Food Research International 129 (2020) 108866

Contents lists available at ScienceDirect

Food Research International

journal homepage: www.elsevier.com/locate/foodres

Review

Gap analysis of nickel bioaccessibility and bioavailability in different food matrices and its impact on the nickel exposure assessment

Mehrnoosh Babaahmadifooladi[a,b,*], Liesbeth Jacxsens[a], Tom Van de Wiele[c], Gijs Du Laing[b]

[a] Department of Food Technology, Safety and Health, Faculty of Bioscience Engineering, Ghent University, Coupure Links 653, 9000 Gent, Belgium
[b] Department of Green Chemistry and Technology, Faculty of Bioscience Engineering, Ghent University, Coupure Links 653, 9000 Gent, Belgium
[c] Center for Microbial Ecology and Technology (CMET), Faculty of Bioscience Engineering, Ghent University, Coupure Links 653, 9000 Gent, Belgium

ARTICLE INFO

Keywords:
Nickel
Dietary intake assessment
Exposure assessment
Bioavailability
Bioaccessibility

ABSTRACT

The metal nickel is well known to cause nickel allergy in sensitive humans by prolonged dermal contact to materials releasing (high) amounts of nickel. Oral nickel exposure via water and food intake is of potential concern. Nickel is essential to plants and animals and can be naturally found in food products or contamination may occur across the agro-food chain. This gap analysis is an evaluation of nickel as a potential food safety hazard causing a risk for human health. In the first step, the available data regarding the occurrence of nickel and its contamination in food and drinks have been collected through literature review. Subsequently, a discussion is held on the potential risks associated with this contamination. Elevated nickel concentrations were mostly found in plant-based foods, e.g. legumes and nuts in which nickel of natural origin is expected. However, it was observed that dedicated and systematic screening of foodstuffs for the presence of nickel is currently still lacking. In a next step, published studies on exposure of humans to nickel via foods and drinks were critically evaluated. Not including bioaccessibility and/or bioavailability of the metal may lead to an overestimation of the exposure of the body to nickel via food and drinks. This overestimation may be problematic when the measured nickel level in foods is high and bioaccessibility and/or bioavailability of nickel in these products is low. Therefore, this paper analyzes the outcomes of the existing dietary intake and bioaccessibility/bioavailability studies conducted for nickel. Besides, the available gaps in nickel bioaccessibility and/or bioavailability studies have been clarified in this paper. The reported bioaccessibility and bioavailability percentages for different food and drinks were found to vary between < LOD and 83% and between 0 and 30% respectively. This indicates that of the total nickel contained in the foodstuffs only a fraction can be absorbed by the intestinal epithelium cells. This paper provides a unique critical overview on nickel in the human diet starting from factors affecting its occurrence in food until its absorption by the body.

1. Introduction

Elementary nickel (Ni) plays an essential role in the growth of bacteria, plants and animals. The necessity of the Ni for growth of a bacterium, i.e. *Alcaligenes*, a cyanobacterium, i.e. *Oscillatoria*, and a green alga, i.e. *Chlorella vulgaris*, has been proven (Welch, 1981). Furthermore, some pine tree species require Ni for their optimum growth (Welch, 1981). Nickel occurs as a structural component in urease and hydrogenase enzymes involved in the nitrogen fixation in legumes (Lavres, Castro Franco, & de Sousa Câmara, 2016). Thus, nitrogen fixating plants, e.g. soybeans, alfalfa and peanuts, have a high level of naturally occurring Ni. Nickel can also be found in almost all organs of vertebrates (Anke, Groppel, Kronemann, & Grun, 1984). Nickel deficiency may lead to lower life expectancy of the reproducing animals as well as development of anemia through reducing the iron resorption. It can also accelerate parakeratosis-like damages through disturbing calcium incorporation in the skeleton (Anke et al., 1984). However, these deficiency symptoms have not yet been observed in animals and humans since the Ni administered by their body always exceeded the requirements, i.e. 25 to 35 μg/day/person (Anke, Angelow, Glei, Müller, & Illing, 1995). Excess intake of Ni can result in Ni dermatitis in sensitive individuals (Anke et al., 1995). This can occur either via exogenous, i.e. skin contact, or endogenous, i.e. oral and inhalation, exposure. Worldwide prevalence of the dermal Ni sensitivity, i.e. Ni

* Corresponding author at: Department of Food Technology, Safety and Health, Faculty of Bioscience Engineering, Ghent University, Coupure Links 653, 9000 Gent, Belgium. Tel.: +32 09 264 61 31.

E-mail addresses: mebabaah.babaahmadifooladi@ugent.be (M. Babaahmadifooladi), liesbeth.jacxsens@ugent.be (L. Jacxsens), tom.vandewiele@ugent.be (T. Van de Wiele), gijs.dulaing@ugent.be (G.D. Laing).

https://doi.org/10.1016/j.foodres.2019.108866
Received 25 June 2019; Received in revised form 5 November 2019; Accepted 24 November 2019
Available online 02 December 2019
0963-9969/

allergy, for adults and children is around 8.6%. The Ni allergy affects females 3–10 times more than males due to their regular daily contact with jewelries and garments. Prevalence of Ni allergy among young females can even increase up to 17% (Torres, Das Graças, Melo, & Tosti, 2009).

Public health agencies are concerned about the presence of essential and toxic trace elements in the diet of the worldwide population. Among different routes of the exposure to the trace elements, e.g. skin contact, oral and inhalation, alimentary routes are the predominant pathway of the trace elements to reach the human body (Aung, Yoshinaga, & Takahashi, 2006; EFSA, 2015). Toxic trace elements such as Cd, Pb and Hg were initially in the focus of public health policies since they pose a risk for human health. Thus, these toxic trace elements have been included in legislation and are now monitored in foods. Other trace elements like Ni have recently become the focus of concern as the European Food Safety Authority (EFSA) recently stated that the current level of acute exposure of the population to Ni via alimentary routes may increase the risk of eczematous flare-up skin reactions to occur for Ni sensitized individuals (EFSA, 2015).

A range of different food products and multiple sources of contamination of Ni to food have been reported (Noël et al., 2012). It has been shown that tofu, dark chocolate and cereals are administering the highest level of the Ni into the human body (Noël et al., 2012). Compatible to the study conducted by Leblanc et al. (2005) and Noël et al. (2012) stated that the food groups with elevated Ni concentration are nuts, oilseeds, chocolate and breakfasts cereals. There are several (European) studies available evaluating the dietary exposure of the population to Ni in different countries (Alberti-Fidanza, Burini, Perriello, & Fidanza, 2003; Arnich et al., 2012; Bocio, Nadal, & Domingo, 2005; Rose, Baxter, Brereton, & Baskaran, 2010). Arnich et al. (2012) have reported a Ni dietary exposure level of 2.33 μg/kg bw/day in adults (18–79 years) and 3.83 μg/kg bw/day in children (3–17 years) in France. In the United Kingdom, a mean dietary exposure of 1.49–1.63 μg/kg bw/day was obtained for the adults (Rose et al., 2010). Almost all available dietary exposure estimation studies in different (European) countries are based on the total Ni concentration in food items which is not the most effective fraction.

According to the EFSA opinion on Ni intake via food, the bioaccessibility and bioavailability of Ni in the food matrix needs to be included when an exposure assessment is conducted (EFSA, 2015). The soluble fraction of the total Ni released from the food matrix into the digestive fluids at the time of digestion is the so-called bioaccessible fraction. This is the maximum possible amount of Ni that can be absorbed by body through consuming every food item (Junli et al., 2013). The bioavailability refers to the fraction of the element passing through the intestinal epithelium and entering blood stream (Wei, Shohag, & Yang, 2012). These two fractions, as the most effective fraction causing the health risk, must be taken into account in the Ni exposure assessment study.

Therefore, one of the important objectives of the current review paper is highlighting the importance of the bioaccessibility and bioavailability studies in the exposure assessments and demonstrating the scarcity of the available studies on estimation of the Ni exposure including bioaccessibility and bioavailability of metals.

2. Materials and methods

More than 80 articles in Ni related fields, i.e. the Ni amounts and sources in different foods, water and drinks, Ni exposure through diet, Ni bioavailability and bioaccessibility in different foods either via *in vivo* or *in vitro* studies, were screened in the current study. These papers have been explored for the several related terms, e.g. Ni intake, exposure assessment, chronic versus acute exposure, deterministic versus probabilistic exposure and type of the diet applied in the studies.

A majority of the articles were available in MEDLINE database, i.e. the PubMed and Elsevier Database. Following key words were applied: Ni, dietary intake assessment, exposure assessment, bioavailability, and bioaccessibility.

All obtained information regarding the Ni occurrence in different food, drinks and water has been summarized and classified per reference/year in Tables 1–3. Similarly, the summary information obtained for Ni intake/exposure has been classified per reference/year and presented in Table 4. Studies on Ni bioaccessibility/bioavailability in different types of foods were limited. Collected information on bioaccessibility and bioavailability has been summarized and classified in Tables 5 and 6, respectively. These tables include the main information presented in the reference articles such as type of the food, type of the study (*in vivo* or *in vitro*), type of exposure, etc. Besides, gaps occurring in these studies were identified and listed in the tables.

3. Results and discussion

3.1. Overview of the nickel prevalence and contamination in different types of food, water and drinks

3.1.1. Animal based foods

Table 1 summarizes available studies on Ni content for animal based foods, including sea foods, meat products, eggs, dishes-meals, dairy products, honey and beeswax. Besides, the Ni content, origin country, sample size as well as the reference article have been specified in the table for each study. More details regarding the different food categories are provided in the following sections. All Ni concentrations specified in the Sections 3.1.1.1–3.1.1.6 are based on wet weight (ww) unless specified otherwise.

3.1.1.1. Seafood (including fish). The main sources of Ni pollution in seafood and aquatic systems, e.g. oceans, are domestic wastewater effluent and non-ferrous metal smelters (Cempel & Nikel, 2006). Studies in the Northeastern coastal area of the Mediterranean Sea and Turkey found average Ni values in fish grown in non-contaminated water ranging from 0.2 μg/g to 2 μg/g dry weight. However, significantly higher values were found in areas subject to pollution. It has been shown that blue fish accumulates greater amounts of Ni in comparison to white or semi-oily fish. Furthermore, in some shellfish species such as oysters, clams or mussels high amounts of Ni have been detected (Demirezen & Uruç, 2006; Mutlu, Türkmen, Türkmen, & Tepe, 2011).

In a study focused on the assessment of the Ni concentration in fish and seafood (N = 159) available on the French market, Ni was found at an average level of 0.074 μg/g in fish and 0.299 μg/g in seafood (Table 1). In the fish group, tuna, pilchard and pout had the highest levels (0.341, 0.236 and 0.161 μg/g, respectively). In the seafood group, cockle contained the highest level (2.8 μg/g), followed by periwinkle (0.709 μg/g) (Guérin et al., 2011). In Poland, the Ni content ranged from 0.007 to 0.178 μg/g (mean 0.040 μg/g) in nine samples of freshwater fish (roach, bream and carp) (Skibniewskaa et al., 2009). Bouchoucha et al. (2019) evaluated the effect of red mud, a bauxite processing residue, on the trace elements concentrations in fishes obtained from the northwest French Mediterranean coastal area. Red mud is an alumina refinery residue disposed in the aforesaid area from 1995 to 2015 at an estimated amount of 20 million tons (Bouchoucha et al., 2019). They found a mean Ni concentration of 0.023 μg/g and 0.013 μg/g in *Sardine pilchurdus* and *Scyliorhinus canicula* fish species, respectively. Furthermore, a clear inverse relation between the fish length and the trace element concentrations, including Ni, was found (Bouchoucha et al., 2019). Gu, Ning, Ke, and Huang (2018) studied 12 fish species from the South China Sea. The Ni concentration ranged from 6.63 μg/g to 20.03 μg/g. In the investigation conducted on fish-based baby foods by Vella and Attard (2019), an average Ni content of 0.81 μg/g was reported. Besides, studies showed that plastics can play the role as a vector to convey trace elements into the aquatic organisms (Bradney et al., 2019). Particular types of plastics can absorb inorganic pollutants, e.g. trace elements including Ni, from the aquatic

Table 1
Nickel content in animal based food products (with product type, sample size and origin). All data are based on the fresh (wet) weight (ww) of the edible portion.

