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HEALTH RISK IN TRANSPORT WORKERS PART II. DIETARY COMPOUNDS AS MODULATORS OF OCCUPATIONAL EXPOSURE TO CHEMICALS

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Abstract
Professional drivers are exposed to a number of factors that have a negative influence on their health status. These include vibrations, noise, the lack of fresh air in the car cabin, shift work (frequently at night), monotony resulting from permanent repetition of certain actions, static loads due to immobilization in a sitting position, stress resulting from the need to ensure safety in heavy traffic, as well as air pollution (dust, volatile organic substances, nitrogen and sulfur oxides, polycyclic aromatic hydrocarbons, heavy metals, dioxins, furans and others). Factors associated with the specificity of the profession of a driver, including exposure to chemical substances, result in an increased risk of the development of many diseases, i.e., obesity, diabetes, heart disease, hypertension, extensive genitourinary pathology experienced by taxi drivers, lung cancer and other forms of cancer. In the case of drivers, especially those covering long distances, there are also actual difficulties related to ensuring a proper diet. Although attempts at interventional research that would change the principles of nutrition, as well as ensure physical activity and weight reduction, have been made, their results have not been satisfactory. The paper focuses on the discussion on the role of a diet and dietary phytochemicals in the prevention of adverse health effects of such chemicals as a mix of chemicals in the polluted air, benzo(a)pyrene, benzene and metals (lead, cadmium, chromium, nickel), which are the main sources of exposure in the case of transport workers. Int J Occup Med Environ Health. 2019;32(4):441–64

Key words:
diet, heavy metals, benzene, dietary supplements, transport workers, benzo(a)pyrene

INTRODUCTION

Professional drivers are exposed to a wide spectrum of factors that have a negative influence on their health status. These are, *inter alia*, vibrations, noise, the lack of fresh air in the car cabin, shift work (often at night), monotony resulting from permanent repetition of certain actions, static loads due to immobilization in a sitting position, stress resulting from the need to ensure safety in heavy traffic, as well as air pollution (dust, volatile organic substances, nitrogen and sulfur oxides, polycyclic aromatic hydrocarbons, heavy metals, dioxins, furans and others) [1–5].

In the case of drivers, especially those covering long distances, there are also actual difficulties related to ensuring a healthy diet and lifestyle. Due to considerable distances that they have to cover, they do not always come back home. Irregular working hours and frequent work at night, which characterize the profession of a driver, are also associated with sleep disorders [6]. The majority of long-distance driv-

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ers sleep, eat their meals and spend their free time at car parks, which does not provide them with a chance for a calm sleep environment, inexpensive healthy food products or performance of additional physical activity, e.g., doing favorite sports [3–5]. Some drivers use dangerous stimulants or tobacco as a way to help them stay awake during long and monotonous hours of driving [7,8]. Professional drivers also have a habit of frequent "snacking" during their work. The range of products consumed this way is, to a large extent, determined by what drivers can purchase at catering outlets and stores located along the route. That is why they eat few vegetables and fruit, but a lot of snacks such as fast-food products, and drink a lot of sweet beverages, thus consuming lots of salt and saturated fatty acids [9–11].

The above-mentioned factors related to the specificity of the profession of a driver, including exposure to various chemical substances, result in an increased risk of the development of numerous diseases, i.e., obesity, diabetes, heart disease, hypertension, extensive genitourinary pathology experienced by taxi drivers, lung cancer and other forms of cancer [6,12–19].

Even though attempts at interventional research altering dietary principles, as well as ensuring physical activity and body weight reduction, have been made [20], their results have not been satisfactory. Randomized studies carried out for over 18 months, involving 1061 bus drivers in Minneapolis, U.S., who were overweight, revealed that certain diet modifications, consisting in the introduction of more fruit and vegetables, coupled with an exact determination of consumed fats and a recommendation of a greater physical activity, did not result in favorable changes in the level of physical activity or weight [21]. Similarly, a study carried out by Sorensen et al. [22] in a group of 227 lorry drivers and docks workers who had not smoked for at least 4 months, and 89% of whom were overweight, did not show the impact of a modified diet on the reduction of body weight. Hedberg et al. [23] also conducted an 18-month intervention study, mainly aiming at an improvement of the cardiovascular risk factors among a group of German workers, including bus drivers. In this study, interventions included health education, group or individual activities involving physical exercise, diet, and stress coping techniques. Despite the actions taken in the intervention period, in both the intervention and control groups no effect on the body mass index (BMI) was observed. In contrast, a study performed by Puhkala et al. [24] showed a positive influence of a healthier diet and an increased physical activity on the reduction of body weight in overweight drivers. During 12 months of the study, the drivers emphasized the large support from their families and friends, concerning the maintenance of the diet regime and an increased physical activity. One may assume that men are less likely to follow the lifestyle change than women, but when they decide to do so, they are no less successful [25].

The lack of effectiveness of the undertaken actions in the field of body weight reduction may result from the fact that the basis for obesity development is multi-factorial, with nutritional factors, as well as lifestyle and environmental factors, playing a very important role. A reduced consumption of vegetables, fruit and natural herbs results in lower intakes not only of elementary vitamins and minerals but also of a whole spectrum of significant bioactive components, such as polyphenols. Studies performed over the past few years have shown that many dietary compounds can modulate the body response to chemicals absorption, distribution, metabolism and excretion, which may significantly reduce the risk of a number of chronic diseases [26–29]. There are no publications comprehensively describing the current state of knowledge about dietary compounds as modulators of occupational exposure to chemicals in transport workers. Bearing in mind the beneficial effect of dietary habits on health, it is important to pay attention to those components of the diet which may be particularly beneficial for transport workers.

The work focuses on the role of a diet and dietary phytochemicals in the prevention of adverse health effects of

such chemicals as a mix of chemicals in the polluted air, benzo(a)pyrene (BaP), benzene and metals (lead, cadmium, chromium, nickel), which are the main sources of exposure in the case of transport workers.

