carried out after weaning (about 36 d of age), the second at 60 d of age, and the third before slaughter (~90 d of age). Samples were collected into polyvinyl fluoride bags and subjected to chromatographic analysis. The animals were kept in cages (length 80 cm, width 60 cm and height 40 cm) in accordance with welfare requirements (Rommers *et al.,* 2015). Manure in the buildings was removed three times a week using mechanical scrapers. All animals were subject to appropriate prophylaxis for the species and fed according to their energy requirements (*ad libitum*) in compliance with feeding standards (Gugołek *et al.,* 2017). Their housing was equipped with natural and mechanical ventilation. The animals were healthy, and after reaching slaughter weight (3.5 kg) upon completion of the production cycle, they were slaughtered on the farm.

Immediately after slaughter, samples were taken from 20 animals for analysis to determine the level of residual pollutants in the tissues (blood, perirenal fat and lung). Headspace gas chromatography (GC) was performed on the tissue samples to test for volatile toxic substances and hydrocarbon derivatives (modified method based on 'Blood Alcohol Analysis by Static Headspace with Dual FID/Megabore Capillary Columns'. Terry Rankin, Jessie Crockett Butler, Thermo Electron Corporation Application Note: 10076, Milan, Italy). To prepare the material, 200 µL of blood or 200 mg of tissue was measured into 10 mL glass headspace vials, 200 µL of an internal standard (*tert*-butanol) was added, and the vials were capped. The headspace phase was analysed using the Thermo TriPlus HS Autosampler with the following operational parameters: sample incubation temperature 60°C, incubation time 6 min, injection volume 400 µL and syringe temperature 62°C. Chromatographic separation was carried out using a Thermo Trace GC Ultra gas chromatograph with two FID detectors equipped with two capillary columns. The headspace phase samples were introduced into the dispenser and separated by a Y-splitter into two separate mobile-phase streams containing the analytes, which then underwent chromatographic separations in parallel on two types of columns, followed by independent FID detection. Two capillary columns were used: Restek BAC-1 and BAC-2. Grade 5 helium at a constant flow of 15 mL/min was used as the mobile phase. The procedure included two consecutive independently prepared analyses of samples of the research material. Two separate results were generated from each sample, obtained from the two columns and the detectors coupled with them. Each final result was calculated as the average of four measurements (2 independent samples×2 separate GC methods: BAC1 and BAC2). The results were analysed statistically and presented in the table and figure (StatSoft, Inc. 2007).

RESULTS

Numerous gaseous pollutants released into the air were identified in the air of the rabbit farm (Figure 1). During the fattening period (55-60 d), the animals were exposed to contaminants released from manure pits in the barns. This is a 'natural' mixture of gases released in buildings with a low standard of hygiene. During the research, we did not interfere with the odour in the buildings where the rabbits were kept. The predominant gases were 1-pentanol (20.35 µg/m^3), isobutanol (15.5 µg/m^3), 1-propanol (17.77 µg/m^3) and toluene (17.61 µg/m^3). The lowest levels among organic compounds were obtained for cyclobutanol (0.42 µg/m^3) and dodecane (1.09 µg/m^3). The microclimatic conditions in the rabbit housing were optimal for this group of animals, with a temperature of 16-18°C
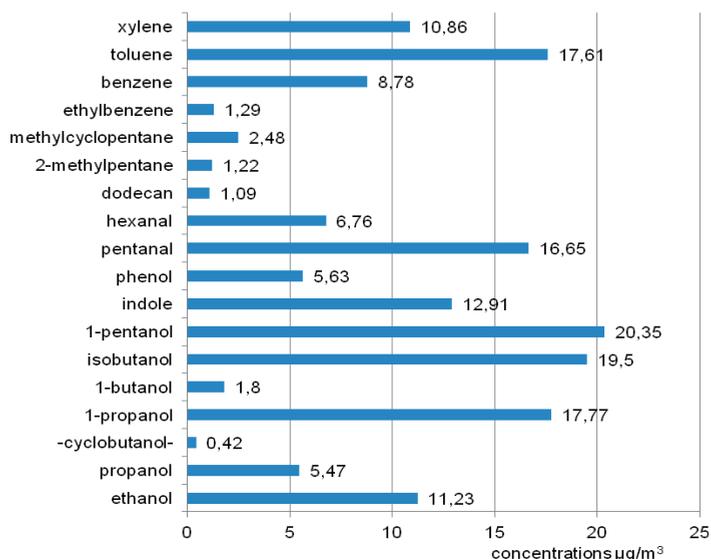
Figure 1: Mean concentrations of gaseous pollutants identified in the air of the rabbit farm (µg/m^3)