Food category	Product type	Reference	Sample size	Origin	Ni content: mean, mean ± SD or range (μg/g ww)
Sea foods	Sea food	(Guérin et al., 2011)	N = 159	France	Mean: 0.299
	Fish				Mean: 0.074
	Fresh water fish	(Skibniewskaa et al., 2009)	N = 9	Poland	Mean: 0.040
	Sardina pilchardus fish	(Bouchoucha et al., 2019)	N = 68	France	Mean: 0.023
	Scyliorhinus canicula fish	(Bouchoucha et al., 2019)	N = 82	France	Mean: 0.013
	Fish	(Gu et al., 2018)	N = 282	China	6.63–20.03
	Fish-based baby formula	(Vella & Attard, 2019)	N = 8	Malta	Mean: 0.81
Meat products	Chicken meat	(Uluozlu et al., 2009)	N = 3	Turkey	Mean: 2.08
	Poultry	(Noël et al., 2012)	N = 38	France	UB[a]: 0.027–0.148
	Lamb		N = 80		UB[a]: 0.027–0.316
	Offal		N = 16		UB[a]: 0.027–0.255
	Poultry-based baby formula	(Vella & Attard, 2019)	N = 4	Malta	Mean: 1.07
	Breast of chicken	(Abduljaleel et al., 2012)	N = 36	Selangor (Malaysia)	Mean: 0.119
	Breast of quail	(Abduljaleel et al., 2012)	N = 36	Selangor (Malaysia)	Mean: 0.330
Eggs	Eggs and egg products	(Noël et al., 2012)	N = 30	France	0.027–0.328
	Chicken eggs	(Nisianakis et al., 2009)	N = 24	Greece	0.077–0.280 yolk: 0.059 ± 0.005 Egg white: 0.074 ± 0.007
	Duck eggs	(Nisianakis et al., 2009)	N = 24	Greece	yolk: 0.058 ± 0.006 egg white: 0.050 ± 0.006
Dishes and Meals	Prepared dishes	(Noël et al., 2012)	N = 68	France	0.027–0.554
	Ready meals and fast foods	(Cabrera-Vique et al., 2011)	N = 170	Granada (Spain)	0.018–0.095
	Ready-to-eat meal for babies	(EFSA, 2015)	NA [d]	NA	Mean[b]: 0.033–0.165 (LB-UB[c])
		(EFSA, 2015)	NA	NA	Mean[b]: 0.036–0.091 (LB-UB[c])
Dairy products	Milk	(Noël et al., 2012)	N = 38	France	0.027–0.086
		(Vahčić et al., 2010)	N = 72	Croatia	0.072–0.097
		(Ghimpeteanu, 2009)	N = 12	Romania	0.005–0.039
		(Lukáčová et al., 2012)	N = 30	Slovakia	0.25–1.65
		(Rey-Crespo et al., 2013)	N = 360	Spain	0.015, 0.014
		(Rose et al., 2010)	NA	UK	Below the LOD of 0.007–0.04
		(Güler, 2007)	N = 3	Turkey	Mean: 1.38
	Butter	(Noël et al., 2012)	N = 6	France	0.001–0.233
	Milk based products	(Pandelova et al., 2012)	N = 42	France, Germany, Italy, Portugal, Sweden and the United Kingdom	< 0.05
	Cheese	(Noël et al., 2012)	N = 16	France	0.112–0.409
		(Gogoasa et al., 2006)	N = 10	Romania	0.002–0.010
		(Moreno-Rojas et al., 2010)	N = 57	Spain	0.050–1.10
		(EFSA, 2015)	N = 145	NA	Mean[b]: 0.09–0.11 (LB-UB[c])
	Fermented milk products	(EFSA, 2015)	N = 58	NA	Mean[b]: 0.007–0.076 (LB-UB[c])
	Cow's milk	(Saribal, 2019)	N = 21	Turkey	Mean: 0.038
Honey and beeswax	Honey	(Bommuraj et al., 2019)	N = 32	Israel	Mean: 1.24
	Beeswax	(Bommuraj et al., 2019)	N = 32	Israel	Mean: 4.15
	Honey	(EFSA, 2015)	N = 183	NA	Mean[b]: 0.14–0.16 (LB-UB[c])
	Honey	(Madejczyk & Baralkiewicz, 2008)	N = 30	Poland	0.023–1.33
	Honey	(Nowak et al., 2011)	N = 6	Poland	0.42–1.83
	Honey	(Lanjwani & Channa, 2019)	N = 8	Pakistan	0.06–0.33

(a) UB = Upper bound scenario at which results below LOD were replaced with value reported as the LOD.
(b) Refers to the occurrence values used for Ni exposure assessment through food consumption.
(c) LB-UB = Lower bound-upper bound scenarios. LB = Lower bound scenario at which results below LOD /LOQ were substituted with zero.
(d) Abbreviation of not available.

environment. Consequently, Ni in seafood can end up in the human body through the diet (Bradney et al., 2019). In summary, waste water effluents, refinery residues containing trace elements and some plastics in the aquatic environment could increase the concentration of trace elements, including Ni, in fish and seafood. However, it should be noted that it is often not easy to evaluate the effect of human activities on the contamination of the seafood with trace elements (Bouchoucha et al., 2019).

3.1.1.2. Meat products. Compared to other meat products, poultry is typically lower in price. Therefore, poultry meats are consumed more frequently by households on a global scale. Due to these two important facts, i.e. low price and high frequency of consumption by households, a majority of the studies have been conducted on poultry meat products (Abduljaleel, Shuhaimi-Othman, & Babji, 2012; Uluozlu, Tuzen, & Soylak, 2009). As shown in Table 1, a concentration range of 0.027–0.148 μg/g was found in 38 poultry samples in France. In the same study, concentration ranges of 0.027–0.316 μg/g and 0.027–0.255 μg/g were found in lamb and offal samples, respectively. Concentration ranges for meat products collected in other studies are also included in Table 1. The Ni concentrations in four different poultry-based baby foods were measured by Vella and Attard (2019). They reported a mean Ni concentration of 1.07 μg/g in these samples. It seems that the animal species play an important role in the final trace element concentration of the meat. Different animals have a different capability for accumulating the trace elements, e.g. Ni, in their tissues (Abduljaleel et al., 2012). Besides, the distribution of Ni throughout their body is not equal for the different species (Abduljaleel et al., 2012; Uluozlu et al., 2009). All the aforesaid factors affect the final Ni concentration in the meat products.

3.1.1.3. Dairy based foods. According to EFSA (2015), milk and dairy products play an important role in dietary exposure to Ni in some subgroups of the population, e.g. young populations, especially

Table 2
Nickel content in plant-based food products (with product type, sample size and origin). All data are based on the fresh (wet) weight (ww) of the edible portion.

Food category	Product type	Reference	Sample size	Origin	Ni content: mean, mean ± SD or range (μg/g ww)
Vegetables	Edible vegetables	(Junli et al., 2013)	N = 60	Hung Kong	0.26–1.1
	Green beans	(Nakaona et al., 2019)	N = 30	Zambia	Mean: 44.1
	carrots	(Nakaona et al., 2019)	N = 20	Zambia	Mean: 31.9
	Rape	(Nakaona et al., 2019)	N = 30	Zambia	Mean: 25.8
	cabbage	(Nakaona et al., 2019)	N = 30	Zambia	Mean: 39.4
Cereal and cereal based products	Breakfast cereals	(Noël et al., 2012)	N = 6	France	0.077–0.280
		(EFSA, 2015)	N = 313	NA [c]	Mean[a]: 0.63–0.71 (LB-UB[b])
	Pasta	(Noël et al., 2012)	N = 4	France	0.053–0.121
		(EFSA, 2010)	N = 150	NA	Mean[a]: 0.12–0.160 (LB-UB[b])
	Rice	(Noël et al., 2012)	(N = 5) [d]	France	0.053–0.066
		(Sommella et al., 2013)	N = 110	Italy	0.15–0.48
Coffee and coffee drinks	Coffee	(Noël et al., 2012)	N = 30	France	0.024–0.214
		(EFSA, 2010)	N = 83	NA	Mean[a]: 1.2–1.2 (LB-UB[b])
Fat and oils	Edible vegetable oils	(Noël et al., 2012)	N = 10	France	0.027–0.087
		(EFSA, 2010)	N = 151	NA	Mean[a]: 0.305–0.36 (LB-UB[b])
	Margarines	(Noël et al., 2012)	N = 4	France	0.027–0.077
		(Lodyga-Chruścińska et al., 2012)	N = 10	Poland	0.11–1.76
Seasonings	Herbs and spices	(Noël et al., 2012)	N = 12	France	0.024–0.533
Sugar and Sugar based products	Sugar	(Noël et al., 2012)	N = 8	France	0.026–0.186
		(EFSA, 2010)	N = 95	NA	Mean[a]: 0.011–0.15 (LB-UB[b])
	Sugar and confectionaries	(EFSA, 2015)	N = 1170	NA	Mean[a]: 1.5–1.6 (LB-UB[b])
	Sugar plants	(EFSA, 2015)	N = 30	NA	Mean[a]: 0.064–0.084 (LB-UB[b])
	Cookies	(Noël et al., 2012)	(N = 24)[d]	France	0.027–0.639
Soy and soy based products	Soybean	(Pandelova et al., 2012)	(N = 42)[d]	France, Germany, Italy, Portugal, Sweden and the United Kingdom	< 0.05
	Tofu	(Noël et al., 2012)	N = 2	France	0.309–0.392
	Tofu (soybean)	(Ščančar et al., 2013)	N = 3	Slovenia	Mean: 2.130
	Fermented soy milk	(Ščančar et al., 2013)	N = 3	Slovenia	Mean: 5.950
Legumes	Dried beans	(EFSA, 2010)	NA	NA	Mean: 3.1
Nuts	Almonds	(Ščančar et al., 2013)	N = 3	Slovenia	Mean: 0.830
	Hazelnut	(EFSA, 2010)	N = 48	NA	Mean: 2.2
Cacao based products	Chocolate	(Noël et al., 2012)	N = 10	France	0.422–3.26
		(EFSA, 2010)	N = 490	NA	Mean[a]: 3.231–3.236 (LB-UB[b])
Fruits	Grape	(Amer et al., 2019)	N = 9	Egypt	Mean: 0.805
	Orange	(Amer et al., 2019)	N = 9	Egypt	Mean: 0.228
	Apple	(Amer et al., 2019)	N = 9	Egypt	Mean: 0.25
	Prune-based baby formula	(Vella & Attard, 2019)	N = 4	Malta	Mean: 0.86
	Apple-based baby formula	(Vella & Attard, 2019)	N = 6	Malta	Mean: 0.63
	Pear-based baby formula	(Vella & Attard, 2019)	N = 6	Malta	Mean: 0.85
Dishes	Kimchi[f]	(Hwang et al., 2019)	N = 75	South Korea	0.056–0.263
Tubers	Wild yam (*Dioscorea* spp)	(Padhan et al., 2018)	N = 8	India	0.03–0.089
Edible wilde mushroom	Ectomycorrhizal Fungi (*Boletaceae*)	(Zhang et al., 2019)	N = 74	China	0.1–1.2

(a) Refers to the occurrence values used for Ni exposure assessment through food consumption.
(b) LB = Lower bound scenario at which results below LOD /LOQ were substituted with zero, UB = Upper bound scenario at which results below LOD were replaced with value reported as the LOD and those lower than LOQ were substituted with the LOQ value.
(c) Abbreviation of not available.
(d) Reported values are based on dry weight.
(f) Korean traditional dish made mainly from nepa cabbage.

toddlers**.** This could originate from the high consumption of dairy products, e.g. milk, by toddlers. EFSA (2015) reported a mean concentration of 0.071 μg/g of Ni in 631 samples of milk and dairy products. In another study conducted by Noël et al. (2012), a mean concentration of Ni ranging from 0.027 to 0.086 μg/g was reported for milk samples. Saribal (2019) has reported a mean Ni concentration of 0.038 μg/g for 21 samples of cow's milk collected from supermarkets in Istanbul (Turkey). A Ni concentration ranging from 0.112 to 0.409 μg/g was reported by Noël et al. (2012) for cheese samples. The higher concentration of Ni in the cheese samples may originate from Ni contamination in the food processing and production stage along with the nickel-absorbing characteristic of the caseins and the fats at the flocculation stage of the cheese making process (Ziarati, Shirkhan, Mostafidi, & Tamaskani Zahedi, 2018). Generally, different factors, i.e. the cattle's diet, genetic variation among the cattle breeds, herbicide used in the grazing area, geographical origin of the cattle and seasonality, can affect the trace element content of the cattle's milk (Pechová, Pavlata, Dvořák, & Lokajová, 2008).

3.1.1.4. Eggs. According to the study conducted by Noël et al. (2012), eggs are not included in the list of food products containing elevated concentrations of Ni. They reported a concentration of 0.027–0.328 μg/g for eggs and egg products (Table 1). Nisianakis, Giannenas, Gavriil, Kontopidis, and Kyriazakis (2009) studied trace element contents of the eggs produced by poultry breeders, i.e. chicken, turkey, duck, goose, and pigeon. They reported a mean Ni content of 0.059 μg/g for chicken egg yolk and 0.074 μg/g for chicken egg white (Table 1). According to Nisianakis et al. (2009), diet and geographical origin of the chicken are the major determining factors for the final concentration of the trace elements in the eggs. Besides, different feeding behavior among the avian species as well as their different ability for digesting the ingested soil and grass can lead to different trace element contents in the eggs, including the content of Ni (Nisianakis et al., 2009).

Table 3
Nickel content reported for water and drinks (with product type, sample size and origin).