METHODS

The study was conducted using electronic databases, such as MEDLINE, Web of Science and GOOGLE Scholar. Articles relevant for the study were searched for using the following keywords: air pollution, benzo(a)pirene, benzene, lead, cadmium, chromium, nickel, nutrition, diet, supplement, and phytochemical. For the preparation of the article, recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [30] were applied.

Original peer-reviewed articles in English, describing studies on people, as well as *in vitro* and *in vivo,* were used. The articles which did not analyze the influence of a diet or specific food components on the risk related to exposure to air pollution, benzo(a)pyrene, benzene, lead, cadmium, chromium and nickel were excluded from the study. Six hundred and twenty-eight publications were collected, 479 of which did not meet the study criteria or were duplicated. One hundred and forty-nine articles concerning the above-mentioned area were included in the study. The work mainly cites the results of original research dated 1974–2018. In the case of research on mixed exposure, benzo(a)pirene, chromium and nickel, > 85% of the original articles were published after 2000. For benzene, lead and cadmium exposure publications, this percentage was smaller (66–70%), with only few original papers on this subject released after 2000.

RESULTS

Prevention of adverse health effects of chemicals – the role of a diet and dietary phytochemicals

Mixed exposure (air pollution)

Recent studies indicate that environmental air pollutants, and in particular diesel exhaust fumes, constitute an additional potential cause of obesity. In an animal study using pregnant mice which were affected by diesel fuel exhaust, more obese male progeny as well as higher inflammation were reported [31]. In C57BL/CBA mice which had inhaled heavy industry pollution (< 2 μm particulate matter adsorbed with polycyclic aromatic hydrocarbons) for several days, higher lipid formation in the lungs, possibly acting as a pollutant storage or cell signaler to generate reactive oxygen species (ROS), was observed. Prenatal diesel fuel exhaust exposure in mice caused fetal brain cytokine response (systemic inflammation) and contributed to obesity in the male offspring. Additionally, anxiety and insulin levels were increased, and physical activity was reduced [32].

A human study with mothers who gave birth to children in the boroughs of New York City revealed that those who had experienced higher polycyclic aromatic hydrocarbon exposure pre-disposed their children to a significantly higher body mass and body fat, contributing to obesity at the age of 5 [33]. Thus, air-pollution during pregnancy, both in mice as well as in humans, was shown to cause lipid formation connected with an increased systemic inflammation, adipocyte accumulation and obesity in the offspring.

Some herbal extracts, also known as xenobiotics, modify the excretion of air pollutants via xenobiotic metabolizing enzymes [34]. For example, glutathione S-transferases, which are key enzymes in detoxification, are responsible for transportation of conjugated toxins, following phase II processing outside of the cells [35]. Phenolic metabolites of air pollutants may accumulate in fat tissue and can then be released upon ingestion of lipolytic substances such as green tea catechins. The elimination of conjugated toxins from the cells occurs via the trans-membrane p-glycoprotein, and then via the bile or urine [36]. A lot of attention is focused on the green tea catechins with regard to reducing the obesity risk. Green tea may modulate the body fat mass in response to air pollutants, acting as a phytochemical protective mechanism connected with its antioxidant properties [37].

Green tea is a source of many bioactive ingredients, such as catechins, methylxanthine and caffeine [38]. In mice bearing a solid Ehrlich ascites carcinoma, green tea catechins (a dosage of 20 mg/kg or 40 mg/kg) reduced systemic inflammation (serum CRP), oxidative stress, lipid peroxidation and inhibited tumor growth [39]. In a study using female LEWIS rats fed with chow and 0.1% green tea extracts, reduced or inhibited hepatic necrosis, oxidative stress (measured as 4-hydroxynonenal), IL-6 cytokine release and apoptosis were shown [40]. Yanget et al. observed that in a 2-month dietary intervention in humans, with a diet inducing obesity, daily consumption of catechins-rich tea (650 ml) increased lipolysis and reduced body weight by up to 20% [41]. Both in the case of an *in vitro* study with human lymphocytes pre-incubated in green tea and subjected to oxidant challenge induced by H_2O_2, and in a supplementation study with healthy volunteers (4 weeks 2×150 ml/d green tea), a decrease in DNA damage was observed [42]. It was also shown that catechins affected the lipid droplets size in vascular endothelial cells and indirectly reduced obesity [43].

To sum up, many animal as well as human studies have demonstrated that green tea catechins can prevent the effects of genetic and diet-induced obesity, insulin resistance and hypertension, thanks to their anti-oxidative effects, metabolism modulation, increased glucose utilization, reduced dietary fat absorption, decreased DNA damage and *de novo* lipogenesis [44,45]. A shift from natural dietary sources of vitamins, minerals, bioactive compounds and fiber to high-calories food with a small amount of regulating ingredients, along with the additive effect of environmental pollutants that induce systemic inflammation observed in drivers, may be one of the key factors contributing to the development of obesity and related chronic diseases.

Benzo(a)pyrene (BaP)

Polycyclic aromatic hydrocarbons (PAHs) are environmental contaminants which are related, *inter alia*, to the operation of combustion engines. Some PAHs compounds have been recognized as mutagenic, carcinogenic and teratogenic to humans [46]. Benzo(a)pyrene, which is often used as a toxicological model for all carcinogenic PAHs, is one of the most widely studied and powerful PAHs [47]. The main routes of BaP exposure occur through the intake of food with a high content of BaP and by inhalation [48]. Studies over the last decades have shown that a diet can modulate the bodily response to chemicals absorption, distribution, metabolism and excretion [49,50]. The results of many studies carried out on humans, as well as *in vitro* and in animal models, have been published, where the influence of various bacterial strains, individual nutrients and their constellations on the reduction of the negative impact of BaP on health has been analyzed.

