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REVIEW ARTICLE

FOOD AS A SOURCE OF EXPOSURE TO NICKEL

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ABSTRACT

According to the European Food Safety Authority (EFSA), food is the main source of nickel intake by the general population. Based on the risk assessment, EFSA determined the tolerable daily intake of this element (TDI) from all sources at the level of 2.8 µg/kg body weight, which is for an adult 196 µg, while for a child 56 µg. The Benchmark Dose Lower Confidence Limit ($BMDL_{10}$) associated with dermatitis at 1.1 µg/kg body weight was also determined as well as the Margin of Exposure (MOE). Nickel intake in the Member States varies and depends on consumption habits. CONTAM Panel of EFSA considered the unlikely possibility of developing cancers related to the intake of nickel with food. According to experts, other harmful effects on the human body are more often identified. An additional aspect requiring further investigations that will allow an actual estimation of exposure associated with intake of this element by various groups of population is the issue of nickel absorption in the human body. The review of the EFSA opinion on the request of the European Commission planned in the near future based on the collected data as part of the action of the Commission Recommendation (EU) 2016/1111 on monitoring the presence of nickel in food will contribute to taking appropriate actions related to consumer protection, including the most vulnerable groups of population.

Key words: *nickel/toxicity, foodstuffs, dietary exposure, sources of exposure*

STRESZCZENIE

Według Europejskiego Urzędu ds. Bezpieczeństwa Żywności (EFSA), głównym źródłem pobrania niklu przez populację generalną jest żywność. Na podstawie dokonanej oceny ryzyka EFSA wyznaczył wartość tolerowanego dziennego pobrania tego pierwiastka (Tolerable Daily Intake TDI) ze wszystkich źródeł na poziomie 2,8 µg/kg masy ciała, co stanowi dla osoby dorosłej 196 µg, natomiast dla dziecka 56 µg. Określono również najniższą dawkę wyznaczającą (Benchmark Dose Lower Confidence Limit) – $BMDL_{10}$ związaną z występowaniem zapaleń skórnych na poziomie - 1,1 µg/kg masy ciała oraz wyznaczono wartość marginesu narażenia (Margin of Exposure – MOE). Pobranie niklu w państwach członkowskich jest zróżnicowane i zależne od nawyków żywieniowych. Panel CONTAM EFSA uznał za mało prawdopodobną możliwość powstawania nowotworów związanych z pobraniem niklu z żywnością. Zdaniem ekspertów znacznie częściej identyfikowane są inne efekty szkodliwe na organizm człowieka. Dodatkowym aspektem wymagającym dalszych badań, który pozwoli na rzeczywiste oszacowanie narażenia związanego z pobraniem tego pierwiastka przez różne grupy populacji, jest kwestia wchłaniania niklu w organizmie człowieka. Planowana w najbliższym czasie na wniosek Komisji Europejskiej rewizja opinii EFSA, w oparciu o zgromadzone dane w ramach zalecenia Komisji (UE) nr 2016/1111 w sprawie monitorowania obecności niklu w żywności, przyczyni się do podjęcia odpowiednich działań związanych z ochroną konsumentów, w tym najbardziej wrażliwych grup populacji.

Słowa kluczowe: *nikiel/toksyczność, środki spożywcze, żywność, narażenie człowieka z dietę, źródła narażenia*

INTRODUCTION

Nickel is an element widely distributed in nature and is present in water, soil, plants and animals [28, 30]. Its biological function in humans is not clear and there is no data indicating its essential role for humans [4, 28]. However for plants and some animals Ni is an essential micronutrient. In higher plants this element is an integral part of enzymes which participate in the metabolism of nitrogen [31]. Higher concentrations could lead to several harmful alterations in plants. It was found that its optimal concentration in plants tissues should not exceed 3 mg/kg. The higher levels affect the development of plants in a degree depending on their sensitivity [15]. This element is also present in all animal tissues at levels up to several ppm. Due to its chemical properties, such as: hardness, high melting point, ductility, nickel is used as part of alloys.

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It imparts such desirable properties as corrosion resistance, heat resistance, hardness, and strength [14, 19].

Nickel containing stainless steel is widely preferable in the food industry because of its durability, lack of reactivity with foods and excellent conductivity [19]. Nickel alloys are also use for production of coins, jewelry while compounds of this element find application in ceramic production as pigments and in battery production [17, 28].