Category	Type	Reference	Sample size	Origin	Ni content in water (μg/L) and drinks (μg/kg)
Water	Fresh	(Barceloux, 1999)	NA[a]	US	Mean: 0.3
		(Borg, 1987)	N = 59	Northern Sweden	0.11–0.54
		(Mannio et al., 1995)	N = 116	Finland	0.25[b]
Water	Drinking	(IARC, 1990)	N = 2503	US	< 20
		(WHO, 2000)	NA	European countries	2–13
		(Frengstad et al., 2010)	N = 18	Norway, Sweden, Finland, Iceland	0.045–1.59
		(Hussain & Habib-Ur-Rehman, 2019)	N = 20	Pakistan	Mean: 1306
		(Nakaona et al., 2019)	N = 150	Zambia	20–2580
Drinks	Soft drinks	(Noël et al., 2012)	N = 26	France	27–457
		(EFSA, 2015)	N = 35	NA[a]	Mean[c]: 37–41 (LB-UB[d])
	Alcoholic drinks	(Noël et al., 2012)	N = 10	France	25–271
		(EFSA, 2015)	N = 110	NA	Mean[c]: 2–16 (LB-UB[d])
		(Gama et al., 2017)	N = 30	Brazil	Mean[e]: 160

(a) Expressed as not available.
(b) Expressed as median.
(c) Refers to the occurrence values used for Ni exposure assessment through drink consumption.
(d) LB = Lower bound scenario at which results below LOD /LOQ were substituted with zero, UB = Upper bound scenario at which results below LOD were replaced with value reported as the LOD and those lower than LOQ were substituted with the LOQ value.
(e) Only obtained for the beers.

3.1.1.5. Honey and beeswax. Bommuraj et al. (2019) reported a mean Ni content of 1.24 μg/g and 4.152 μg/g for honey and beeswax samples collected from 32 different apiaries across Israel. Concentrations of the trace elements in honey are significantly lower than those in the beeswax samples. Thus, Bommuraj et al. (2019) stated that beeswax might function as detoxifying agent to remove Ni along with other trace elements from the honey. In EFSA (2015), a mean concentration of 0.14–0.16 (LB-UB) μg/g was reported for 183 honey samples collected across Europe. Madejczyk and Baralkiewicz (2008) have reported a Ni concentration ranging from 0.023 to 1.33 μg/g for 30 samples of honey collected in Poland. In another study conducted by Nowak, Dziezyc, and Piotrowski (2011), a concentration range of 0.42–1.83 μg/g was defined for Ni in 6 different honey samples. In the study conducted by Lanjwani and Channa (2019), the Ni concentration ranged from 0.06 μg/g to 0.33 μg/g for 8 samples of honey collected in Pakistan. In general, it seems that artificial feeding practices may lead to a lower concentration of the trace elements in honeys (Bommuraj et al., 2019).

3.1.1.6. Dishes and meals. In the study conducted by Cabrera-Vique, Mesías, and Bouzas (2011), 170 samples of highly consumed fast foods were analyzed to determine their Ni content. As represented in Table 1, the average Ni concentration ranges from 0.018 to 0.095 μg/g. Though, the most Ni contaminated dishes were pork-meat based with an average Ni content of 0.065–0.095 μg/g. A mean Ni concentration ranging from 0.033 to 0.091 μg/g was reported for ready-to-eat baby meals (EFSA, 2015) (Table 1). In another study conducted by Noël et al. (2012), a mean Ni concentration of 0.137 μg/g was obtained for 68 samples of cooked dishes. These researchers have also analyzed a wide range of other food products, i.e. sweeteners, confectioneries, cereals, chocolate, tofu, etc. Among all of these products, cooked dishes showed an intermediate level of Ni contamination in comparison to other food products. According to Cabrera-Vique et al. (2011), processing of the foods and some ingredients added to ready-to-eat meals primarily affect the final Ni content of these dishes. Additional ingredients can lead to lowering the Ni content of the ready-to-eat meal as well, through dilution of the initial Ni content (Cabrera-Vique et al., 2011).

3.1.2. Plant-based food products

All obtained information from reviewing the available data on Ni content in the plant-based foods is summarized in Table 2. The food products are classified in 14 main food categories, i.e. cereal products, coffee products, seasonings, oils and fats, sugary products, soy-based products, legumes, nuts, cacao-based products, fruits, dishes, tubers and mushroom. Every food category contains a few types of foods. Reference of the article, the country of origin, sample size as well as the Ni contents per study are presented in Table 2. All Ni concentrations discussed in this section are on wet weight (ww) base unless specified otherwise.

In four different regions of Egypt, mean Ni concentration froms 0.30 μg/g to 1.78 μg/g and 0.06 μg/g to 0.38 μg/g were reported for grapes and oranges, respectively (Amer, Sabry, Marrez, Hathout, & Fouzy, 2019). Vella and Attard (2019) reported Ni concentrations of 0.63, 0.85 and 0.86 μg/g for apple, pear and prune-based baby foods, respectively. Babies are a vulnerable age group and their diet is more restricted that the adults. Therefore, it is recommended to monitor the baby foods to make sure they are safe enough to be consumed.

Hwang et al. (2019) reported a mean Ni concentration of 0.114 μg/g in kimchi dish, i.e. a traditional Korean dish mainly made of *nepa cabbage*. They stated that the characteristics of the production area, e.g. soil compounds and the climate, may have a significant effect on the final trace element concentration of the cabbage rather than the characteristics of the plant itself. In wild yam (*Dioscorea* spp.) grown in India, a Ni concentration range of 0.03–0.089 μg/g was reported by Padhan, Biswas, Dhal, and Panda (2018). Wild yam is a foodstuff that is highly consumed by the tribal population of Koraput, India. They stated that not only the Ni concentration range in wild yam but also the concentrations of other trace elements are lower than tolerable levels proposed by the WHO Expert committee. So wild yam is considered safe enough to be consumed by humans (Padhan et al., 2018). A Ni concentration range from 0.1 μg/g to 1.2 μg/g was reported for Ectomycorrhizal fungi (*Boletaceae*) collected in the Yunnan province, China. This wild mushroom is one of the *Boletus* genus consumed a lot globally (Zhang, Baralkiewicz, Hanc, Falandysz, & Wang, 2019). The Ni concentration in tea leaves ranged from 1.21 μg/g to 14.4 μg/g. The environmental conditions during growth (e.g. the total/bioavailable Ni in soil, the use of fertilizers or use of Ni containing phytosanitary agents) determined the final Ni concentration in the tea leaves (Bolle et al., 2011). The ionic form of Ni is highly soluble in tea leaves resulting in Ni values greater than 14.4 μg/g in green tea leaves (Ščančar, Zuliani, Žigon, & Milačič, 2013). The same authors found Ni concentrations between 0.422 and 3.260 μg/g in 10 chocolate samples (Table 2).

Generally, elevated concentrations of Ni have been found in some vegetable-based food products including chocolate, soy, nuts, oatmeal, cabbage, spinach tea and coffee (Table 2). As previously mentioned, some of these high concentrations, e.g. in soy, can be explained by the essentiality of Ni for the function of plant enzymes, e.g. urease. Therefore, the Ni level is high as a result of natural processes. Nickel is an essential structural component of some enzymes, e.g. urease and

Table 4
Dietary intake/exposure of Ni (mg/day/person) via various foods and water in different countries, with description of the method used, exposure type and type of exposure assessment, type of food/diet involved, and type of study (single- or multi-element); the studies are ranked chronologically according to publication year.

Country	Year	Method used	Mean Ni exposure (mg/day/person)[a]	Type of exposure assessment	Acute versus chronic exposure	Type of food/diet	Ni only/Multi-element study	Reference
United Kingdom	1999	Food analysis and food consumption	0.120	Deterministic	Chronic (daily)	Total diet	Multi-element	(Ysart et al., 1999)
Germany	2000	Food analysis and food consumption	0.025–0.035	NA [b]	Chronic (daily)	Multiple food	Ni only	(Anke et al., 2000)
Denmark	2002	Food analysis andfood consumption	0.167	Deterministic	Chronic (daily)	Multiple food	Multi-element	(Larsen et al., 2002)
Poland	2004	Food analysis andfood consumption	0.124–0.166	NA	Chronic (daily)	Total diet	Multi-element	(Marzec, 2004)
Spain (Tarragona)	2005	Food analysis andfood consumption	0.138	Deterministic	NA	Multiple food	Multi-element	(Bocio et al., 2005)
Japan	2005	Food analysis andfood consumption	0.172	Deterministic	Chronic (daily)	Market basket study	Multi-element	(Shiraishi, 2005)
France	2005	Food analysis and surveysfrequency of food consumption	0.0924	Deterministic	Chronic	Total diet	Multi-element	(Leblanc et al., 2005)
Japan	2006	Duplicate diet analysis	< 0.198	Deterministic	Chronic (daily)	Drinking water,snacks and beverages	Multi-element	(Aung et al., 2006)
Italy	2008	Food analysis and tablesfrequency of food consumption	0.361	Deterministic	Chronic (daily)	Total diet	Multi-element	(Turconi et al., 2009)
Germany	2009	Record food consumption and tables withfood composition	0.030–1.050	Deterministic	Chronic (daily)	Total diet	Ni and Zn	(Wittsiepe et al., 2009)
Germany	2009	Analysis of duplicate portions and tables withNi levels in food	0.012–0.560	Deterministic	Chronic (daily)	Total diet	Ni and Zn	(Wittsiepe et al., 2009)
United Kingdom	2010	Data collected in British National Dietand Nutrition Survey	0.130	Deterministic	Chronic (daily)	Total diet	Multi-element	(Rose et al., 2010)
Spain (Canary Islands)	2010	Food analysis and questionnairesfrequency of food consumption	0.093	NA	NA	Most commonly consumed food and beverages	Ni only	(González-Weller et al., 2010)
Lebanon	2010	Food analysis and surveysfood consumption	0.126	Deterministic	Chronic (daily)	Total diet	Multi-element	(Nasreddine et al., 2010)
Spain (Peninsula)	2012	Food analysis and surveysfood consumption	0.109	NA	NA	Duplicate diet study	Multi-element	(Domingo et al., 2012)
Hong Kong	2013	Population-based food consumption survey	0.099 0.036[c]	NA	NA	Vegetables	Multi-element	(Junli et al., 2013)
Canada	2018	NA	0.005	NA	NA	Prenatal supplement	NA	(Schwalfenberg et al., 2018)
Zambia	2019	Face-to-face interview and Ni level in drinking water	4.64 8.94	NA	NA	Drinking water Vegetables	Multi-element	(Nakaona et al., 2019)
South Korea	2019	Survey on Korean consumption of kimchi in 2016	Male 0.009 Female 0.007	NA	NA	Single food	Multi-element	(Hwang et al., 2019)

(a) The reported values are based on the total Ni concentration in food unless specified otherwise.
(b) Not available.
(c) Bioaccessible estimated daily intake.

Table 5
Range of Ni bioavailability (%) in water and drinks, with description of the food matrix, study type (*in vitro/in vivo*), exposure type, subject studied, risk threshold and gaps arising in the studies; the studies are ranked chronologically according to publication year.

Authors	Year	Matrix (food type)	Food specification	Range of BAV[a]	In vitro/ *in vivo*	Exposure type	Subject	Risk threshold	Population group	Gaps
Sunderman et al.	1989	Ingestion of $NiSO_4$ via drinking water or food	NA[b]	25% of Ni ingested in drinking water and 1% of Ni in food	In vivo	Oral	Healthy human volunteers	NA	NA	NA
Nielsen et al.	1999	Water solution	NA	1–5% in presence of food 12–27% under fasting Max 30% BAV when BAC[d] is 100%	In vivo	Oral	NA	NA	NA	Lack of estimations on the Ni absorption from the foods
Cempel and Janicka	2002	Food and drinking water	NA	1.7–10%	NA	oral	rats	NA	NA	Lack of information on Ni toxicity and distribution in human body
Cabrera-Vique et al.	2011	Ready meals and fast foods	Dishes with beef, chicken or pork, fish, eggs, sauces, etc	4.5–7.8%.	In vitro	NA	NA	NA	NA	Limited information available on Ni speciation in food and its bioavailability
ECB, 2008	2012	Drinking tap water	NA	30%	In vivo	Oral	NA	20 µg Ni/l	5% of the EU population	It is not possible to assess the magnitude of the EU population beyond the 95th percentile intake.
Latorre et al.	2018	Wine	Chilean natural wines	0%[c]	In vitro	NA	NA	NA	NA	NA

(a) Bioavailability.
(b) Not available/specified.
(c) Indicated as not bioavailable.
(d) Bioaccessibility.

Table 6
Range of Ni bioaccessibility (%) in different foodstuffs, with description of the food matrix and type of foodstuff, risk threshold and gaps arising in the studies.