and 60-70% humidity. Gas residues of 11 compounds were determined in the samples of blood, perirenal fat and lungs (Table 1). The highest values were found in the perirenal fat samples for ethylbenzene (4.23 mg/100 g) and 2-propanone (1.80 mg/100 g). In the blood samples, the concentration of ethylbenzene was 2.4 mg/100 g and was statistically significant. Ethanol predominated in the lung samples (2.31 mg/100 g), and these values were statistically significant relative to its level in the blood. High levels were also obtained in these samples for ethylbenzene (2.1 mg/100 g), 2-propanol (1.74 mg/100 g) and 2-propanone (1.58 mg/100 g). The lowest concentrations were found for 1-propanol (0.001 mg/100 g) and 2-butanol (0.003 mg/100 g) in the perirenal fat.

Table 1: Mean concentrations of substances identified in rabbit tissues (mg/100 g).

Compound	Gas residues in tissues		
	blood	fat	lung
methanol	0.715±0.749	0.108±0.131	0.215±0.140
ethanol	0.043±0.071	0.643±0.620	2.311±2.168
2-propanol	0.070±0.095	1.063±1.296	1.744±1.548
2-propanone	0.982±0.151	1.796 ±0.778	1.578±0.691
(acetone)	0.025±0.019	0.001±0.003	0.003±0.004
1-propanol	0.005±0.004	0.003±0.002	0.024±0.053
2-butanol	0.005±0.003	0.029±0,040	0.004±0.004
ethyl acetate	0.084±0.117	0.048±0.045	0.171±0.235
benzene	0.025±0.018	0.050±0.043	0.202±0.378
1-butanol	0.061±0.051	0.359±0.751	0.068±0.078
toluene	0.049±0.037	0.698±0.387	1.041 ±0.778
1-pentanol	2.395±2.753	4.227±3.264	2.103±3.229
ethylbenzene	0.278±0.306	0.086±0.192	0.211±0.265
m-xylene	0.136±0.102	0.039 ±0.060	0.130±0.158
o-xylene	0.063±0.077	0.446±0.671	0.249±0.447

DISCUSSION

In recent years, a great deal of attention has been paid to animal feeding and housing conditions, as this translates into their health and the final quality of the product – meat (Konéab *et al.,* 2019; Tillmann *et al.,* 2019). Inadequate housing conditions may reduce the health status of animals and alter product quality. Michl and Hoy (1996) kept rabbits in an air-conditioned chamber to determine the microclimatic conditions, i.e. the magnitude of released gaseous pollutants. The ammonia concentration reached a maximum of 12.3 ppm in a short time, while the concentration of nitric oxide ranged from 253 to 317 ppb. The amount of CO_2 increased with the activity of the animals. These concentrations were lower than in our research. Research by Da Borso *et al.* (2016) indicates that the ventilation system and activities associated with animal management (manure removal) have a decisive influence on the concentration of gases in the air. The authors suggest that the indoor air quality could be improved by introducing automatic monitoring of ventilation. This system should be based on sensors not only of temperature, but also CO_2 and NH_3.