Zhao et al. [51] analyzed the properties of 15 strains of *Lactobacillus* with regard to reducing the absorption of BaP from the digestive tract of rats. Two strains, namely *L. plantarum* CICC 22135 and *L. pentosus* CICC 23163, were found to display high efficiency in removing BaP from the water environment. Also, the mechanism of cell-BaP complexes formation was examined by analyzing the ability of various cell components to bind BaP. It was shown that peptidoglycans play a significant role in BaP binding. The authors also indicated that these 2 strains might play a considerable role in detoxification, both in the case of humans and animals [51].

In a rat model of colon cancer (Pirc), the influence of the Western diet, rich in saturated fatty acids, on the rate of BaP development inducing colon tumorigenesis in a polyposis was analyzed. The Western diet accelerated tumor formation and proliferation, and was connected with an increase in the concentration of insulin, leptin and inflammatory molecules [52]. *In vivo* studies indicated that exposure to BaP while using a high-fat diet might increase the risk of type 2 diabetes by inducing pro-inflammatory production of cytokines and the expression of genes related to type 2 diabetes [53]. Apart from the quantitative aspect

concerning the fat content in a diet, studies regarding the influence of various fatty acids on health, with a simultaneous exposure to BaP, are being carried out.

In a mouse model of colon cancer, an increased accumulation of BaP metabolites in the plasma, colon and liver tissues was observed in the mice fed on a diet rich in saturated fats (coconut oil), as compared to those fed with unsaturated fats. Additionally, the distribution of BaP-DNA adducts reflecting the distribution of these metabolites, and a strong association between the adducts level and the occurrence of adenomas, were observed [54]. Zhou et al. [55] showed that dietary fish oil played a protective role in BaP-induced hepatic carcinogenesis and significantly reduced the DNA adducts level in the mice model [55]. In the case of *in vitro* studies, clear anti-inflammatory properties of docosahexaenoic acid under exposure to BaP were shown [56]. Docosahexaenoic acid treatment increased BaP membrane accumulation connected with the induction of phases I and II metabolizing and detoxifying enzymes, as well as reduction of DNA adducts and BaP metabolites in the supplemented cells [57].

As regards the natural products which contain a wide spectrum of bioactive components, studies have been undertaken focusing on the use of green tea, coffee and algae, in which the influence of these products on the reduction of the negative action of BaP has been analyzed.

Popular all over the world, green tea is, *inter alia*, a very good source of catechins (e.g., epigallocatechin gallate, epicatechin gallate, epigallocatechin, epicatechin). It has been demonstrated that green tea strongly inhibits the process of digestion and absorption of lipids and lipophilic compounds in the intestines, as well as their excretion [58]. Studies on rats with lymph- and bile duct cannulation have shown that green tea powder considerably reduces the absorption of BaP from the intestines and increases its biliary secretion. It is assumed that the obtained effect results from specific properties of tea associated, *inter alia*, with luminal lipolysis and micellar solubilisation. The dose of the green tea powder, as applied in the studies, in terms of the weight of an adult, corresponded to about 2–3 cups/day [59].

Coffee is another drink that is extremely popular all over the world. It constitutes a rich source of phenols, polyphenols, flavanoids and nonflavanoids with antioxidant properties. The *in vitro* studies performed using hepatocarcinoma cell lines HepG2, human esophageal squamous carcinoma cell line KYSE 70, as well as transgenic UGT1A mice, indicated that coffee inhibited the generation of oxidative stress induced by BaP. The observed effect was related to UDP-glucuronosyltransferases activation [60].

Using a male and female mice model, Chamorro-Cevallos et al. [61] showed a protective effect of Arthrospira (Spirulina) against the BaP-induced genetic damage of germ cells. On the market, there are many dietary supplements with Spirulina, which is the commercial name of Cyanophyceae belonging to the Oscillatoriales order. They are a rich source of plant protein, essential amino acids, vitamins, carotenoids, minerals, essential fatty acids (g-linolenic acid and sulfolipids), and such compounds as phycocyanin, photosynthetic biliprotein, and phycocyanobilin. Taking into consideration a wide spectrum of bioactive components of green tea, coffee and Spirulina, the obtained beneficial effect seems to be the outcome of a synergistic effect of a broad spectrum of bioactive components and antioxidants.

Apart from the studies aiming at analyzing the influence of individual products with a specific content on the cascade of changes induced by BaP, there are many papers describing the influence of isolated single compounds, such as vitamin C, β-carotenoids, retinol, retinoic acid, phenethyl isothiocyanate, luteolin, chrysin, naringenin, quercetin, damnacanthal, proanthocyanidine, resveratrol, berberine, catechin, anthocyanins, apigenin or kaempferol. The mechanisms of action of the selected phytochemicals and the above-mentioned dietary compounds are presented in Table 1 [52–57,59–73].

Table 1. Mechanisms of action of selected nutrients and phytochemicals during exposure to benzo(a)pyrene (BaP) – a review of original research dated 1974–2018