Authors	Year	Matrix (food type)	Food specification	Range of BAC[a]	Risk threshold	Gaps
Junli et al.	2013	Vegetables	60 varieties of edible vegetables	29–64%.	BEDI[e] < TDI[f]	NA
Bertin et al.	2016	*Sarcocornia ambigua* plant	Specific type of plant food	< LOD[d]	NA	The data provided by this study can be a starting point for more complex and in-depth studies.
Liu et al.	2017	Cereal grains	Spring wheat, maize and rice	32–56%	NA	To add robustness to the study outcomes, more studies like this one are needed in other related regions.
Machado et al.	2017	Artichoke heads	Raw edible	41.3–54.7%	NA	Further investigation is needed to establish a RDI for this type of non-traditional foods.
Schulze et al.	2017	Euterpe edulis Martius	Juçara fruits	7.4–42.5%	NA	Further studies regarding the bioavailability of these compounds and elements in juçara fruits is needed.
Gu et al.	2018	Marine organisms	Fishes and cephalopods species	59.93%	THQ[g] < 1	NA
Lam & Lai	2018	Ipomoea aquatica Forsk	Water spinach	27–40%[h]	NA	NA
Gedik	2018	Sea food	NA[b]	83.11%	HQ[c] < 1	The role of portion size needed to be taken into account in risk assessment.

(a) Bioaccessibility.
(b) Not available/specified.
(c) Hazard quotient.
(d) Limit of detection.
(e) Bioaccessible estimated daily intake.
(f) Tolerable daily intake.
(g) Target hazard quotient.
(h) This range obtained under the effect of blanching and inoculation with arbuscular mycorrhizal fungi.

hydrogenase, performing nitrogen metabolism in many legume species (Lavres et al., 2016). Therefore, these foods are frequently reported as being the main source of Ni exposure for humans via food (Noël et al., 2012). Water content also affects the Ni concentration in food crops, when concentrations are expressed on fresh weight basis. It has been shown by López-López, López, Madrid, and Garrido (2008) that the Ni content of olives can increase, to almost double concentrations, with ripening (0.220 μg/g versus 0.145 μg/g). This is explained by the fact that during the ripening process, water is lost from the olives.

Generally, many different factors can affect the trace element contents present in vegetable oils, e.g. composition of the soil, the presence of environmental pollutants during the extraction/packing process, etc (Zhu, Fan, Wang, Qu, & Yao, 2011). In the study conducted by Li et al. (2012), concentrations exceeding the maximum allowable level of Ni in food were observed in approximately 29.3% of the samples of vegetables and fruits cultivated in reclaimed farmland in 26 villages of the Pearl River Estuary in China. Moreover, a high average concentration of 2.34 μg/g dry weight was found for rice grown on these reclaimed farmlands. A maximum level of 1 μg/g (reported based on the edible portion) was found for Ni present in the food in China (Clever & Jie, 2014). Crops grown in areas close to highly polluting industries (e.g. electronics, metallurgy and mining) contained elevated concentrations of Ni (Amin, Hussain, Alamzeb, & Begum, 2013; Lemos et al., 2007). In the study conducted by Nakaona, Maseka, Hamilton, and Watts (2019), a Ni concentration ranging from 25.8 μg/g to 44.1 μg/g is reported for vegetables cultivated in Zambia. They reported that this Ni concentration exceeded the safe level assigned by WHO/FAO, i.e. 1.5 μg/g, in all vegetables. These vegetables were cultivated in the so-called copper-belt province where mining activities drastically affect the environment and cause a serious health concern. As conclusion, some crops contain naturally high Ni concentrations as Ni is essential in enzymes involved in the nitrogen metabolism. However, anthropogenic activities can also have a drastic impact on the final trace elements concentrations (including Ni) in plant-based foods. The trace elements absorption by plants was reported to be higher when industrially contaminated water was used for irrigation of the plant or when the plant was cultivated in industrially contaminated soil, e.g. cultivation sites in the vicinity of mining activities.

3.1.3. Water and other drinks

In Table 3, summary information regarding the Ni occurrence in water and drinks is presented. Water is specified as fresh water (surface water) and drinking water, drinks are classified as soft drinks and alcoholic drinks. Similar to the previous summary tables, Table 3 is also representing the reference article, sample size and origin of the water or drinks.

Nickel enters the surface waters from the degraded bedrocks and soil via precipitation (WHO/IPCS, 1991). According to Barceloux (1999), the Ni concentration in uncontaminated fresh water is typically 0.3 μg/L in Europe. The Ni concentration in samples collected from fresh waters in Finland, Lapland, and northern Sweden ranged on average from 0.11 to 0.54 μg/L (Borg, 1987; Mannio, Jarvinen, Tuominen, & Verta, 1995; Verta et al., 1990). In a study conducted by (Frengstad, Lax, Tarvainen, Jaeger, & Wigum, 2010), a Ni concentration ranging from 0.045 to 1.59 μg/L was reported for Finland, Norway, Sweden and Iceland. According to a recent study conducted by Khan, Kujala, Nieminen, Raisanen, and Ronkanen (2019), increasing mining activity in the Arctic region of Finland results not only in elevated Ni concentration in surface waters but also elevated concentration of other toxic trace elements, e.g. arsenic. However, they stated that peatlands are effective towards removing these contaminants from the surface water. The average removal of Ni from the contaminated surface water was 20 μg/L (Khan et al., 2019).

Various factors have an effect on the Ni concentration in tap (potable) water, e.g. origin of the water, pipes/tap materials and stagnation time (EFSA, 2015). In the European Council Directive 98/83/EC and in the European Commission Directive 2003/40/EC, the maximum level of Ni in drinking water was set at 20 μg/L in European Union. The reported level of Ni in drinking water of European countries, 2–13 μg/L (IARC, 1990; WHO, 2000), is still below this limit. The World Health Organization (WHO, 2008) assigned a maximum level of 70 μg/L for Ni in drinking water in its guidelines. A Ni concentration of < 20 μg/L was reported for drinking water (N = 2503) in the US (IARC, 1990), whereas the Environmental Protection Agency of the US (EPA) has defined a maximum level of 100 μg/L for Ni present in drinking water.

Hussain and Habib-Ur-Rehman (2019) has reported the Ni concentration to range from 4 to 7190 μg/L for 20 drinking water (ground water) samples collected from different cities in Pakistan. They stated that the Ni concentration drastically exceeded the maximum level of 70 μg/L in many cities and it poses a serious health threat for the citizens. They recommended that polluted water should not be consumed for drinking purposes unless it undergoes proper treatment. In Zambia, a Ni concentration range of 20–2580 μg/L is reported for 150 samples collected from the local wells (Nakaona et al., 2019). They reported that the drinking water obtained from the wells is highly contaminated. It seems that groundwater (e.g. local wells) used for drinking purposes could be highly contaminated with trace elements especially in poor and developing countries, e.g. Pakistan and Zambia. Therefore, more strict regulations are needed especially in these countries. Noël et al., 2012 reported a Ni content between 27 and 475 μg/kg for soft drinks (N = 26). Furthermore, the concentration of Ni was reported to vary between 37 and 41 μg/kg for soft drinks (N = 35) in EFSA (2015). According to EFSA (2015), the range of Ni concentrations was lower for alcoholic drinks (N = 110), i.e. 2–16 μg/kg, in comparison to soft drinks (Table 3). A mean Ni concentration of 160 μg/L was reported for 30 beer samples collected on the Brazilian market (Gama, Nascentes, Matos, Rodrigues, & Rodrigues, 2017). In this study, it was observed that the variation in the concentrations, as observed for Ni, is also detected for other trace elements in the beers. The authors attributed this to different levels of contamination at the production and processing sites (Gama et al., 2017). As previously discussed, the availability of the trace elements, e.g. Ni, in the soil for plant uptake is generally important for drinks of plant origin such as beers. Besides, the quality of the irrigation water as well as the quality of the water being used for the beer production have a significant effect on the final Ni contamination in the beers as well (Gama et al., 2017).

3.1.4. Food supplements

Nickel can also be present as a contaminant in commercialized multi-mineral and multi-vitamin food supplements (Adolfo et al., 2019). These food supplements are produced in a pharmaceutical form and typically consumed to compensate for deficiencies in a normal diet. These products are highly consumed worldwide. Though, a lot of concerns have been raised recently regarding the health risk and safety of these products, particularly as regulation is still limited and they are highly susceptible towards contamination during manufacturing and storage (Adolfo et al., 2019). In the study conducted by Adolfo et al. (2019), a Ni concentration range of 0.133–1.3 μg/g was obtained in seven samples of multi-mineral and multi-vitamin supplements. A Ni content of 0.48–5.7 mg/kg was reported in herbal dietary supplements in Brazil by Barrella et al. (2017). These authors concluded that they can pose a threat on the local population health. Particularly as these products are promoted also as a solution for the prevalent obesity, their consumption can be significant. A strict regulation and competent certification system is needed in different countries, such as Brazil, to assure the safety of these dietary supplements. Furthermore, a regular monitoring and reporting system should be developed to assure their safety for the population (Schwalfenberg, Rodushkin, & Genuis, 2018).

3.2. Nickel intake or exposure through diet

Nickel intake through the diet is highly variable, as it is affected by geographical variation in natural Ni concentrations in the food, the diet, the proportion of animal- and vegetable–based foods, environmental pollution where foods are sourced, migration of this element during processing and storage or via various kitchen utensils made with Ni (Aung, Yoshinaga, & Takahashi, 2006; Leblanc et al., 2005; Rose et al., 2010).

In the background document established for drinking-water quality by WHO (2008), a TDI, i.e. tolerable daily intake, of 22 μg Ni/kg bodyweight (bw)/day was reported. This TDI was derived from the critical no-observed-adverse-effect level (NOAEL), i.e. 2.2 mg Ni/kg bw/day, for all endpoints studied. An oral intake study was conducted on two generations of the rats through administering Ni sulphate hexahydrate via gavage. For the individuals sensitized to Ni this NOAEL of 2.2 mg Ni/kg bw/day was found to be not protective enough to prevent eliciting an eczematous flare-up reaction. Hence, a lowest-observed-adverse-effect level (LOAEL), i.e. 12 μg Ni/kg bw/day, was established for Ni sensitized patients under fasting conditions (Nielsen et al., 1999). According to the WHO (2008), this is the worst-case scenario since the absorption of Ni from food is almost 10–40 fold lower than its absorption from water ingested in an empty stomach (EFSA, 2015).

When using these TDI values for comparison with exposure study outcomes in the frame of risk characterization, researchers should be careful. When the bioavailability is taken into account in the exposure estimation, this estimation is reflecting real exposure of the consumers to the Ni via the food. This already has considered the effects of release of Ni from the food matrix during digestion and absorption of the Ni by the intestinal cells (Fig. 1). However, the TDI of 2.8 μg Ni/kg bw/day defined by WHO (2008) was obtained through oral ingestion of soluble Ni salts, in absence of a food matrix and digestion effects, which may alter the accessibility of Ni to the human body. This TDI only reflects the effect of the intestinal absorption. The other reported TDI of 12 μg Ni/kg bw/day was obtained through provision of a supplementary high Ni diet for 4 days in a single-blind cross-over study. The diet had about five times the average Ni content of the daily Danish diet (Nielsen, Jepsen, Jørgensen, Grandjean, & Brandrup, 1990). In this study both effects of the digestion and absorption may have played a role, but Ni did not occur naturally in the diet, i.e. it concerned a fortified diet, wherein the accessibility and availability of Ni may not have been the same as in a natural diet.

There are a number of research papers in which an estimated average Ni intake or exposure through the diet and foods have been specified (Hwang et al., 2019; Larsen et al., 2002; Marzec, 2004; Rose et al., 2010). In Table 4, intake data of Ni from different studies conducted in different countries in recent years are presented. For this table, papers have been investigated for the related terms to exposure, e.g. chronic versus acute exposure, deterministic versus probabilistic exposure and type of the diet applied in the studies, to make the exposure assessment as explicit as possible. Chronic exposure occurs when an individual has a regular intake of Ni, e.g. daily. Acute exposure may occur as a result of one high-exposure event (Reichwaldt, Stone, Barrington, Sinang, & Ghadouani, 2016). As specified in Table 4, the majority of the studies were based on the chronic (daily) exposure approach (although 6 of the studies did not mention the approach). In the deterministic approach, measured food consumption and concentrations are averaged for each food. Single value of average consumption and average concentration are multiplied to calculate the final deterministic exposure (Mekonen et al., 2015). The probabilistic approach is performed using for instance @Risk® 5.7 software program for Microsoft Excel 2010 (Palisade Corporation, USA) in which the consumption and contamination distribution are combined to provide the exposure distribution (Mekonen et al., 2015). Except for the 5 studies with no specification regarding the deterministic/probabilistic exposure approach used, 11 other studies were performed via the deterministic approach (Table 4).