SOURCES OF EXPOSURE TO NICKEL

Nickel can occur in the environment in the various form, generally occurs in the divalent form, as this is its most stable oxidation state [12, 28]. Plants are one of the major sources of exposure to nickel. The concentration of nickel in plants is dependent on the content of this element in the soil [25, 31]. Ni in agricultural soils has been reported at concentrations in the range from 3 mg/kg to 1000 mg/kg [28, 31]. According to monitoring data of Institute of Soil Science and Plant Cultivation – State Research Institute the average content of nickel in soils in Poland is 9.8 mg/kg. The highest nickel contamination is observed in the malopolskie voivodship, which is caused in large measure by industrial activity.

Significant sources of nickel contamination besides natural presence as an effect of volcanic eruptions, windblown dust, forest fires include anthropogenic activity, such as: coal burning processes, liquid fuels, primarily expelled by Diesel engines, the mining industry, production of paints, enamels and plastics [17, 20, 28, 30]. Nickel is commonly used as a raw material in metallurgical and electroplating industry is also use as a catalyst in chemical industry [17, 31] as well as in the fat industry, in the production of margarines and other food fats where nickel is used as a catalyst in the hydrogenation process. Occupational exposure to nickel is connected with elevated levels of this element in blood, urine and body tissues.

The main source of nickel exposure for general population is food and water [12, 17, 36, 37], other sources like dermal contact as well as air inhalation can contribute to exposure to this element. In the air, mainly its inorganic compounds occur such as sulfates, sulfides and nickel oxides. The levels found are usually much lower that hose typically found in occupational situations. Nickel can also release from food contact materials covered with nickel plated or containing this element as an alloy component. The research indicate that migration is higher in the presents of acidic food or food ingredients such as rhubarb and citric acid.

Foodstuffs that are the main contributors to the dietary exposure to nickel in case general population are: grain and grain-based products, nonalcoholic beverages (except milk-based beverages), sugar and confectionery, legumes, nuts and oilseeds, and vegetables and vegetable products (including fungi), milk and dairy products especially for the young population, in particular in toddlers. Chocolate and chocolate-based product as well as sugar and confectionery, non-alcoholic beverages are important contributors to nickel intake for children and adolescents [28].

TOXICITY AND EFFECT ON HUMANHEALTH

Toxicity of nickel is dependent on the chemical form, the route of exposure and solubility of nickel compounds. In 2012 compounds of this element were classified by the International Agency for Research on Cancer (IARC) as carcinogenic to humans (Group 1), while metallic nickel and nickel alloys as possibly carcinogenic to humans (Group 2B) [12, 14, 28]. For occupationally exposed population the respiratory tract and the skin are the major routes of exposure. Ni compounds are carcinogenic to humans after inhalation causing cancers of the lung, nasal cavity and paranasal sinuses [14]. Allergic contact dermatitis is the most frequent effect of Ni in the general population [17, 28, 37]. In humans, the non-carcinogenic effects of oral exposure to nickel include effects on the gastrointestinal, hematological, neurological and immune system [12, 17, 28].

Absorption on nickel from the gastrointestinal tract varies between 3-40 % depending on whether the nickel was in drinking water or food, with greater absorption occurring with drinking water. Fasting individuals have also been shown to absorb more nickel from the gastrointestinal tract than when food is present [12]. One of the factors that can influence, reducing the absorption of nickel from food is the co-ingestion of vitamin C and iron [26]. Most of the absorbed nickel is excreted in the urine, regardless of the route of exposure. About 20%÷35% of the inhaled nickel that is retained in the lungs is absorbed into the blood [28].

The mechanism of nickel carcinogenic action is still the subject of numerous studies and still requires clarification, similar to the absorption from the gastrointestinal tract. It has been proved that this element causes disturbance of DNA synthesis, inhibition of its repair processes and loss of DNA sequence [1, 24, 30]. In 2008 WHO set a TDI of 0.012 mg/kg bw/day this value was confirmed in 2011. In 2005 the EFSA Scientific Panel on Dietetic Products, Nutrition and Allergies was not be able to establish a tolerable upper intake level for intake of nickel from food due to inadequate data for dermal reactions [20].