Diet/Nutrient/Phytochemical	Mechanism of actions	Research model	References
Western diet (WD)	In rats fed with a WD compared to animals fed with unsaturated fat/normal rodent chow: • visceral and subcutaneous fat depots were higher • tumor formation was increased • adenoma progression to a high-grade dysplasia in the colon was observed • increased levels of cholesterol, triglycerides and leptin were reported	rat model of polyposis in the colon (PIRC)	52
High-fat diet (HFD)	HFD with BaP: • enhanced the expression of IL-1β in the liver and TNF-α throughout the bowel and in the liver • increased the expression of genes related to type 2 diabetes in the bowel and liver (uncoupling protein UCP2) • significantly decreased the expression of the incretin glucagon-like peptide 1 which plays an important role in insulin secretion	male C57B6/6J mice	53
Coconut oil (saturated fat – SF)	• induction of BaP biotransformation enzymes and extensive metabolism of BaP was observed • BaP metabolites were generated to a greater extent in the colon and liver, and their concentrations were dose-dependent • BaP metabolites formed BaP-DNA adducts which may contribute to colon tumors	Apc^{Min} mice – multiple intestinal neoplasia mouse model	54
Fish oil (FO)	• the levels of total hepatic DNA adducts were significantly decreased in FO groups compared to control groups • FO significantly enhanced gene expression of Cyp1A1	B6C3F1 male mice	55
Docosahexaenoic acid (DHA)	• the highest expression of COX-2 and CB2 was observed in macrophages supplemented with DHA, and activated with lipopolysaccharide and BaP – anti-inflammatory properties of DHA	American Type Cell Culture, RAW 264.7, TIB-71	56
Docosahexaenoic acid (DHA)	• DHA treated cells exhibited lower pyrene-like metabolites indicative of lower DNA adducts compared to control bovine serum albumin, oleic acid or linoleic acid treated cells • DHA reduced the abundance of the proximate carcinogen BaP 7,8-dihydrodiol and the 3-hydroxybenzo(a)pyrene	human adenocarcinoma alveolar basal epithelial cell line – A549	57
Green tea extract (GTE)	• GTE had a profound inhibitory effect on the intestinal absorption of BaP and promoted the excretion of absorbed BaP via the biliary route	male Sprague-Dawley rats	59
Coffee	• exposure to coffee led to a reduction of BaP-induced production of reactive oxygen species *in vitro* and in htgUGT1AWT mice, even in the presence of low function SNP variants	cell culture (HepG2, KYSE70 cells) and htgUGT1A-WT mice	60

Spirulina maxima (SP)	• SP treatment reduced the detrimental effect of BaP on the quality of mouse semen • SP exhibited a protective effect against BaP-induced genetic damage to germ cells in male and female mice	male and virgin female CF1 mice	61
Curcumin	• reverted histopathological deviations in the lung tissues due to benzo[a]pyrene ingestion • reduced the activation of NF-ϰB and MAPK signalling and COX-2 transcription in lung tissues	male Swiss albino mice	62
Vitamin C	BaP intakes were associated with: • significant reductions in birth weight and length in women with low vitamin C intakes • an increased risk of small size for gestational age in women with low dietary vitamin C intakes (the strongest associations in those carrying the GSTP1 Val allele, associated with a lower contaminant detoxification activity)	657 women (Barcelona) during the first trimester of pregnancy	63
β-carotene, β-apo-8-carotenal, retinol, retinoic acid	• β-carotene and retinol significantly reduced BaP-induced oxidative stress • carotenoids and retinoids reacted reversely leading to the reduction of the induced phase I metabolizing enzymes and induction of phase II and III metabolizing enzymes	human HepG2 cell line	64
Phenethyl isothiocyanate (PEITC)	• PEITC inhibited BaP-induced rise in rat liver CYP1A1 mRNA in a dose-dependent manner, as well as the apoprotein levels of CYP1A (the major enzyme required for PAHs bioactivation)	liver of male Wistar albino rats	65
Luteolin (L)	• negated the upregulated expression of PCNA, CYP1A1 and NF-ϰB • counteracted such alterations as LPO, lung specific tumor markers such as CEA, NSE, decreased enzymatic antioxidants: SOD, CAT, GR, GPx and GST, and non-enzymatic antioxidants such as GSH, vitamins E and C	male Swiss albino mice	66
Chrysin	• downregulated the expression of COX-2 and NF-ϰB, and maintained cellular homeostasis • significantly attenuated increased lipid peroxides and carcinoembryonic antigen with a concomitant decrease in the levels of both enzymatic antioxidants and non-enzymatic antioxidants	male Swiss albino mice	67
Naringenin (NRG)	• significantly counteracted the alterations of BaP-induced increased lipid peroxidation, proinflammatory cytokines (TNF-α, IL-6 and IL-1β) decrease in activities of tissue enzymic antioxidants (SOD, CAT, GPx, GR, GST) and non-enzymic antioxidants (GSH and Vit-C) • effectively negated the BaP-induced upregulated expression of CYP1A1, PCNA and NF-ϰB genes	Swiss albino mice	68
Quercetin (QC)	• quercetin metabolites (Q3G, Q30S, IS) inhibited BaP+BC-induced cell death • Q30S, Q3G and IS decreased BaP+BC-induced DNA damage • Q30S, Q3G and IS suppressed BaP+BC-induced cytochrome P450 (CYP)1A1/1A2 expression • Q3G and Q30S decreased the intracellular reactive oxygen species formation induced by BaP+BC	American Type Culture Collection – A549 cells	69
Quercetin (QC)	• the amount of unmetabolised BaP was significantly lower after incubation with lung microsomes from the offspring that received quercetin during gestation • BaP-induced DNA adduct formation liver microsomes were significantly lower in the offspring exposed to quercetin during gestation • prenatal diet led to persistent alterations in phase I and II enzymes of adult mice and might have affected the cancer risk	liver and lung of 129/SvJ:C57BL/6J mice	70

Table 1. Mechanisms of action of selected nutrients and phytochemicals during exposure to benzo(a)pyrene (BaP) – a review of original research dated 1974–2018 – cont.

Diet/Nutrient/Phytochemical	Mechanism of actions	Research model	References
Quercetin (QC), damnacanthal (DAM), proanthocyanidine (PA)	• in QC, DAM and PA decreased interferon-γ l • in PA and QC decreased IL-1β and TNF-α • in QC, DAM and PA decreased oxidative stress markers (NO, MDA, TOS) and OSI, increased antioxidant GSH levels • QC and DAM upregulated apoptotic gene expression and downregulated anti-apoptotic gene expression, decreased TOS, OSI, NO; GSH, MDA	A549 alveolar cell line	71
Resveratrol, berberine, quercetin (QC), catechin, anthocyanins	• all of the polyphenols completely prevented the increase in ROS generation • anthocyanins and berberine inhibited BaP increased mitochondrial superoxide generation • quercetin, berberine, resveratrol and cyaniding strongly inhibited the increase in mRNA expression of the UCP2 gene • QC and catechin increased the expression of SOD2 • QC, cyanidin and catechin strongly inhibited the increased mRNA expression of TNF-α • resveratrol, QC, catechin and cyanidin blocked cell proliferation • most polyphenols, and especially resveratrol, helped to decrease neoplastic transformation	Bhas 42 cells (v-Ha-ras-transfected mouse embryo fibroblast cells)	72
Flavonoids: apigenin (A), luteolin (L), quercetin (QC), kaempferol (K)	• flavonoids containing a 4' B-ring hydroxyl substitution and a 2–3 C-ring double bond (A, L, QC, K) protected against BaP-induced increase in intercellular adhesion of molecule-1 (ICAM-1) in endothelial cells	human umbilical vein endothelial cells (HUVEC) – model for vascular inflammatory diseases	73