The outcomes of the reported total diet studies (in total 8 studies) listed in Table 4 are more or less comparable, with the exception of one study performed by Turconi, Minoia, Ronchi, and Roggi (2009) in Italy, where the exposure values were about three times higher compared to the data collected in other studies (i.e. 361.1 μg Ni/day/person). Assuming a mean body weight of 65 kg, this exposure value in Italy would be 5.5 μg Ni/kg bw/day. In the aforesaid study, milk and dairy products were the highest contributors to the total daily exposure to Ni. Besides

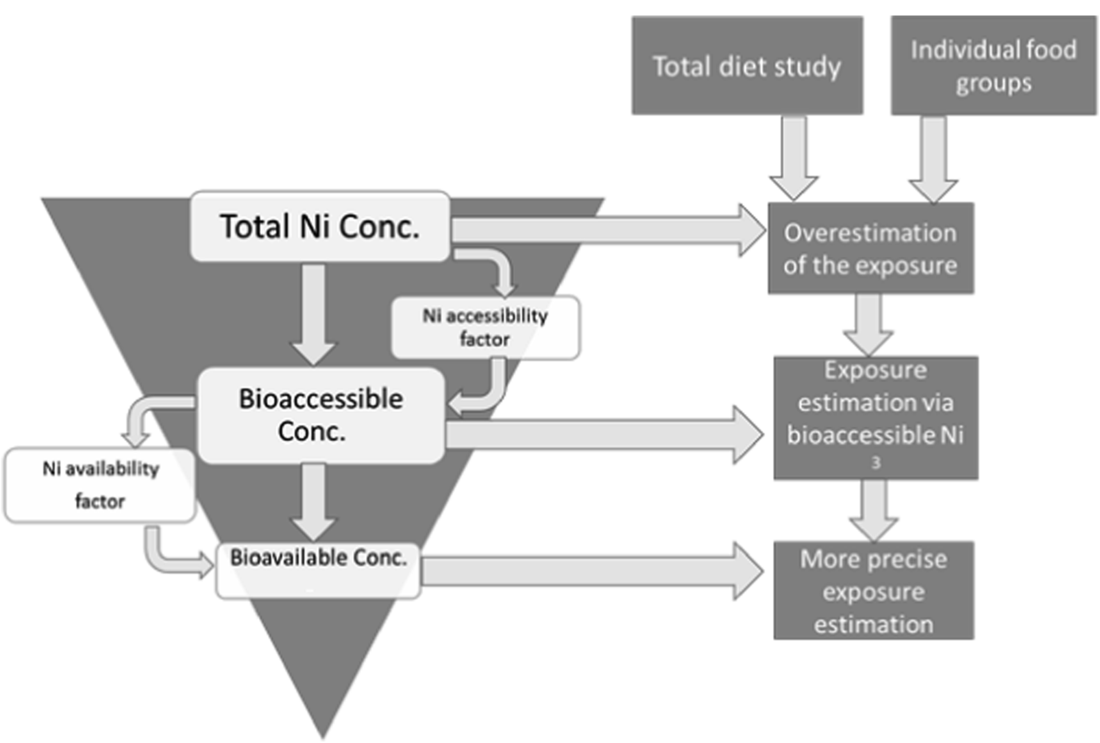

Fig. 1. Schematic of the relations among overestimation of the exposure using the total Ni concentration, exposure estimation using the bioaccessible fraction of Ni and precise estimation of the exposure using the bioavailable fraction of Ni.

cereals, tubers and vegetables are high suppliers not only of Ni but also for other types of trace elements. Turconi et al. (2009) stated that this elevated Ni concentration may be explained by Ni release from the metal contact materials (e.g. steel cookware). Nickel intake is of course closely related to the origin, natural Ni content and degree of Ni contamination of food as well as food habits in each country (Tables 1–3).

Jensen , Menné, and Duus Johansen (2006) conducted a meta-analysis study on the results of oral exposure to Ni and eliciting the systemic contact dermatitis reaction as a consequence. This study aimed to assess and to estimate the best possible Ni threshold doses to observe systematic contact dermatitis in Ni sensitive patients. The study results for two groups with most sensitive members demonstrated that systemic contact dermatitis occurred in 1% of the patients tested after normal daily exposure to Ni (i.e. 0.22–0.35 mg/day/person through drinking water or food (Jensen et al., 2006). Junli et al. (2013) studied the bioaccessible estimated daily intakes (BEDIs) of the trace elements through consuming market vegetables in the population of Hong Kong. They reported a total daily intake of 0.58 µg Ni/kg bw/day (i.e. 0.036 mg/day by taking the average population's body weight of 62 kg into account). They generally stated that obtained BEDI values for the trace elements, including Ni, were far below the tolerable daily intake defined by JECFA (1989). In the single food study on Kimchi, i.e. a cabbage-base food product, conducted by Hwang et al. (2019) in South Korea, average daily intakes of 0.009 mg Ni/day/person and 0.007 mg Ni/day/person were reported for Korean males and females, respectively. These researchers concluded that a normal daily intake of Kimchi will not cause any health risk for the Korean male and female population. The daily intake of Ni together with other trace elements was also estimated for people living in the Copper-belt province of Zambia by Nakaona et al. (2019). They reported an estimated daily intake of 4.79 mg Ni/kg bw/day through consuming the ground water, obtained from the locall wells, and the locally cultivated vegetables, i.e. green beans, beans leaves, pumpkin leaves, carrots, sweet potato leaves, rape, cabbage and cassava leaves. Furthermore, these researchers reported a daily intake of 4.64 mg Ni/day/person for the well's water merely. They argued that ground water and vegetables contamination by trace elements, including Ni, is the reason behind these high levels of the exposure. Though, more in depth studies are needed to specify the health implications of these levels of exposure. Monitoring of the drinking water, vegetables and soil should be implemented regularly. This should be done in line with a definition of the probable exposure routes (Nakaona et al., 2019). The Ni exposure through daily intake of prenatal supplements has been studied in Canada by Schwalfenberg et al. (2018). They reported a value of 5 µg Ni/day/person and 34 µg Ni/day/person for mean and maximum Ni exposure, respectively. According to the USP (United States Pharmacopeia) guidelines, the upper limit of exposure for Ni is 60 µg Ni/day/person (Yetley, 2007). In the aforesaid study, the maximum exposure through prenatal supplements did not exceed the critical value of 60 µg Ni/day/person. However, as previously also mentioned in other studies, a self-monitoring system to report on the status of trace elements in these types of supplements is still lacking.

According to the World Health Organization, for assessing a total daily intake of trace elements, a total diet study is the proper approach assuring that chemicals are present at a safe level in the diet (WHO, 2011). The process consists of purchasing the foods (i.e. diet representatives) from the retailer, processing them according to the actual ways of consumption, then homogenizing and analyzing them for the elements of concern (Moy, 2015). In a multiple food approach, food samples from different food groups, e.g. meat, pulses, cereals, vegetables and fruits, are collected randomly from the market for further analysis of the elements of concern (Bocio et al., 2005). In a single food study, only one food/drink item is focused on in the study and the intake of the trace element through consuming that single food/drink is being evaluated (Hwang et al., 2019; Nakaona et al., 2019). Except in the study conducted by Junli et al. (2013), the bioaccessible and bioavailable fractions of Ni, as having the highest impact on human health risk, have not been included in the studies presented in Table 4. Hence, bioavailability was overestimated when assessing the exposure of the human body to Ni, and reported dietary intake values are not reflecting the actual daily intake of the Ni by the human body.

3.3. Bioaccessibility versus bioavailability

The bioaccessible fraction is the fraction of an element that is released from the food matrix in the gastro-intestinal tract at the time of digestion (Lavu, Van De Wiele, Pratti, Tack, & Du Laing, 2016). This fraction is a maximum possible amount of the element that could be available for absorption (bioavailable). Generally, bioavailability refers to the fraction of the element that reaches the systemic circulation. This usually requires absorption by the body at the intestinal phase of digestion (Wei et al., 2012). As previously mentioned, assessing the level of exposure based on the total metal concentration in foods results in the most conservative and likely overestimation of exposure. To have an accurate estimation, exposure should be calculated based on the amount of the element likely to be released, i.e. the bioaccessible fraction, or absorbed, i.e. the bioavailable fraction. While the bioaccessible fraction is easier to measure, the bioavailable fraction is the most likely to result in a more accurate health risk assessment (Fig. 1).

3.4. Studies on nickel bioavailability

In Table 5, the most important information obtained in Ni bioavailability studies has been summarized. The bioavailability percentages given in Table 5 provide a possibility for quick comparison of different foods used in different studies. The type of the study, *in vivo* or *in vitro*, as well as the exposure type, e.g. oral, are important to be taken into account. It is important to know under which conditions the bioavailable fraction is obtained. Risk thresholds, population group, authors, year of the study and more importantly study gaps are available in Table 5 as well.

The comprehensive study performed by Cabrera-Vique et al. (2011) specified the total Ni concentration in ready meals and fast foods. Furthermore, the bioavailable fraction (dialyzable fraction) of the Ni was assessed through simulated gastro-intestinal digestion for different types of food, i.e. dishes with beef, chicken or pork, fish, eggs, sauces, etc. In total 170 classified samples in 43 different food groups were assessed. The range of the Ni content in average varied between 18.50 and 95.00 ng/g fresh weights of the edible portion. Products with added spices/herbs, whole grains, nuts, cheese and mushrooms demonstrated the highest Ni content. The Ni content was highly variable within every food category with similar products. This could be explained by possible effects of packaging and processing at the food production stage. The bioavailable (dialyzed) fraction ranged from 4.5 to 7.8%. These types of studies are very useful as they give better insights into the current situation with Ni intake and recent changes in eating habits of the population. However, there is still limited information available regarding Ni speciation and bioavailability in food during the digestion process (Cempel & Nikel, 2006).

Cempel and Janicka (2002) cited that food, drinking water and beverages are the main routes of Ni intake in humans. The absorption of Ni (bioavailability) in the human gastro-intestinal tract is reported to be rather low (1.7–10%). This value can be affected greatly by the solubility of the Ni compounds. The Ni bioavailability from drinking water is higher than that from solid food products. According the Cempel and Janicka (2002), there is limited information available regarding toxicity and distribution of the soluble Ni compounds ingested via food and drinking water. In their study, they administered $NiCl_2{\cdot}6H_2O$ in the drinking water to male Wistar rats to evaluate the Ni distribution in the rat organs. They found a direct proportional relationship between the Ni intake and its deposition in the rat organs. This direct proportional relationship was observed between the total Ni intake and Ni absorbed/

transferred into the serum, i.e. bioavailable Ni, as well. The absorption of other essential trace elements (i.e. zinc, copper) may be decreased in presence of high doses of Ni (Cempel & Janicka, 2002).

Mathematical modeling and kinetics of Ni absorption, distribution and elimination from the human body were studied by Sunderman et al. (1989). The study was performed in a group of selected healthy volunteers who ingested $NiSO_4$ via drinking water or food. The average Ni absorption was 27 ± 17% (mean ± SD) for the volunteer group subjected to $NiSO_4$ via drinking water. For the group of volunteers subjected via food, the average Ni absorption was 0.7 ± 0.4% (mean ± SD) at the same doses as the first group. The half time of elimination for absorbed Ni (bioavailable fraction) was 28 ± 9 h in average. This study confirmed the reducing effect of dietary constituents on Ni^{2+} bioavailability. About 25% of ingested Ni^{2+} via drinking water was absorbed (bioavailable), though only 1% of the Ni ingested through food was absorbed. The tap water quality database for Ni was used to estimate exposure of the population to Ni (De Brouwere, Buekers, Cornelis, Schlekat, & Oller, 2012). This database was collected through reviewing the available literature including European Commission (EC) reports regarding the water quality standards for human water consumption in the EU (Directive 98/83/EC). The EU maximum concentration of Ni allowed in tap water is 20 µg/L. According to the database, approximately 5% of the total EU population could be exposed to excessive amounts of Ni when using this threshold. Considering the percentage of Ni absorption (bioavailability) from the drinking water (30%) and solid matrices (5%), drinking water is one of the major routes of Ni oral intake besides the food (ECB, 2008). Furthermore, the Ni can also be ingested from other non-alimentary sources, i.e. soil and dust, at the regional and local level (De Brouwere et al., 2012).

According to the article published by Nielsen et al. (1999), the maximum oral absorption, bioavailability, of Ni is not more than ~30% even if it is 100% bioaccessible. It was shown that a fasting state can increase Ni absorption from water in human volunteers. When ingestion occurred together with food, the oral absorption (bioavailability) ranged from 1 to 5%, whereas the absorption increased to 12–27% under fasting conditions (Nielsen et al., 1999). The bioavailability of the Ni and other trace elements was assessed in 15 wine samples collected from Itata Valley in Chile (Latorre et al., 2018). Bioavailability assessment was conducted through *in vitro* dialyzability approach and no bioavailable fraction of Ni was found in the wine samples. The authors compared the bioavailability % by taking the type of wine, i.e. white or red, and the grape varieties into account, and also no effect of wine type and the grape variety was found in this study. In conclusion, there are rather limited studies addressing the bioavailability of different food or drinks whether via *in vitro* or *in vivo* studies. Besides, studies regarding the Ni species occurring in foods or drinks and their toxicity in the body are lacking as well. However, it has been shown that other dietary constituents can reduce the Ni bioavailability for the body (Nielsen et al., 1999). It seems that these factors have a higher impact on the Ni bioavailability compared to the intrinsic characteristics of the food/drink (Latorre et al., 2018). However, this should be further investigated in future studies.