Table 1. Contents of nickel in different categories of foodstuffs, (µg/kg) [28]

Foodstuffs	n	LC (%)	LB/UB	Concentration (µg/kg)	
				Mean	P95
Grains and grain-based products	4291	26	LB UB	271 321	1069 1078
Vegetables and vegetable products (including fungi)	3738	26	LB UB	742 753	9250 9250
Starchy roots and tubers	664	24	LB UB	123 150	690 690
Legumes, nuts and oilseeds	1218	3	LB UB	1862 1880	7000 7000
Fruit and fruit products	966	31	LB UB	68 91	210 300
Meat and meat products (including edible offal)	2169	66	LB UB	191 239	310 500
Fish and other seafood	718	61	LB UB	77 112	330 390
Milk and dairy products	631	62	LB UB	71 93	435 488
Eggs and egg products	115	74	LB UB	38 57	179 179
Sugar and confectionery	1170	26	LB UB	1504 1586	5170 5170
Animal and vegetable fats and oils	363	58	LB UB	315 378	360 500
Fruit and vegetable juices	505	30	LB UB	35 58	102 120
Non-alcoholic beverages (excepting milk based beverages)	46	24	LB UB	32 35	- -
Alcoholic beverages	892	69	LB UB	28 71	70 150
Drinking water	25700	89	LB UB	1 2	2 3
Herbs, spices and condiments	481	18	LB UB	1259 1277	4640 4640
Food for infants and small children	309	45	LB UB	126 152	500 500
Products for special nutritional use	471	26	LB UB	1999 2051	9100 9100
Composite food (including frozen products)	65	9	LB UB	181 184	490 490
Snacks, desserts, and other foods	73	62	LB UB	111 430	280 1200

n: number of samples; LC: left-censored data (percentage of analytical data below LOD/LOQ); LB: lower bound (results below the LOQ and LOD were replaced by zero in calculations); UB: upper bound (the results below the LOD were replaced by the LOD and those below the LOQ were replaced by the value reported as LOQ; mean; 95th percentile.

EFSA OPINIONS ON NICKEL

In 2015 on request of Hellenic Food Safety Authority the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) published a scientific opinion on the risk to human health associated with the presence of nickel in food and drinking water. Based on available epidemiological data and occurrence data the EFSA established a tolerable daily intake (TDI) of 2.8 µg Ni/kg body weight (b.w.) per day. The benchmark dose lower limit $BMDL_{10}$ of 1.1 µg Ni/kg b.w. associated with dermatitis following oral exposure to Ni based on dose-response analysis was also determined. For risk characterization the CONTAM Panel decided not to establish an acute reference dose, but to adopt a margin of exposure (MOE) approach. Calculated value of MOE taking into account mean and 95th percentile acute exposure for all groups of population was below 10 which indicated to be of health concern. EFSA considered that it is unlikely that dietary exposure to Ni results in cancer in humans and only non-carcinogenic health effects of oral exposure to Ni include effects on the gastrointestinal, haematological, neurological and immune system can occur. Effects of acute exposure to nickel are connected with gastrointestinal and neurological symptoms whiles exposure through skin or by inhalation may lead to Ni sensitization. Whereas oral exposure to Ni is not known to lead to sensitization, oral absorption of Ni is able to elicit eczematous flare-up reactions in the skin in Ni-sensitised individuals [28].

In 2015 EFSA also published scientific opinion concerning risk to animal, public health and the environment related to the presence of nickel in feed. This risk assessment was performed on a request of European Commission. EFSA assessed that any adverse impact of Ni via feed to animals is unlikely. Whereas risks from the presence of Ni in food of animal origin, might be of potential concern in the young population, in particular in toddlers, and other children taking into account chronic average exposure. In case of acute dietary exposure, in Ni-sensitised people different types of skin reactions associated with taking nickel from food of animal origin can occur [29].

OCCURRENCE OF NICKEL IN FOOD

The average content of nickel in food is lower than 0.5 mg/kg, but there are foodstuffs with higher levels of this element [5, 26]. The highest mean concentrations of Ni have been measured in wild growing edible mushrooms, cocoa or cocoa-based products which contain above 10 mg/kg dry weight, beans, seeds, nuts and grains e.g. cocoa beans - 9.8 mg/kg; soybeans - 5.2 mg/kg; soya products - 5.1 mg/kg; walnuts - 3.6 mg/kg; peanuts - 2.8 mg/kg; oats - 2.3 mg/kg; buckwheat - 2.0 mg/kg; and oatmeal - 1.8 mg/kg [14, 27, 28]. Studies of total diet conducted in France indicate slightly lower average nickel contamination for nuts and oilseeds 1.15 mg/kg, chocolate - 0.63 mg/kg and breakfast cereals at 0.55 mg/kg and significantly lower for other groups of foodstuffs – much below 0.5 mg/kg [16]. Subsequent studies from 2012 indicate significantly higher contamination for chocolate and dried fruit, nuts and seeds and lower in case of for breakfast cereals [3].