BC – β-carotene; CAT – catalase; CB2 – cannabinoid receptor 2; CEA – carcinoembryonic antigen; COX-2 – cyclooxygenase-2; GPx – glutathione peroxidase; GR – glutathione reductase; GSH – reduced glutathione; GST – glutathione S-transferase; GSTP1 – glutathione S-transferase P1; ICAM-1 – intercellular adhesion of molecule-1; IL-1β – interleukin 1 β; IL-6 – interleukin 6; IS – isorhamnetin; LPO – lipid peroxides; MAPK – mitogen activated protein kinases; MDA – malondialdehyde; NAD(P)H – nitrite reductase; NF-ϰB – nuclear factor-ϰ B; NO – nitric oxide; NSE – neuron specific enolase; OSI – oxidative stress index; PAH – polycyclic aromatic hydrocarbon; PCNA – proliferating cell nuclear antigen; Q30S – quercetin 30-sulphate; Q3G – quercetin 3-glucuronide; ROS – reactive oxygen species; SNP – single nucleotide polymorphism; SOD – superoxide dismutase; SOD2 – superoxide dismutase 2; TNF-α – tumor necrosis factor α; TOS – total oxidant status; UCP2 – mitochondrial uncoupling protein 2; UGT – UDP-glucuronosyltransferase.

The range of food ingredients that are currently being studied in terms of reducing the negative impact of BaP is very wide. Kasala et al. [74] published a review article on *in vivo* (animal model) and *in vitro* studies concerning the role of dietary phytochemicals in BaP-induced lung cancer. That paper presents results of the studies demonstrating that 28 dietary phytochemicals exerted a protective effect against BaP-induced lung cancer through reducing the bioactivation and/or promoting detoxification. The obtained results of *in vitro* as well as *in vivo* studies are very promising. It seems that there is a number of nutrients that may have a potentially protective effect on the adverse impact of BaP.

Interest in the results of *in vitro* and *in vivo* studies with regard to the reduction of the negative influence of not only BaP but also other air pollutants is great, as evidenced by the dynamically growing market of dietary supplements. In recent years, a lot of dietary supplements have been marketed containing various types of isolated dietary phytochemicals or extracts from plant products. The wide range of these supplements also results from a growing demand. Those supplements are so popular due to their relatively low toxicity when compared to synthetic substances. However, it needs to be emphasized that there are currently no dietary phytochemicals whose beneficial effect, in terms of reducing the negative influence of BaP, has been confirmed in clinical studies in people. Therefore, preventive actions should be targeted at the consumption of food products which are good sources of dietary phytochemicals, rather than on the intake of isolated single compounds or plant extracts.

The results of studies in which vitamin A was supplemented may be an excellent example. Studies carried out at the end of the 20th century indicated that retinoids had the most documented potential chemopreventive effects [75]. This was confirmed by epidemiological studies showing that individuals consuming a diet rich in vitamin A had a reduced risk of lung cancer incidence. However, in clinical trials with the use of vitamin A supplementation, an increase in the number of lung cancer cases has been observed, especially in smokers [76,77]. This is explained, *inter alia*, by the fact that the chemopreventive properties of phytochemicals are based on the results of *in vitro* or *in vivo* studies in which the doses applied are often several times higher than those that can be consumed in a form of food products. Moreover, the final effect of the applied supplementation reflects a whole spectrum of other genetic and environmental factors, including one's lifestyle and diet.

Benzene

Benzene has been suspected of having a toxic effect already since 1900, earning the name of a "bone marrow poison" [78]. Benzene poisoning takes place through steam inhalation, as well as by the absorption through the skin and the digestive system [79]. Benzene fumes induce oxidative stress, inflammatory responses, alterations in cell cycle and DNA damage in mice [80,81]. These changes have been associated with the risk of the development of various diseases, such as myelodysplastic syndromes, acute myeloid leukemia, as well as presumably lymphocytic leukemia and non-Hodgkin lymphoma in humans [82–84]. It has been demonstrated that even a low exposure to benzene (< 1 ppm – the occupational standard in the U.S.) induces a significant decrease in almost all blood cell counts, along with dose-dependent decreases in CD4+ T cells, the CD4+/CD8+ ratio and B cells [85].

Benzene vapors, after getting into the lungs, are adsorbed by lung alveoli and hence transported to the bloodstream, from which they are largely absorbed by adipose tissue. Studies using animals as well as humans showed that, in the case of a higher fat content, benzene was eliminated more slowly from the body than in subjects with a small body fat content [86]. It was also demonstrated that, for example, phenolic metabolites of benzene, such as hydroquinone, catechol and 1,2,4-benzenetriol, may accumulate

in fat tissue, following which they can be released upon the ingestion of lipolytic substances such as green tea catechins [36]. In the case of drivers among whom obesity is a big problem, a larger accumulation of fat mass may be associated with increased susceptibility to chemicals, such as benzene which has a high affinity for adipose tissue.

Due to the role of oxidative stress and inflammatory state in the risk of developing diseases related to exposure to benzene, in the literature there have been several papers in which the influence of selected products and nutrients on the improvement of the antioxidant barrier of a body and, thus, on the reduced intensity of harmful processes associated with exposure to benzene, has been analyzed.