3.5. Studies on nickel bioaccessibility

The information obtained from revision of the Ni bioaccessibility studies has been summarised in Table 6. It is important to clarify the type of the food used in bioaccessibility studies. The Ni bioaccessibility percentage reported in different studies, available risk threshold values and the gaps related to these studies are given in Table 6.

Gedik (2018) studied the bioaccessibility of Cd, Cr, Cu, Mn, Ni, Pb, and Zn in edible soft tissues of the Mediterranean mussels using *in vitor* digestion model. All samples were collected along the coastal area of the southern black sea. Among all of the elements, Pb was the only one exceeding the maximum allowed limits set by European Commission (EC, 2006). The bioaccessibility of the metals (using the *in vitro* digestion protocol of Versantvoort, 2005) was 83.1%, 80.5%, 76.7%, 73.3%, 69.1%, 61.1% and 58.4% for Ni, Cu, Zn, Cd, Mn, Pb and Cr, respectively. Magnesium, lead and nickel showed significant positive linear correlations between their total and bioaccessible concentrations. Taking the bioaccessible fraction into account, the hazard quotients (HQ) were calculated. The hazard quotient, HQ, is the ratio of the potential exposure of a substance and the level at which no adverse effects are expected. The values were lower than the limit, HQ < 1, set by the US Environmental Protection Agency. Thus, there is no concern on potential hazards of the trace elements through consumption of these seafood tissues (Gedik, 2018).

Bertin et al. (2016) reported the bioaccessibility % to be below LOD for Ni in *Sarcocornia ambigua* plants. Several other types of trace elements were found in this plant, e.g. Ca, K, Mg, Li, Al, V, Cr, Mn, Co, Cu, Zn, Se and Pb. The calculated LOD for Ni was 0.2 mg/g. The aerial parts of *Salicornia* and *Sarcocornia* species are enriched in minerals and trace elements so they are considered as proper vegetable food products for human consumption in areas where the plant is accessible.

The bioaccessible fraction of Ni in some cereals (i.e. rice, spring wheat and maize) was measured using the Rijksinstituut voor Volksgezondheid en Milieu (RIVM) *in vitro* simulated digestion (Liu, Ai, Zhang, Huang, & Zhang, 2017; Versantvoort, 2005). The range of bioaccessibility was reported from 32% to 56%. The grains were cultivated in mining and smelting areas of Baiyin district, Gansu province (China).

Vegetables available in the Hong Kong market were systematically screened to measure their trace element content (Junli et al., 2013). The total Ni concentrations ranged from 0.26 to 1.1 mg/kg. After measuring a total metal concentration in nine major groups of fresh vegetables, a bioaccessibility assessment was performed. For these assessments, three representative samples were selected randomly in every vegetable group. The *in vitro* gastro-intestinal method of digestion described by Wang et al. (2011) was used for bioaccessibility measurements. The bioaccessibility percentage was measured as a ratio between the bioaccessible fraction of the trace element and its total concentration. Bioaccessibility percentages of Ni were reported to vary from 29% to 64%. Higher values were observed for legumes, bulb and root vegetables, while the lowest values were observed for cucurbit, brassica and stalk vegetables. The leafy vegetables were reported to vary in the middle of the range. Estimated daily intakes (EDI) based on bioaccessibility (BEDI) were significantly lower than the tolerable limits for Cd, Pb, Cr, Ni, Cu, and Zn in vegetables (Junli et al., 2013). Reference doses, R_fD, from the Integrated risk information systems (USEPA, 2003, 2007a, b) were 1, 1500, 40, 20, not available and 300 (µg/kg bw/day) for Cd, Cr, Cu, Ni, Pb and Zn, respectively (Junli et al., 2013). While, the average estimated daily intakes (EDI) for consumers were 0.12, 0.54, 3.7, 1.6, 0.32 and 8.5 (µg/kg bw/day) for the aforesaid elements in the same order.

In the study conducted by Machado et al. (2017), nutritional properties as well as the food safety of raw edible globe artichoke heads were investigated. Edible globe artichoke heads are a good source of minerals. Machado et al. (2017) reported a total concentration range of 35.8–57.8 mg/kg, 27.7–42.2 mg/kg, 5.4–7.5 mg/kg and 1.9–3.4 mg/kg for Fe, Zn, Cu, and Ni, respectively. All reported concentrations are on a dry weight basis. In vitro bioaccessibility ranged between 71.3–82.3%, 51.2–64.2%, 41.3–54.7% and 39.5–49.7% for Cu, Zn, Ni and Fe, respectively. The research outcomes indicated that raw edible artichoke heads can act as a mineral enriched food, especially for Cu and Zn, and can be an effective contributor to daily intake of these essential elements. This could be the starting point for further investigation to establish a Recommended Daily Intake (RDI) for this type of non-traditional food (Machado et al., 2017).

Schulz et al. (2017) have studied the *in vitro* bioaccessibility of the fifteen minerals and twenty-two phenolic compounds in juçara fruit during seven ripening stages. They reported a range of Ni bioaccessibility percentage from 7.4 to 42.5% during the ripening stages of this fruit. They did not find any explicit pattern in Ni bioaccessibility during the ripening of juçara fruit. In the study conducted by Gu et al. (2018), a bioaccessibility percentage of 59.9% was obtained for Ni in marine organisms including fishes. They also assessed the risk of this bioaccessible Ni for human health. This study together with the study conducted by Junli et al. (2013) are examples of risk assessments that were conducted taking only the bioaccessible fraction into account. The reported THQ value (target hazard quotient for non-carcinogenic effect) for Ni was higher than that of other trace elements in this research. The THQ value is the ratio between the trace element exposure and maximum level for not expecting adverse health effects. However, THQ value of Ni was below a safe level of 1 (Gu et al., 2018). Lam and Lai (2018) studied the bioaccessibility of Ni in the water spinach, i.e. *Ipomoea Aquatica Forsk*, under the effect of blanching and inoculation with arbuscular mycorrhizal fungi. They reported that 27–40% of the Ni was bioaccessible upon digestion with *in vitro* digestive fluids. Thus, blanching led to the leaching out of Ni and reduced its bioaccessibility.

In summary, Ni bioaccessibilty in different foods ranged from < LOD (for *Sarcocornia ambigua* plants) to 83.11% (for Mediterranean mussels). Some studies conducted on specific foods, e.g. *Sarcocornia ambigua* plants and juçara fruit and the studies focused on typically consumed food/drinks in western diet are still lacking. Generally, the higher bioaccessibility percentages were observed for legumes and root vegetables in comparison with the stalk vegetables having lower bioaccessibility percentages. The Ni bioaccessibility in leafy vegetables varied between both. Generally, the reported range of Ni bioaccessibility for cereals (32–65%) was comparable with that of vegetables (29–64%).

3.6. Impact of bioaccessibility on the estimated daily intake

The direct impact of the metal bioaccessibility on the final estimation of daily intake was reported by Junli et al. (2013). As previously mentioned, their study was conducted on available vegetables in the Hong Kong's market. Junli et al. (2013) reported two intake values. The estimated daily intake (EDI) which obtained using the total Ni concentration in the foodstuffs, and the bioaccessible estimated daily intakes (BEDIs) that obtained using the bioaccessible fraction of Ni in vegetables. They used the consumption data that obtained from Population-based Food Consumption Survey 2005–2007 (FEHD, 2010) for their exposure calculations. Junli et al. (2013) reported a Ni bioaccessibility percentage ranging from 29 to 64% in 9 different types of the fresh vegetables available in the Hong Kong market, e.g. leafy vegetables, legume vegetables, tuber vegetables, etc. The EDI was 1.6 μg Ni/kg bw/day for the average consumers and 5.5 μg Ni/kg bw/day for the high consumers, while the BEDI for the average consumers and the high consumers was 0.58 μg Ni/kg bw/day and 2.2 μg Ni/kg bw/day, respectively. It is clear that EDIs values are higher than the BEDIs, which highlights the importance of taking the bioaccessibility into account at the time of dietary intake assessment to avoid overestimation in reported exposure values.

4. Conclusion

A gap analysis is presented in this paper evaluating Ni as a potential food safety hazard causing a risk for human health. In the first step, available literature was critically screened for Ni occurrence and its potential sources of contamination in food and drinks. The foods with high Ni content are mostly from plant-based origin, e.g. legumes, soy-based products and nuts, compared to foods of animal origin such as meat, fish, and honey, having lower Ni contents. The elevated Ni content can be explained by the essential role of Ni in the nitrogen metabolism in some plants, e.g. legumes, soy and nuts. Drinks including drinking water were only analyzed in limited studies. Several studies (are available that calculated Ni intake via food, where mainly chronic impact on human health was evaluated. However, more exposure studies are needed to address the level of contamination in drinks consumed in different countries around the world. Comparing to the other approaches of intake assessment such as multiple food, single food and duplicate diet study, a total diet studies were applied as a predominant approach in majority of the studies. Furthermore, most of the risk assessment studies still rely on risk estimations based on the total concentration of the contaminants in food. However, the concentration of a contaminant posing a real health risk is the absorbed (bioavailable) fraction in the body. In order to have a real exposure estimation, it is indispensable to take a bioavailable fraction or at least its conservative estimator, i.e. the bioaccessible fraction into account. The Ni bioavailability% reported in different studies ranged from 0 to 30%. Compared with the bioavailability studies, bioaccessibility was assessed for more typically consumed foods, i.e. seafood, cereal and vegetables. In general, the bioaccessibility of Ni ranged from < LOD to 83% in different foods. To obtain better insights in factors affecting bioaccessibility and bioavailability in foodstuffs, it is indispensable to conduct more studies on different food products, especially those with high Ni contents, e.g. legumes, chocolate, nuts, and soy products. Besides, bioaccessibility/bioavailability factors should be taken into account in exposure calculations to reduce overestimation in Ni intake studies.

Acknowledgement

The research that yielded these results was funded by the Belgian Federal Public Service of Health, Food Chain Safety and Environment through the contract RT 16/4 INNIBEL. This research was also supported by the Nickel Institute, Toronto, Canada.

We thank Tony Newson, Adriana Oller, Marco Vallini and Kate Heim from the Nickel Institute for their revision and useful comments on this paper.

References

Abduljaleel, S. A., Shuhaimi-Othman, M., & Babji, A. (2012). Assessment of trace metals contents in chicken (Gallus gallus domesticus) and quail (Coturnix coturnix japonica) tissues from Selangor (Malaysia). *Environmental Science & Technology, 5*, 441–451. https://doi.org/10.3923/jest.2012.441.451.

Adolfo, F. R., do Nascimento, P. C., Leal, G. C., Bohrer, D., Viana, C., de Carvalho, L. M., & Colim, A. N. (2019). Simultaneous determination of iron and nickel as contaminants in multimineral and multivitamin supplements by solid sampling HR-CS GF AAS. *Talanta, 195*, 745–751.

Alberti-Fidanza, A., Burini, G., Perriello, G., & Fidanza, F. (2003). Trace element intake and status of Italian subjects living in the Gubbio area. *Environmental Research, 91*, 71–77.

Amer, M. M., Sabry, B. A., Marrez, D. A., Hathout, A. S., & Fouzy, A. S. M. (2019). Exposure assessment of heavy metal residues in some Egyptian fruits. *Toxicology Reports, 6*, 538–543.

Amin, N. U., Hussain, A., Alamzeb, S., & Begum, S. (2013). Accumulation of heavy metals in edible parts of vegetables irrigated with waste water and their daily intake to adults and children, District Mardan, Pakistan. *Food Chemistry, 136*, 1515–1523. https://doi.org/10.1016/j. foodchem.2012.09.058.

Anke, M., Trüpschuch, A., Dorn, W., Seifert, M., Pilz, K., Vormann, J., & Schäfer, U. (2000). Intake of nickel in Germany: Risk or normality. *Journal of Trace and Microprobe Techniques, 18*, 549–556.

Anke, M., Angelow, L., Glei, M., Müller, M., & Illing, H. (1995). The biological importance of nickel in the food chain. *Journal of Analytical Chemistry, 352*(1–2), 92–96.

Anke, M., Groppel, B., Kronemann, H., & Grun, M. (1984). Nickel an essential element. *IARC Scientific Publications, 53*, 339–365.

Arnich, N., Sirot, V., Rivière, G., Jean, J., Nöel, L., Guérin, T., & Leblanc, J. C. (2012). Dietary exposure to trace elements and health risk assessment in the 2nd French Total Diet Study. *Food and Chemical Toxicology, 50*, 2432–2449.

Aung, N. N., Yoshinaga, J., & Takahashi, J. I. (2006). Dietary intake of toxic and essential trace elements by the children and parents living in Tokyo Metropolitan Area, Japan. *Food Additives & Contaminants, 23*, 883–894. https://doi.org/10.1080/02652030600699643.