Ni concentrations of about 30 µg/L and of 100 µg/L have been found in beer and wine; respectively [28]. Concentration of nickel in food is depending on different factors such as: the type of food, growing conditions (i.e. higher concentrations have been observed in food grown in areas of high environmental or soil contamination), and food preparation techniques (e.g. Ni content of cooking utensils, although the evidence for leaching from stainless steel cookware is somewhat mixed) [14, 26]. The nickel content in food also varies according to climate and season. Higher concentration of this element was observed in crops fruit and vegetables grown in spring and autumn in comparison to crops from summer. For above mentioned reasons content of nickel in foodstuffs very often appear to vary according to the sources, and differences are sometimes significant [26].

A total diet study conducted in Spain revealed nickel concentration between 2.35 mg/kg in nuts and 0.002 mg/l in drinking water [13].

Other studies on the nickel content in foods for infants and young children conducted in UK showed an average contamination of this group of foods at the level of 0.1 mg/kg (0.002 mg/kg - 1.4 mg/kg) [28]. Occurrence data collected by EFSA in 15 different European countries between 2003 and 2012 most of them in Germany (80 %) concerned mainly drinking water, food data were relatively scarce. Data collected by EFSA are presented in Table 1.

INTAKE OF NICKEL WITH FOOD

Intake of nickel with food can vary widely not only among different population groups but also in a single individual in different seasons and different days. Factors which can may have influence on the intake are also national and regional dietary habits, diversity of foodstuffs consumed, contamination of drinking water, migration from food contact materials, preparation process of food, absorption in the gastrointestinal tract etc.

According to EFSA mean chronic dietary exposure to Ni across the different dietary surveys and age classes ranged from 2.0 µg/kg b.w. per day (elderly) to 13.1 µg/kg b.w. per day (toddlers). The 95th percentile dietary exposure ranged from 3.6 µg/kg b.w. per day (elderly) to 20.1 µg/kg b.w. per day (toddlers). The highest dietary exposure to Ni was observed in the age classes toddlers and other children. The adult population showed, in general, lower exposure than the young population (2.2 µg/kg b.w. per day ÷ 3.6 µg/kg b.w. per day). Similar results were obtained in investigation of daily diets led in Poland and covering Lublin province. The average daily intake of nickel was 99 µg - 133 µg and 130 µg - 178 µg in women and men diets [18]. Studies of total diet conducted in France indicate that the main contributors to the dietary exposure in children aged 13-36 months are chocolate-based products [2]. The main contributors to the dietary intake of this element by adults are: alcoholic beverages and fruits (9%), followed by water (8%) and vegetables excluding potatoes (7%) [3]. Assessed in other studies mean exposure of the French population to nickel was 2.33 µg/kg b.w. per day in adults and 3.83 µg/kg b.w per day in children. At the 95th percentile, exposure was estimated 3.76 µg/kg b.w per day in adults and 7.44 µg/kg b.w. per day in children and was higher than in the earlier investigations in this area about 25-50% [3].

Studies conducted in UK concerning intake of nickel with foodstuffs concluded that dietary exposure to nickel were unlikely to be of toxicological concern [11, 12].

MIGRATION OF NICKEL FROM FOOD CONTACT MATERIALS

Food contact materials can be additional important source of human exposure to nickel by migration of this element into food or drinking water. Nickel is widely use in the production of high quality, corrosion resistant alloys with iron, copper, aluminum, chromium, zinc and molybdenum. Nickel containing stainless steels are very commonly used for production of e.g. process equipment, cook wares, milk and wine tanks. Nickel plated items are less durable and corrosion resistant than stainless steels and therefore not commonly used for articles in contact with food. EFSA in their opinion concluded that release of nickel may not be negligible for food contact materials made of poor quality stainless steel, or of other nickel containing metal alloys [28].

Other nickel compounds like nickel oxide is used for enamel frits and in ceramic glazes. Nickel carbonate is used for colouring ceramics and in glazes [34]. At present, as recommended by the Council of Europe, manufacturers of food preparation and handling tools and equipment made of stainless steel should respect the migration of Ni compliant with a specific release limit (SRL) of 0.14 mg/kg food [19].

Currently, mainly due to the lack of legal requirements in the EU legislation regarding the migration of nickel from food contact materials, Member States conduct such tests in a very limited scope.