By examining gasoline station attendants exposed to low-dose benzene, Costa et al. [87] observed a significantly higher urinary concentration of trans, trans-muconic acid – a biomarker of benzene exposure – than in unexposed male office workers. Additionally, in the workers exposed to benzene, a significantly higher advanced oxidation protein products level and serum reactive oxygen metabolites (measured using d-ROMS test), negatively correlated with fruit and vegetables consumption, were observed. The influence of vegetables on benzene-induced hematologic and immunologic disorders was also analyzed in a rat model. In the groups fed with vegetable cocktail juice (made from carrot, beetroot, celery and radish), in comparison with the group not receiving this cocktail, such parameters as red blood cells, hemoglobin and lymphocytes were significantly higher. In the group without the cocktail, spleen necrosis and cell injuries were observed, whereas similar changes did not occur in the cocktail treated groups [88].

In vivo studies have also analyzed the influence of various plant extracts on the reduction of the negative effect of benzene. Mukhopadhyay et al. [89] analyzed the chemopreventive effect of flavonoids present in the bark extract of *Saraca asoca* (folk medicinal plants) on the acute myeloid leukemia (AML) in mice. In this study, the bark extract of *Saraca asoca* effectively attenuated benzene-induced secondary AML in bone marrow.

The anti-leukemic effect of an extract from Wheat grass (with anticancer and antioxidant potential) has also been investigated in the murine model. In various experimental groups with benzene-induced leukemia, hematological parameters have demonstrated anti-leukemic effect connected with phagocytosis of killed *Candida albicans* and with a significant chemotactic activity [90].

Akanni et al. [91], using a benzene-induced model of leukemia, evaluated the potential chemotherapeutic activities of bark, fruit and leaf extracts of *Kigelia africana* (a tropical plant commonly referred to as the "sausage tree"). In the rats treated with the stem bark, fruit and leaf extracts, there were significantly alleviated anemia signs and reduced leukocytosis in comparison with the leukemia control group. Anti-leukemic properties were the most effective in the bark extract, and the least effective in the leaf extract.

In the same rat model of leukemia, the protective and ameliorative roles of an aqueous leaf extract of *Andrographis paniculata* (an herbaceous plant constituting a rich source of flavonoids and diterpenoids) were also examined [92]. Organs histology showed varying lesions of the heart, as well as degeneration and necrosis of the hepatocytes and renal tissue in the groups exposed to benzene carcinogen, but the hepato-renal and heart histio-architectures were intact in the extract pre-treatment and post-treatment groups.

Metals

Lead

Lead is classified as probably carcinogenic to humans, and is related to cardiovascular, neurodevelopmental, hematological and renal disorders [93,94]. In adults, after absorption to the circulatory system, about 94% of lead is accumulated in bones and the remaining amounts in such tissues as the liver, brain or kidneys. The half-life of

lead in blood and soft tissue is about 30 days but, once accumulated in bones, it may be released to the blood for many years [95]. Many studies have indicated that both macro- and micro-nutrients can modulate Pb absorption and accumulation.

In rats fed on a diet with a high fat content, increased blood and liver concentrations of Pb were reported, and this effect was probably connected with the formation of soluble complexes, which were readily absorbed. Also in rats fed on low as well as high protein diets, a higher concentration of Pb in soft tissue was observed, but in those fed on a diet with a normal protein content this effect did not occur [96,97]. A rat model showed that dietary fiber, especially guar gum, reduces the levels of absorption and accumulation of Pb [98].

Also, lactic acid bacteria (*Lactobacillus plantarum* CCFM8661) were found to decrease the blood and tissues concentrations of this metal via the formation of complexes with Pb. This probiotic also prevented alterations in the levels of oxidative stress markers, such as malondialdehyde, superoxide dismutase, glutathione, glutathione peroxidase in the blood and kidneys, and recovered blood δ-aminolevulinic acid dehydratase activity [99].

Just like in the case of other toxic elements, the presence of some minerals can influence lead absorption and accumulation, as well as reduce its toxic effects. In children inhabiting areas highly contaminated with lead, a significant dependence between the Fe-deficient children and the blood concentration of lead was observed, with the blood levels of lead being higher in iron-deficient children, as compared to those with an adequate iron status [100]. Another study revealed that Fe supplementation resulted in a reduced lead absorption only in the population suffering from anemia, whereas in the population with a normal Fe status it did not reduce the blood Pb level [101].

In addition, a low dietary intake of Ca would intensify the intestinal absorption of Pb via the stimulation of Ca transporter proteins, which also transport Pb [102]. A high consumption of phosphate is also connected with the formation of insoluble Pb-P complexes, which triggers a decrease in their absorption [103]. Calcium and Zn supplementation in a mouse model was found to reduce lead-induced perturbations in the aminergic system of the brain [104], while protecting lead-induced perturbations in antioxidant enzymes and lipid peroxidation [105]. In a rat model, supplementation with dietary antioxidants, such as ascorbic acid, α-tocopherol, L-methionine and quercetin, reduced the impact of Pb toxicity through reducing the oxidative stress and inflammation in soft tissue [106,107]. In animals experimental models, it was shown that some plant extracts (garlic, olive leaf, green tea) could also reduce various types of symptoms connected with Pb toxicity [108–110].

Epidemiological research indicates that a high consumption of vitamin C is connected with a lower blood concentration of Pb, which is probably related to the chelating ability of vitamin C [111]. Simultaneously, supplementation with vitamin D3 increases the intestinal absorption of Pb [112].

Cadmium

The International Agency for Research on Cancer has classified Cd as Group 1 – carcinogenic to humans when inhaled [113]. The toxicity mechanism of Cd includes, *inter alia*, generation of oxidative stress and inflammation, alteration in gene expression, DNA repair impairment, interactions with Zn and Mg, and changes in cellular signaling pathways [114,115]. Cadmium in the body is mainly accumulated in the liver and kidneys [116]. This element has a very long half-life, i.e., 45 years [117]. Taking into consideration the fact that Cd toxicity is associated, *inter alia*, with the intensification of oxidative stress and inflammatory state, one may assume that certain dietary components can counteract Cd toxicity by their antioxidant and anti-inflammatory activity.