Barceloux, D. G. (1999). Nickel. *Journal of Toxicology: Clinical Toxicology, 37*, 239–258.

Barrella, M. V., Heringer, O. A., Cardoso, P. M. M., Pimentel, E. F., Scherer, R., Lenz, D., & Endringer, D. C. (2017). Metals content in herbal supplements. *Biological Trace Element Research, 175*(2), 488–494.

Bertin, R. L., Maltez, H. F., Gois, J. S. D., Borges, D. L. G., Borges, G. D. S. C., Gonzaga, L. V., & Fett, R. (2016). Mineral composition and bioaccessibility in Sarcocornia ambigua using ICP-MS. *Journal of Food Composition and Analysis, 47*, 45–51.

Bocio, A., Nadal, M., & Domingo, J. L. (2005). Human exposure to metals through the diet

in Tarragona, Spain. *Biological Trace Element Research, 104*(3), 193–201.
Bolle, F., Brian, W., Petity, D., Boutakhrit, K., Feraille, G., & Van Loco, J. (2011). Tea brewed in traditional metallic teapots as a significant source of lead, nickel and other chemical elements. *Food Additives & Contaminants: Part A,* 1287–1293. https://doi.org/10.1080/19440049.2011.580010.
Borg, H. (1987). Trace-metals and water chemistry of forest lakes in Northern Sweden. *Water Research, 21*, 65–72.
Bouchoucha, M., Chekri, R., Leufroy, A., Jitaru, P., Millour, S., Marchond, N., ... Guerin, T. (2019). Trace element contamination in fish impacted by bauxite red mud disposal in the Cassidaigne canyon (NW French Mediterranean). *Science of the Total Environment, 690*, 16–26.
Bommuraj, V., Chen, Y., Klein, H., Sperling, R., Barel, S., & Shimshoni, J. A. (2019). Pesticide and trace element residues in honey and beeswax combs from Israel in association with human risk assessment and honey adulteration. *Food Chemistry, 299*, 125123.
Bradney, L., Wijesekara, H., Palansooriya, K. N., Obadamudalige, N., Bolan, N. S., Ok, Y. S., ... Kirkham, M. B. (2019). Particulate plastics as a vector for toxic trace-element uptake by aquatic and terrestrial organisms and human health risk. *Environment International, 131*, 104937.
Cabrera-Vique, C., Mesías, M., & Bouzas, P. R. (2011). Nickel levels in convenience and fast foods: In vitro study of the dialyzable fraction. *Science of the Total Environment, 409*, 1584–1588. https://doi.org/10.1016/j. scitotenv.2010.12.035.
Cempel, M., & Janicka, K. (2002). Distribution of nickel, zinc, and copper in rat organs after oral administration of nickel (II) chloride. *Biological Trace Element Research, 90*(1), 215.
Cempel, M., & Nikel, G. (2006). Nickel: A review of its sources and environmental toxicology. *Polish Journal of Environmental Studies, 15*, 375–382.
Clever, J., & Jie, M. (2014). China's Maximum Levels for Contaminants in Foods, USDA Foreign Agricultural Service, Global Agricultural Information Network, CH14058.
De Brouwere, K., Buekers, J., Cornelis, C., Schlekat, C. E., & Oller, A. R. (2012). Assessment of indirect human exposure to environmental sources of nickel: Oral exposure and risk characterization for systemic effects. *Science of the Total Environment, 419*, 25–36.
Demirezen, D., & Uruç, K. (2006). Comparative study of trace elements in certain fish, meat and meat products. *Meat Science, 74*, 255–260.
Domingo, J. L., Perelló, G., & Bordonaba, J. G. (2012). Dietary intake of metals by the county population of Tarragona (Catalonia, Spain): Results from a duplicate diet study. *Biological Trace Element Research, 146*, 420–425. https://doi.org/10.1007/s12011-011-9269-5.
EC (European Commission regulation) no. 790/2009 amending, or the Purposes of Its Adaptation to Technical and Scientific progress, regulation (EC) No. 1272/2008 of the European Parliament of the Council on Classification, Labelling and Packaging Substances and Maxtures.EC. 2006.
EC (European Commission regulation) no. 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs. Official Journal of European Union L364:5–24, pp. 26–28.
EC (European Commission Regulation). Synthesis report on the quality of drinking water in the Member States of the EU in the period 2002–2004. Directives 80/778/EC and 98/83/EC. EC; 2007.
ECB (European Chemicals Bureau). European Union Risk Assessment Reports on Nickel and Nickel Compounds. ECB. (2008). Available at: http://esis.jrc.ec.europa.eu/doc/existing-chemicals/ risk assessment/REPORT/nickelreport311.pdf.
EFSA (European food safety authority) (2015). Scientific Opinion on the risks to public health related to the presence of nickel in food and drinking water. EFSA Journal, 13(2), 4002.
EFSA (European food safety authority) (2010). Management of left-censored data in dietary exposure assessment of chemical substances. EFSA Journal 2010; 8(3):1557, 96 pp. Doi:10.2903/j.efsa.2010.1557.
FEHD (2010). Hong Kong population-based food consumption survey 2005–2007, Final report. Food and Environmental Hygiene Department (FEHD), Hong Kong Special Administrative Region Government, China.
Frengstad, B., Lax, K., Tarvainen, T., Jaeger, Ø., & Wigum, B. J. (2010). The chemistry of bottled mineral and spring waters from Norway, Sweden, Finland and Iceland. *Journal of Geochemical Exploration, 107*, 350–361. https://doi.org/10.1016/j.gexplo.2010.07.001.
Gama, E. M., Nascentes, C. C., Matos, R. P., Rodrigues, G. C., & Rodrigues, G. D. (2017). A simple method for the multi-elemental analysis of beer using total reflection X-ray fluorescence. *Talanta, 174*, 274–278.
Gedik, K. (2018). Bioaccessibility of Cd, Cr, Cu, Mn, Ni, Pb, and Zn in Mediterranean mussel (Mytilus galloprovincialis Lamarck, 1819) along the southeastern Black Sea coast. *Human & Ecological Risk Assessment, 24*, 754–766.
Ghimpeteanu, O. M. (2009). Researches concerning heavy metals in milk. *Scientific Works, C series, 3*, 126–132.
Gogoasa, I., Gergen, I., Rada, M., Parvu, D., Ciuobanu, C., Bordean, D., ... Moigradean, D. (2006). AAS detection of heavy metal in sheep cheese (the Banat area, Romania). *Buletinul USAMV-CN, 62*, 240–245.
González-Weller, D., Gutierrez, Á. J., de la Torre, A., Armendáriz, C., & Armendariz, A. (2010). Dietary intake nickel in the Canary Islands (Spain): A total diet study. *Toxicology, 278*, 377. https://doi.org/10.1016/j. tox.2010.08.142.
Gu, Y. G., Ning, J. J., Ke, C. L., & Huang, H. H. (2018). Bioaccessibility and human health implications of heavy metals in different trophic level marine organisms: A case study of the South China Sea. *Ecotoxicology and Environment Safety, 163*, 551–557.
Guérin, T., Chekri, R., Vastel, C., Sirot, V., Volatier, J.-L., Leblanc, J.-C., & Noël, L. (2011). Determination of 20 trace elements in fish and other seafood from the French market. *Food Chemistry, 127*, 934–942.
Güler, Z. (2007). Levels of 24 minerals in local goat milk, its strained yoghurt and salted yoghurt (tuzluyogurt). *Small Ruminant Res, 71*, 130–137.
Hussain, S., & Habib-Ur-Rehman, M. (2019). Health risk assessment of different heavy metals dissolved in drinking water. *International Journal of Environmental Research and Public Health, 16*(10).
Hwang, I. M., Yang, J. S., Jung, J. H., Lee, H. W., Lee, H. M., Seo, H. Y., & Khan, N. (2019). Dietary intake assessment of macro, trace and toxic elements via consumption of kimchi in South Korea. *Journal of the Science of Food and Agriculture*. https://doi.org/10.1002/jsfa.9926.
IARC (International Agency for Research on Cancer) (1990). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Chromium, nickel, and welding. WHO, Lyon. 49, 257–445.
JECFA, 1989. Evaluation of certain food additives and contaminants. Thirty-third Report of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Technical Report Series 776, Geneva.
Jensen, C. S., Menné, T., & Duus Johansen, J. (2006). Systemic contact dermatitis after oral exposure to nickel: A review with a modified meta-analysis. *Contact Dermatitis, 54*(2), 79–86.
Junli, H., Fuyong, W., Shengchun, W., Zhihong, C., Xiangui, L., & Ming, H. W. (2013). Bioaccessibility, dietary exposure and human risk assessment of heavy metals from market vegetables in Hong Kong revealed with an in vitro gastrointestinal model. *Chemosphere, 91*, 455–461.
Khan, U. A., Kujala, K., Nieminen, S. P., Raisanen, M. L., & Ronkanen, A. K. (2019). Arsenic, antimony, and nickel leaching from northern peatlands treating mining influenced water in cold climate. *Science of the Total Environment, 657*, 1161–1172.
Lam, C. M., & Lai, H. Y. (2018). Effect of inoculation with arbuscular mycorrhizal fungi and blanching on the bioaccessibility of heavy metals in water spinach (Ipomoea aquatica Forsk.). *Ecotoxicology and Environment Safety, 162*, 563–570.
Lanjwani, M. F., & Channa, F. A. (2019). Minerals content in different types of local and branded honey in Sindh, Pakistan. *Heliyon, 5*(7), e02042. https://doi.org/10.1016/j.heliyon.2019.e02042.
Larsen, E. H., Andersen, N. L., Møller, A., Petersen, A., Mortensen, G. K., & Petersen, J. (2002). Monitoring the content and intake of trace elements from food in Denmark. *Food Additives & Contaminants, 19*, 33–46. https://doi.org/10.1080/02652030110087447.
Latorre, M., Pena-Farfal, C., Neira, Y., Herbello-Hermelo, P., Dominguez-Gonzalez, R., Bermejo-Barrera, P., & Moreda-Pineiro, A. (2018). In vitro human bioavailability of major, trace and ultra-trace elements in Chilean 'natural' wines from Itata Valley. *Food & Function, 9*(10), 5381–5389.
Lavres, J., Castro Franco, G., & de Sousa Câmara, G. M. (2016). Soybean seed treatment with nickel improves biological nitrogen fixation and urease activity. *Frontiers in Environmental Science, 4*(37).
Lavu, R. V. S., Van De Wiele, T., Pratti, V. L., Tack, F., & Du Laing, G. (2016). Selenium bioaccessibility in stomach, small intestine and colon: Comparison between pure Se compounds, Se-enriched food crops and food supplements. *Food Chemistry, 197*, 382–387.
Leblanc, J. C., Guérin, T., Noël, L., Calamassi-Tran, G., Volatier, J. L., & Verger, P. (2005). Dietary exposure estimates of 18 elements from the 1st French total diet study. *Food Additives & Contaminants, 22*, 624–641. https://doi.org/10.1080/02652030500135367.
Lemos, V. A., dos Passos, A. S., dos Santos Novaes, G., de Andrade Santana, D., de Carvalho, A. L., & da Silva, D. G. (2007). Determination of cobalt, copper and nickel in food samples after pre-concentration on a new pyrocatechol-functionalized polyurethane foam sorbent. *Reactive & Functional Polymers, 67*(6), 573–581.
Liu, B., Ai, S., Zhang, W., Huang, D., & Zhang, Y. (2017). Assessment of the bioavailability, bioaccessibility and transfer of heavy metals in the soil-grain-human systems near a mining and smelting area in NW China. *Science of the Total Environment, 609*, 822–829.
Li, Q., Chen, Y., Fu, H., Cui, Z., Shi, L., Wang, L., & Liu, Z. (2012). Health risk of heavy metals in food crops grown on reclaimed tidal flat soil in the Pearl River Estuary, China. *Reactive & Functional Polymers, 227–228*, 148–154. https://doi.org/10.1016/j.jhazmat.2012.05.023.
Lodyga-Chruścińska, E., Sykuła-Zając, A., & Olejnik, D. (2012). Determination of nickel in Polish brands of margarines. *Food Additives and Contaminants: Part B, 5*, 25–254.
López-López, A., López, R., Madrid, F., & Garrido, A. (2008). Heavy metals and mineral elements not included on the nutritional labels in table olives. *Journal of Agriculture and Food Chemistry, 56*, 9475–9483. https://doi.org/10.1021/jf801690k.
Lukáčová, A., Massányi, P., Greń, A., & Golian, J. (2012). Concentration of selected elements in raw and Ultra-heat treated cow milk. *Journal of Microbiology and Biotechnology, 2*, 795–802.
Marzec, Z. (2004). Alimentary chromium, nickel, and selenium intake of adults in Poland estimated by analysis and calculations using the duplicate portion technique. *Nahrung, 48*, 47–52. https://doi.org/10.1002/food.200300355.
Machado, I., Cesio, M. V., & Pistón, M. (2017). In vitro bioaccessibility study of As, Cd, Cu, Fe, Ni, Pb and Zn from raw edible artichoke heads (Cynara cardunculus L. subsp. Cardunculus). *Microchemical Journal, 133*, 663–668.
Madejczyk, M., & Baralkiewicz, D. (2008). Characterization of Polish rape and honeydew honeyaccording to their mineral contents using ICP-MS and F-AAS/AES. *Analytica Chimica Acta, 617*, 11–17.
Mannio, J., Jarvinen, O., Tuominen, R., & Verta, M. (1995). Survey of trace-elements in lake waters of Finnish Lapland using the ICP-MS technique. *Science of the Total Environment, 160–161*, 433–439.
Mekonen, S., Lachat, C., Ambelub, A., Steurbaut, A., Kolsteren, P., Jacxsens, L., ... Spanoghe, P. (2015). Risk of DDT residue in maize consumed by infants as complementary diet in southwest Ethiopia. *Science of the Total Environment, 511*, 454–460.
Moreno-Rojas, R., Sánchez-Segarra, P. J., Cámara-Martos, F., & Amaro-López, M. A.