After entering the body, gaseous pollutants can undergo a number of conversions, transformations and often bioaccumulation, depending on factors such as the chemical structure and concentration of the xenobiotic. Nowakowicz-Dębek and Łopuszyński (2004) showed an increase in histopathological (inflammatory) changes in the liver and kidneys of animals exposed to air pollution compared to the control group. This may be manifested by irritation of the respiratory system and reduced reproductive and production parameters. Studies in animals subjected to prolonged exposure to ethylbenzene have shown an increase in the incidence of renal and testicular tumours in rats and of lung and liver tumours in mice (Saghir *et al.,* 2009; Huff *et al.,* 2010). The Environmental Protection Agency (EPA) does not classify ethylbenzene as carcinogenic to humans. Studies in rats confirm that ethylbenzene has moderate toxicity in cases of acute exposure. Long-term exposure has been found to cause central nervous system (CNS) toxicity, changes in the lungs, liver and kidneys, as well as eye irritation (ATSDR, 2010; Dikshith, 2013). The mechanism of action of benzene and its compounds is similar, and symptoms of metabolic acidosis may appear (Dickson and Luks, 2009; Vitale and Gutovitz, 2018). Exposure to organic solvents may lead to poisoning, necrosis or fatty degeneration of organs, accompanied by anaemia and bone marrow aplasia (Lauwerys *et al.,* 1985; Peckham *et al.,* 2014). Nowakowicz-Dębek and Łopuszyński (2004) observed bronchoconstriction and higher lung reactivity in blue foxes exposed to elevated pollution levels. Amoore and Hautala (1983) showed conflicting results regarding the effect of inhalation exposure on blood parameters. The odour detection threshold of ethylbenzene in that study was 2.3 ppm. It breaks down in the air in less than three days under the influence of sunlight. Long-term exposure to ethylbenzene (several months or years) has been shown to cause kidney damage in animals (ATSDR, 2010). Ethylbenzene is easily absorbed by the respiratory tract, distributed throughout the body, and excreted mainly in the urine (Ogata *et al.,* 1984; Howard, 1989). In rats exposed to a mixture of m-xylene and ethylbenzene, m-xylene metabolites were excreted faster than ethylbenzene metabolites (Elovaara *et al.,* 1984; OECD SIDS, 2002). According to Tang *et al.* (2000), daily exposure of a human population to ethylbenzene at around 130 µg/person (inhalation) or about 1.8 µg/kg d (food) corresponds to an annual exposure of about 46 mg/person. In the blood and lungs of rabbits, ethylbenzene was at a similar level, while it was higher in the perirenal fat samples. In our study, the levels of 2-propanone (acetone) were significantly higher in the samples of rabbit blood and perirenal fat than in the blood, at 1.796 and 0.982 mg/100 g, respectively (Table 1). Studies in rodents have shown that 2-propanone is rapidly absorbed by the inhalation route, with peak blood levels occurring quickly after the onset of exposure. The equilibrium state is reached 2 h, 6 h and 3-4 d after exposure to 150 ppm, 500 ppm, and 2210 ppm 2-propanone, respectively (Geller *et al.,* 1979; Wigaeus *et al.,* 1982). The time needed to reach equilibrium state increased with the concentration, which suggests concentration-dependent kinetics. Data presented by DiVincenzo *et al.* (1973) and Wigaeus *et al.* (1981) indicate that the body absorbs about 40-50% of inhaled 2-propanone. The low solubility of 2-propanone in lipids is believed to cause resistance during absorption from the air in the nasal tissue into the bloodstream. Absorption through the skin occurs rapidly in humans. Studies in animals indicate that 2-propanone can be found in the blood, lungs, kidneys, liver, brain, pancreas, spleen, thymus, heart, testes, vas deferens, muscles and subcutaneous and intraperitoneal white adipose tissue (Wigaeus *et al.,* 1982). After 24-h exposure to ^{14}C-labelled 2-propanone at 500 ppm (1200 mg/m^{3}), a low level of accumulation was observed in the tissues, with the exception of brown adipose tissue and the liver. The concentration of 2-propanone is usually higher in the blood than in other tissues, which was not confirmed by our study. The rate and manner of elimination of 2-propanone (respiratory and urinary) after exposure is influenced by the concentration and duration of exposure, as well as the level of physical

activity and gender. 2-Propanone is exhaled in both non-metabolised form and as carbon dioxide after metabolism (Kawai *et al.,* 1992; Scholl and Iba, 1997). While total clearance in rats is independent of concentration, the half-life for elimination from the blood has been found to be 2.4 h to 4.9 h to 7.2 h when the exposure was 196.1 mg/kg body weight (BW), 784.4 mg/kg BW and 1961 mg/kg BW, respectively (Plaa *et al.,* 1982). In many studies on irritation, the irritation threshold was found to increase with exposure time or multiple exposures, indicating that adaptation may occur. Several changes in blood parameters were observed, particularly in men. The changes were 10% or less, except for the reduction in the reticulocyte count, which varied between 68 and 80% (152-179×10³/μL) of control values, depending on the concentration. In rats exposed to high concentrations of 2-propanone vapours, mild reversible neurobehavioral changes have been demonstrated (Christoph *et al.,* 2003).

CONCLUSIONS

The same chemicals were present in the air of the farm and the animal tissues, which may indicate their capacity for bioaccumulation. The concentration of these gases persisted in the air during the study period. We recommend that the results presented here should be used to develop guidelines for the welfare of meat rabbits and requirements for laboratory rabbits. Pollutants present in the air are introduced into the respiratory system and penetrate individual organs and systems. The introduction of air quality monitoring would have a positive impact on animal welfare and reduce worker exposure.

Automatic ventilation should be introduced on farms to ensure good air quality. It should take into account not only the temperature inside the rabbit barns, but also the concentration of gases.

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