Colacino et al. [118] analyzed data from the 2003–2010 National Health and Nutrition Examination Survey, and

looked for certain dependence between the antioxidant and anti-inflammatory diet score (ADS) and urinary cadmium, as well as markers of oxidative stress and inflammation. They showed that an increase in urinary cadmium was associated with an increase in C-reactive protein, γ-glutamyl transferase and alkaline phosphatase. However, an increase in ADS was associated with a decrease in C-reactive protein, γ-glutamyl transferase, alkaline phosphatase, total white blood cell count, and an increase in serum bilirubin. The authors suggested that dietary interventions focused on high ADS might be an important tool in reducing cadmium toxicity.

In laboratory animals as well as in humans, it has been shown that the administration of some minerals also reduces the absorption and toxicity of Cd. The absorption of Cd from the digestive tract and its accumulation in the body are influenced, *inter alia*, by Fe and Zn body status. In humans with a lower serum ferritin concentration, the absorption of Cd from a test meal was higher than in people with a normal ferritin concentration. Also in animals fed on a Fe-deficient diet, an elevated Cd absorption was reported [119]. Moreover, a deficiency of Zn is associated with an increased absorption of Cd [120]. Amara et al. [121] found that Zn administration decreased oxidative damage and reversed the impairment of spermatogenesis and testosterone synthesis during oral Cd exposure. The protective effect of Zn may also result from the fact that it works as a co-factor in the superoxide dismutase. Sarić et al. [122] found that in rats exposed to Cd, the administration of Zn resulted in a lower accumulation of Cd in body organs. Groten et al. [123] demonstrated that the administration of several important minerals (Ca, P, Zn, Fe) reduced plasma transaminase activities and anemia caused by Cd exposure. The protective effect related to the reduction of the risk of hepatic, renal, skeletal and reproductive disorders, as well as teratogenic and genotoxic changes related to Cd exposure, has also been shown after the administration of curcumin [124], quercetin [125], naringenin [126], green tea extracts [127], aronia melanocarpa berries [128], garlic [129] and grapefruit juice [130]. Also other dietary components, such as fiber, phytic acid, glycinin and ovalbumin, have significantly lowered the gastrointestinal absorption of Cd and its accumulation in soft tissue [131–133].

As in the case of lead, the absorption of cadmium can be modulated by the intestinal flora. Zhai et al. [134] showed that *Lactobacillus plantarum* CCFM8610 reduced the intestinal absorption and accumulation of Cd in the liver and kidneys, as well as oxidative stress both in the case of acute exposure and prolonged treatment in mice. Also Jama et al. [135] demonstrated that in Cd exposed rats a mixture of lyophilized probiotics bacteria (*Lactobacillus rhamnosus*, *Lacidophilus*, and *Bifidobacterium longum*) significantly reduced its genotoxicity.

Chromium

Chromium exists in a series of oxidation states but trivalent (Cr(III)) and hexavalent (Cr(VI)) compounds are the ones which are the most significant biologically. The Cr(III) is an essential dietary mineral but only in low doses. Its deficiency has been associated with such complications as impaired glucose tolerance, fasting hyperglycemia, glucosuria, elevated body fat percentage, decreased lean body mass, cardiovascular disease, decreased sperm count and impaired fertility [136]. Hexavalent Chromium quickly crosses the cell membranes with anionic sulphate-ion transporters and, after that, it is converted into Cr(III) by antioxidants (ascorbate, glutathione, cysteine). For a long time Cr(III) was considered relatively non-toxic, but recently it has been found that it is more harmful than Cr(VI) and that it exerts genotoxicity action in cell-free systems [137]. It has been stated that Cr(III)picolinate interacts with DNA and leads to DNA strand breaks, oxidative DNA modifications and DNA-protein crosslinks [136–138].

Hexavalent Chromium is commonly used in industrial processes and is a proven endocrine disruptor, toxin, mu-

tagen, teratogen and a group A carcinogen. Cytotoxicity of Cr(VI) is related, *inter alia*, to the oxidative stress generation, DNA damage, apoptotic cell death and altered gene expression. The increased use and insufficient utilization of Cr waste contributes to its increased environmental exposure. Occupational exposure to Cr is found among approximately half a million workers in the U.S. and several millions worldwide [138].

Banu et al. [139] investigated the mechanisms involved in Cr(VI)-induced ovotoxicity, and the protective role of vitamin C. Those authors demonstrated that vitamin C pretreatment protected ovary and granulosa cells from harmful effects of Cr(VI) and, therefore, vitamin C could play an important role in the prevention of Cr(VI)-induced ovotoxicity. Banu et al. [140] analyzed the molecular mechanism of Cr(VI)-induced infertility and the effect of resveratrol administration to mitigate the impact of this metal on lactating rats. Resveratrol, as a strong antioxidant and a phytoestrogen, was found to alleviate the effects of Cr(VI) by upregulating cell survival proteins and antioxidants, and to restore the estradiol levels by means of inhibiting phase I/II metabolic enzymes in the ovary, kidney and liver, as well as by inhibiting hydroxylation, glucuronidation and sulphation.

Susa et al. [141] investigated the effect of vitamin E on Cr(VI)-induced cytotoxicity and lipid peroxidation in primary cultures of rat hepatocytes. The pre-treatment of cultures of rat hepatocytes with a-tocopherol succinate for 20 h prior to the exposure to Cr(VI) resulted in a clear decline of cytotoxicity. The results of that study indicated the protective effect of vitamin E against Cr(VI)-induced lipid peroxidation as well as cytotoxicity. Its authors suggested that this might be preferably associated with the level of non-enzymatic antioxidants than with the enzymatic antioxidant barrier. The effectiveness of various antioxidants in reducing the negative impact of Cr(III) on oxidative DNA damage (8-hydroxydeoxyguanosine) in isolated calf thymus DNA was also evaluated. Alike melatonin, ascorbate as well as vitamin E markedly inhibited the formation of 8-hydroxydeoxyguanosine. However, melatonin was 60- and 70-fold more effective than ascorbate or vitamin E [142].