CONTACT ALLERGY TO NICKEL

The most frequently observed effects of nickel toxicity on the human body are different type skin allergic reactions [17, 26, 28, 32, 33]. Well known and described in literature are cases of sensitization caused by the use of kitchen utensils containing nickel and its alloys as well as use of jewelry covered with nickel. In recent years, quite common practices of piercing various parts of the body have paid special attention [26]. This type of treatments may also be associated with exposure to this allergen and the occurrence of various specific reactions. Studies confirm that rubbing the skin and sweating increase the release of nickel from jewelry and other everyday items therefore the intensification of contact hypersensitivity symptoms is mainly observed during the warm seasons [26].

Additional route of exposure to nickel and its compounds is iatrogenic exposure, which can results from implants and prostheses made from nickel containing alloys, from intravenous or dialysis fluids and from radiographic contrast media [30]. Scientific research confirms that about 20% of the general population in Europe suffering from nickel allergy [26].

FOOD LEGISLATION

There are currently no maximum levels in the EU legislation for Ni in food. Also at the *Codex Alimentarius* level such requirements have not been established.

The highest acceptable levels of nickel in drinking water, natural mineral, spring and table waters at the level of 0.020 mg/l are regulated by the ordinances of the Minister of Health implementing Directives 98/83/EC and 2003/40/EC [22, 23]. Codex Standard for natural mineral water 108-1981 also set limit for nickel in waters at the level of 0.02 mg/l [6]. For food additives, nickel is included in the purity criteria in the range 1 mg/kg to 200 mg/kg.

In Poland, prior to accession to the EU, in accordance with national legislation, nickel content limits were applicable in such foodstuffs as hydrogenated fats and oils and margarine at the level 0.20 mg/kg [21].

There is also no regulatory limit for release of Ni from food contact materials in the EU except specific release limit (SRL) from metals and alloys used in food contact materials and articles, but this limit is not obligatory [19].

EUROPEAN COMMISSION RECOMMENDATIONS

Due to the limited amount of representative data from the entire EU area in the scope of nickel contamination of food and feed, enabling appropriate actions in the area of risk management, the European Commission has decided to monitor the level of this contaminant during the years 2016-2018 [7, 8].

For food, the focus was first on data collection for those foodstuffs that have a significant contribution in dietary exposure and for which only limited occurrence data on the presence of nickel were available. Foodstuffs included in the monitoring were as follows: cereals, cereal-based products, infant formula, follow-on formula, processed cereal-based food for infants and young children, baby food, food for special medical purposes intended specifically for infants and young children, food supplements, legumes, nuts and oil seeds, milk and dairy products, alcoholic and non-alcoholic beverages, sugar and confectionery (including cocoa and chocolate), fruits, vegetables and vegetable products (including fungi), dry tea leaves, dry parts of other plants used for herbal infusions and bivalve molluscs.

The European Commission has extended the monitoring of levels of this element also to feed due to the use of metallic nickel as a catalyst in their production, although EFSA did not directly confirmed that any adverse impact of Ni via feed to animals is possible.

Concerning the assessment of human health risks from the presence of Ni in food of animal origin, EFSA concluded that in the average population the current levels of chronic exposure to Ni, considering only foods of animal origin, might be of potential concern in the young population. In case of acute dietary exposure the Authority concluded that nickel-sensitized individuals are also at risk of developing eczematous flare-up skin reactions through the consumption of food of animal origin.

In order to ensure that the samples are representative for the sampled lot, Member States used procedure laid down in Commission Regulation (EC) No 152/2009 [9]. In case of food samples in order to ensure representatives for the sampled lot sampling was performed in accordance with the rules described in Commission Regulation (EC) No 333/2007 [10].

Member States were obligated to transmit data to EFSA according to reporting format as set by EFSA to enable evaluation of results and risk assessment.

Currently EFSA has been requested by the Commission to update the scientific opinion on the risk to public health related to the presence of nickel in food and drinking water taking into account the new occurrence data. This in view of possible future risk management measures.

NOTIFICATIONS WITHIN THE RASFF

In the years 2010-2018, within the Rapid Alert System for Food and Feed (RASFF), there were a total of 204 notifications regarding high content or migration of nickel. 197 of them concerned the migration of nickel from food contact materials, among others: knives and kitchen utensils, grates, kitchen utensils (pots, pans) etc. mainly originated from China. The remaining few notifications were associated with the finding of high nickel content in dietary supplements. The highest value was detected in food supplement from India – 89 mg/kg [35]. A small number of food notifications are associated with a limited number of studies in this area.

CONCLUSION

Due to the toxic effects of nickel and its compounds, the most sensitive population groups should be protected. For the purpose of proper risk management, it is appropriate to collect representative data on the contamination of various groups of foodstuffs with nickel taking into account different geographical area.

Conflict of interest

The authors declare no conflict of interest.

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