(2010). Heavy metal levels in Spanish cheeses: Influence of manufacturing conditions. *Food Additives and Contaminants: Part B, 3*, 90–100.
Moy, G. G. (2015). Total diet studies protecting the public from chemical hazards in food. *Ernahrungs Umschau, 62*(8), 132–139.
Mutlu, C., Türkmen, M., Türkmen, A., & Tepe, Y. (2011). Comparison of metal concentrations in tissues of blue crab, Callinectes sapidus from Mediterranean lagoons. *Bulletin of Environmental Contamination and Toxicology, 87*, 282–286. https://doi.org/10.1007/s00128011-0363-3.
Nakaona, L., Maseka, K. K., Hamilton, E. M., & Watts, M. J. (2019). Using human hair and nails as biomarkers to assess exposure of potentially harmful elements to populations living near mine waste dumps. *Environmental Geochemistry and Health*. https://doi.org/10.1007/s10653-019-00376-6.
Nasreddine, L., Nashalian, O., Naja, F., Itani, L., Parent, D., Nabhani, M., & Hwalla, N. (2010). Dietary exposure to toxic trace elements and essential from a complete diet study in an adult urban population Lebanese. *Food and Chemical Toxicology, 48*, 1262–1269. https://doi.org/10.1016/j.fct.2010.02.020.
Nielsen, G. D., Jepsen, L. V., Jørgensen, P. J., Grandjean, P., & Brandrup, F. (1990). Nickel-sensitive patients with vesicular hand eczema: Oral challenge with a diet naturally high in nickel. *The British Journal of Dermatology, 122*, 299–308. https://doi.org/10.1111/j.1365-2133.1990.tb08277.x.
Nielsen, G. D., Soderberg, U., Jorgensen, P. J., Templeton, D. M., Rasmussen, S. N., Andersen, K. E., & Grandjean, P. (1999). Absorption and retention of nickel from drinking water in relation to food intake and nickel sensitivity. *Toxicology and Applied Pharmacology, 154*, 67–75.
Nisianakis, P., Giannenas, I., Gavriil, A., Kontopidis, G., & Kyriazakis, I. (2009). Variation in trace element contents among chicken, Turkey, duck, goose, and pigeon eggs analyzed by inductively coupled plasma mass spectrometry (ICP-MS). *Biological Trace Element Research, 128*, 62–71. https://doi.org/10.1007/s12011-008-8249-x.
Noël, L., Chekri, R., Millour, S., Vastel, C., Kadar, A., Sirot, V., & Guérin, T. (2012). Li, Cr, Mn Co, Ni, Cu, Zn, Se and Mo levels in foodstuffs from the second French TDS. *Food Chemistry, 132*, 1502–1513. https://doi.org/10.1016/j.foodchem.2011.12.009.
Nowak, L., Dziezyc, H., & Piotrowski, M. (2011). Content of bioelements and toxic metals in honey of various botanical origin from lower Silesia. *Journal of Elementology*, 437–444.
Padhan, B., Biswas, M., Dhal, N. K., & Panda, D. (2018). Evaluation of mineral bioavailability and heavy metal content in indigenous food plant wild yams. *Journal of Food Science and Technology, 55*(11), 4681–4686. https://doi.org/10.1007/s13197-018-3388-3.
Pandelova, M., Lopez, W. L., Michalke, B., & Schramm, K.-W. (2012). Ca, Cd, Cu, Fe, Hg, Mn, Ni, Pb, Se, and Zn contents in baby foods from the EU market: Comparison of assessed infant intakes with the present safety limits for minerals and trace elements. *Journal of Food Composition and Analysis, 27*, 120–127.
Pechová, A., Pavlata, I., Dvořák, R., & Lokajová, E. (2008). Contents of Zn, Cu, Mn and Se in milk in relation to their concentrations in blood, milk yield and stage of lactation in dairy cattle. *Acta Veterinaria Brno, 77*, 523–531. https://doi.org/10.2754/avb200877040523.
Reichwaldt, E., Stone, D., Barrington, D., Sinang, S., & Ghadouani, A. (2016). Development of toxicological risk assessment models for acute and chronic exposure to pollutants. *Toxins*, 251. https://doi.org/10.3390/toxins8090251.
Rey-Crespo, F., Miranda, M., & López-Alonso, M. (2013). Essential trace and toxic element concentrations in organic and conventional milk in NW Spain. *Food and Chemical Toxicology, 55*, 513–518.
Rose, M., Baxter, M., Brereton, N., & Baskaran, C. (2010). Dietary exposure to metals and other elements in the 2006 UK total diet study and some trends over the last 30 years. *Food Additives and Contaminants: Part A* 19440049.2010.496794.
Saribal, D. (2019). ICP-MS analysis of trace element concentrations in Cow's milk samples from supermarkets in Istanbul, Turkey. *Biological Trace Element Research*. https://doi.org/10.1007/s12011-019-01708-4.
Ščančar, J., Zuliani, T., Žigon, D., & Milačič, R. (2013). Ni speciation in tea infusions by monolithic chromatography—ICP-MS and Q-TOFMS. *Analytical and Bioanalytical Chemistry, 405*, 20412051. https://doi.org/10.1007/s00216-012-6611-5.
Schulz, M., Biluca, F. C., Gonzaga, L. V., Borges, G. D. S. C., Vitali, L., Micke, G. A., de Gois, J. S., de Almeida, T. S., Borges, D. L. G., Miller, P. R. M., Costa, A. C. O., & Fett, R. (2017). Bioaccessibility of bioactive compounds and antioxidant potential of juçara fruits (Euterpe edulis Martius) subjected to in vitro gastrointestinal digestion. *Food Chemistry, 228*, 447–454.
Schwalfenberg, G., Rodushkin, I., & Genuis, S. J. (2018). Heavy metal contamination of prenatal vitamins. *Toxicology Reports, 5*, 390–395.
Shiraishi, K. (2005). Dietary Intakes of eighteen elements and 40 K in eighteen food categories by Japanese subjects. *Journal of Radioanalytical and Nuclear Chemistry, 266*, 61–69. https://doi.org/10.1007/s10967-005-0869-4.
Skibniewskaa, K. A., Guziurb, J., Marecc, Z., Zarębac, S., Grybowskib, M., & Szarek, J. (2009). Nickel in the muscle tissues of freshwater fish from north eastern Poland should not cause human health concerns. *Toxicological & Environmental Chemistry, 91*, 773–778.
Sommella, A., Deacon, C., Norton, G., Pigna, M., Violante, A., & Meharg, A. A. (2013). Total arsenic, inorganic arsenic, and other elements concentrations in Italian rice grain varies with origin and type. *Environmental Pollution, 181*, 38–43.
Sunderman, F. W., Jr., Hopfer, S. M., Sweeney, K. R., Marcus, A. H., Most, B. M., & Creason, J. (1989). Nickel absorption and kinetics in human volunteers. *Proceedings of the Society for Experimental Biology and Medicine, 191*(1), 5–11.
Torres, F., Das Graças, M., Melo, M., & Tosti, A. (2009). Management of contact dermatitis due to nickel allergy: an update. *Clinical, Cosmetic and Investigational Dermatology, 2*, 39–48.
Turconi, G., Minoia, C., Ronchi, A., & Roggi, C. (2009). Dietary exposure estimates of twenty-one trace elements from a total diet study carried out in Pavia, Northern Italy. *British Journal of Nutrition, 101*, 1200–1208.
Uluozlu, O. D., Tuzen, M. D. M., & Soylak, M. (2009). Assessment of trace element contents of chicken products from Turkey. *Journal of Hazardous Materials, 163*, 982–987.
Vahčić, N., Hruškar, M., Marković, K., Banović, M., & Colić Barić, I. (2010). Essential minerals in milk and their daily intake through milk consumption. *Mljekarstvo, 60*, 77–85.
Vella, C., & Attard, E. (2019). Consumption of minerals, toxic metals and hydroxymethylfurfural: Analysis of infant foods and formulae. *Toxics, 7*(2), https://doi.org/10.3390/toxics7020033.
Versantvoort, C. H. M. (2005). Applicability of an in vitro digestion model in assessing the bioaccessibility of mycotoxins from food. *Food and Chemical Toxicology, 43*, 31–40.
Verta, M., Mannio, J., Iivonen, P., Hirvi, J. P., Jarvinen, O., & Piepponen, S. (1990). Trace metals in Finnish headwater lakes effects of acidification and airborne load. In P. Kauppi, P. Anttila, & K. Kenttamies (Eds.). *Acidification in Finland* (pp. 883–908). Berlin, Heidelberg: Springer-Verlag.
Wang, H. S., Zhao, Y. G., Man, Y. B., Wong, C. K. C., & Wong, M. H. (2011). Oral bioaccessibility and human risk assessment of organochlorine pesticides (OCPs) via fish consumption, using an in vitro gastrointestinal model. *Food Chemistry, 127*, 1673–1679.
Wei, Y., Shohag, M. J. I., & Yang, X. (2012). Biofortification and bioavailability of rice grain zinc as affected by different forms of foliar zinc fertilization. *PLoS ONE, 7*(9), e45428.
Welch, R. M. (1981). The biological significance of nickel. *Journal of Plant Nutrition, 3*(1–4), 345–356.
WHO (World Health Organization) (2000). Air Quality Guidelines, Chapter 6.10, and second edition. Regional Office for Europe (Copenhagen). Available at: http://www.euro.who.int/__data/assets/pdf_file/0014/123080/AQG2ndEd_6_10Nickel.pdf.
WHO/IPCS (World Health Organization/International Program on Chemical Safety) (1991). Environmental health criteria 108: Nickel. Available at: http://www.inchem.org/documents/ehc/ehc/ehc108.htm (last accessed on 17 January 2005).
WHO (World Health Organization) (2008). Guidelines for drink ing-water quality incorporating 1st and 2nd addenda (3rd ed., Vol. 1): Recommendations. Geneva: WHO.
WHO (World Health Organization) (2011). Towards a harmonized total diet study approach: a guidance document. Available at: https://www.who.int/foodsafety/publications/tds_guidance/en/.
Wittsiepe, J., Schnell, K., Hilbig, A., Schrey, P., Kersting, M., & Wilhelm, M. (2009). Dietary intake of nickel and zinc by young children - Results from duplicate food portion in comparison to measurements from dietary records calculated data and available data on levels in food groups. *Journal of Trace Elements in Medicine and Biology, 2*(3), 183–194. https://doi.org/10.1016/j.jtemb.2009.03.007.
Yetley, E. A. (2007). Multivitamin and multimineral dietary supplements: Definitions, characterization, bioavailability, and drug interactions. *American Journal of Clinical Nutrition, 85*(1), 269S–276S.
Ysart, G., Miller, P., Crews, H., Robb, P., Baxter, M., De L'Argy, C., & Harrison, N. (1999). Dietary exposure estimates of 30 elements from the UK total diet study. *Food Additives & Contaminants, 16*, 391–403. https://doi.org/10.1080/026520399283876.
Zhang, J., Baralkiewicz, D., Hanc, A., Falandysz, J., & Wang, Y. (2019). Contents and health risk assessment of elements in three edible ectomycorrhizal fungi (boletaceae) from polymetallic soils in Yunnan Province, SW China. *Biological Trace Element Research*. https://doi.org/10.1007/s12011-019-01843-y.
Zhu, F., Fan, W., Wang, X., Qu, L. I., & Yao, S. (2011). Health risk assessment of eight heavy metals in nine varieties of edible vegetable oils consumed in China. *Food and Chemical Toxicology, 49*, 3081–3085. https://doi.org/10.1016/j.fct.2011.09.019.
Ziarati, P., Shirkhan, P., Mostafidi, M., & Tamaskani Zahedi, M. (2018). An overview of the heavy metal contamination in milk and dairy products. *Acta Pharmaceutica Sciencia, 2*(7).