Nickel

All Ni compounds, except for its metallic form, have been classified as human carcinogens by the International Agency for Research on Cancer [143]. Nickel can enter the human body mainly by inhaling Ni-containing air, drinking Ni-contaminated water, eating foods with a high concentration of Ni, or through Ni-containing jewellery. Common food products with a high Ni content are: cocoa, chocolate, soya beans, oatmeal, nuts, almonds, fresh and dried legumes, as well as beverages and dietary supplements with Ni, canned food, Ni-plated utensils and stagnated tap water [144]. However, pulmonary absorption is the major route of Ni-induced toxicity. The chemical form of Ni and its deposition site (size, shape, density and electrical charge) in the lungs affects the extent of absorption [145]. Nickel is a severe neurotoxic, immunotoxic, hematotoxic, genotoxic, reproductive toxic, pulmonary toxic, hepatotoxic, nephrotoxic and carcinogenic agent [146]. Inhalation exposure induces the risk of several lung diseases, such as lung irritation and inflammation, as well as hyperplasia of pulmonary cells, fibrosis, pneumoconiosis and allergic asthma. Occupationally exposed people have a higher risk of respiratory tract cancer due to the inhalation of Ni at their workplace. A high cancer risk is related to less soluble oxidic, and especially sulfidic, Ni species in dust. In the general population, the most harmful health effect related to Ni exposure is allergic contact dermatitis due to a prolonged skin contact with Ni [147].

Chen et al. [148] examined the effects of Ni on human platelets. They observed that Ni significantly inhibited the function of platelet and considerably increased malondialdehyde (MDA) levels, with a reduction in platelet reduced glutathione and α-tocopherol content. However,

treatment with ascorbic acid significantly decreased the levels of MDA, as well as reduced glutathione (GSH) and increased the content of α-tocopherol. Additionally, it has been shown that Ni toxicity is connected with lipid peroxidative damage and that ascorbic acid has a protective effect. Nickel chloride can also induce lipid peroxidation in human plasma. Chen at al. [149] showed that Ni treatment increased the hydroxyl radical production in a concentration-dependent manner. The decreasing trend of α-tocopherol levels in human plasma is believed to be associated with Ni-induced lipid peroxidation. However, glutathione, catechine and mannitol treatment was found to decrease Ni-induced lipid peroxidation and hydroxyl radical production in human plasma [149].

Salnikow et al. [150] revealed that the co-administration of nickel sulphate and vitamin C ameliorated nickel-induced hyperglycemia by augmenting insulin sensitivity in rats, and also enhanced liver glycogen storage. An additional beneficial effect of vitamin C also results from such a property as scavenging activity within the lipid region of the membrane. That study also revealed that the Ni-induced activation of hypoxia-inducible factor (HIF-1) and the upregulation of hypoxia-inducible genes were caused by exhausted intracellular levels of vitamin C. Supplementation of culture medium with vitamin C was found to increase the intracellular vitamin level and reversed the metal-induced stabilization of HIF-1 and HIF-1α dependent gene expression.

Das et al. [146] suggested that vitamin E can also protect nickel-induced changes in the serum lipid profile and glucose level. Moreover, α-tocopherol can protect liver and pancreatic tissues from nickel-induced cellular damage. Vitamin E, located near the cytochrome P-450 in phospholipids of the cell membrane, sweeps away free radicals generated in the cytochrome P-450. The research results described above indicate that a high consumption of dietary L-ascorbic acid and α-tocopherol might ameliorate oxidative stress induced by Ni.

CONCLUSIONS

As it was indicated, a widely understood working environment of professional drivers, along with exposure to a number of xenobiotics, irregular working hours and improper dietary habits, may constitute reasons for the increased risk of the development of some civilization diseases. Literature data prove that some components of a diet may modulate the adverse effects of exposure to:

- mixed air pollution – this can be modulated by green tea catechins;
- benzo(a)pyrene by various bacterial strains, fish oil, green tea, coffee, algae and isolated single compounds: vitamin C, β-carotenoids, retinol, retinoic acid, phenethyl isothiocyanate, luteolin, chrysin, naringenin, quercetin, damnacanthal, proanthocyanidine, resveratrol, berberine, catechin, anthocyanins, apigenin or kaempferol;
- benzene by fruit and vegetables, extracts from folk medical plants: *Saraca asoca*, *Kigelia africana*, *Andrographis paniculata*;
- lead by an adequate intake of protein, Fe and Ca, dietary fiber, lactic acid bacteria, dietary antioxidants: ascorbic acid, α-tocopherol, L-methionine and quercetin, some plant extracts (garlic, olive leaf, green tea);
- cadmium by an adequate intake of Fe, Ca, P and Zn, some strains of probiotics bacteria, foods and dietary compounds such as green tea extracts, aronia melanocarpa berries, garlic and grapefruit juice, curcumin, quercetin, naringenin, fiber, phytic acid, glycinin and ovalbumin;
- chromium by vitamin C and E, resveratrol;
- nickel by vitamin C, α-tocopherol, glutathione, catechine, mannitol.

In recent years, a lot of dietary supplements have been marketed containing various types of isolated dietary phytochemicals or extracts from plant products. However, there are currently no dietary phytochemicals whose beneficial effect, in terms of reducing the negative influence

of the above-mentioned chemicals, has been confirmed in clinical studies in people. Therefore, preventive actions should be targeted at proper nutrition, with the consumption of food products which are a good source of such dietary phytochemicals, rather than on the intake of isolated single compounds or plant extracts. This indicates the necessity for a precise monitoring of the diet and nutritional status, as well as education of this professional group.

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