



Uptake and assimilability of nickel in the course of systemic allergy: Implications for elimination diet



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ABSTRACT

The average nickel uptake in the group of students aged 20 to 25 was determined at 227 µg/day. The same study conducted among 9 senior researchers aged 40 to 50 brought a mean nickel uptake of 161 µg/day. Trace amounts of nickel are present in the majority of foodstuffs. Absorbed from digested aliment, its ions are directly responsible for the occurrence of allergic symptoms. Assimilation of nutrients varies with individual susceptibility and overall health condition. However, it also has a lot to do with dietary habits and food characteristics. In this manuscript, we delineated main parameters related to nickel accumulation, such as its uptake, release from foodstuffs and assimilability. Each of them, their scale and proportions potentially affect allergic response from hypersensitive organism. We analyzed several nickel-rich commodities of various characteristics for their nickel level with a particular interest in the metal amounts being released from digested matter and their proportions. Quantitatively profiled samples of chocolate (3–5 µg nickel/g), popular plant products (1–4 µg/g), nuts (1–10 µg/g) and herbal spices (0.3–10.8 µg/g) underwent simulated digestion followed by atomic absorption spectrometry measurements to evaluate nickel release ratio. Groups of samples composed of analogous food matrices showed consistent release rates. As opposed to chocolate and nuts (both average 50% release), less homogeneous individual herbal spice samples indicated nickel release between 20% and 90%. The release ratio gives an idea of how much metal allergen is available for assimilation out of the total intake of food-borne nickel. Absorption ratio accounts for the amount that ultimately supplies blood serum. We determined mean nickel absorption rate at 16% relative to the daily uptake. Elimination diets should acknowledge release rates specific to individual nutrients as their criterion in designing aware consumption. Apart from crude quantitative approach, specific biochemical food characteristics should be considered in the context of systemic hypersensitivities related to exogenous nickel uptake.

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1. Introduction

Approximately 10% of the overall unselected adult population suffers from allergic contact dermatitis (ACD) caused by cutaneous exposure to nickel (Mortz, Bindslev-Jensen, & Andersen, 2013; Schäfer et al., 2001; Torres, das Gracas, Melo, & Tosti, 2009). Released from jewelry items, clothing accessories, and electronic devices, and present in cosmetics and household chemicals, the metal comes in direct interaction with human skin and causes dermatologic setback in hypersensitive individuals (Sharma, 2006). Up to 10% of the ACD patients additionally develop responsiveness upon systemic exposure (Jellesen, Rasmussen, & Hilbert, 2006; Jensen, Menne, & Johansen, 2006). Systemic nickel allergy evokes inflammatory cutaneous and gastrointestinal symptoms in hypersensitive individuals (Krecisz, Chomiczewska, Kiec-Swierczynska, & Kaszuba, 2011). Occurrence of symptoms follows oral uptake from commodities containing trace amounts of this metal

(Sharma, 2007; Yoshihisa & Shimizu, 2012; Zirwas & Molenda, 2009). The relationship between systemic contact dermatitis and nickel exposure has been elucidated by numerous oral challenge studies (Hindsen, Bruze, & Christensen, 2001; Jensen, Menne, Lisby, Kristiansen, & Veien, 2003). The reported immune response was shown to be dose-dependent and eruptions it caused co-localized with previous nickel patch testing sites (Jensen et al., 2006; Zirwas & Molenda, 2009). Desensitization therapies based on specific oral administration are known to be somewhat successful (Minelli et al., 2010), but their efficiency, outcome and its stability vary on an individual basis (Bonamonte et al., 2011; Tammaro, De Marco, Persechino, Narcisi, & Camplone, 2009).

While it is a futile endeavor to tackle uptake of this ubiquitous food allergen (Karak & Bhagat, 2010; Rose, Baxter, Brereton, & Baskaran, 2010), elimination diets have been insisted on as the best means for alleviating undesired symptoms (Denton, 2012). Low-nickel diets exclude foods considered as hazardous by their high content of nickel, thus reducing intensity of potential allergic feedback (Tammaro, Narcisi, Persechino, Caperchi, & Gaspari, 2011). As such diets are continuously being drawn up for hypersensitive consumers' sake (Mislanar & Zirwas, 2013), they are to an extent encumbered with errors. This kind

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of characterization often fails to acknowledge variability in nickel content between seemingly identical specimens. Plant and animal tissues derive microelements from soil, whose composition varies locally. Analogous plants cultivated in two distinct places will most likely exhibit a difference in nickel uptake. These plants will also accumulate more nickel in spring or autumn, than they would if cultivated in mid-summer (Chen, Huang, & Liu, 2009; Owsianiak, Rosenbaum, Huijbregts, & Hauschild, 2013; Sharma, 2013). Therefore, nickel to be assimilated from an individual bioproduct cannot always be expressed as a default value. Even strict adherence to a specific diet will not put us in control over how much nickel is introduced into our system. Plant tissue, leaves in particular, consumed on a daily basis directs our diet towards larger nickel uptake. Populations where plant products are preferred to meat are more exposed to food-borne nickel (Sharma, 2013). Nickel uptake is, thereby, an aggregate of individual, geographical, seasonal and cultural dietary factors that is cumbersome to standardize.

Different studies approach as little as two borderline stages—when nickel enters the organism and when it is being absorbed/excreted (Darsow et al., 2012). It is, however, misleading when absolute content values of a specific nutrient are not accompanied by its assimilation profile. Firstly, it is not its entire amount that gets to be released from digested foodstuffs. Reportedly, 10% of polyphenol uptake is not subjected to digestion at all and remains intact within the food matrix until excreted (Tarko, Duda-Chodak, & Zajac, 2013). What is more, some of the released nutrients are never absorbed. For example, as little as 30% of the supplied magnesium is assimilated. In addition, numerous co-occurring dietary compounds were identified, that affect either its adsorption or excretion (Blaszczyk & Duda-Chodak, 2013). Absorption of polyphenols, on the other hand, is impaired by binding from certain co-introduced proteins and carbohydrates (Tarko et al., 2013). Chemical speciation determines the absorption rate of iron and selenium (Hunt, 2003). All this goes to say that risk exposure associated with nickel hypersensitivity should not be limited to quantitative standards only, as it normally is. It should be considered along with characteristics specific to a given food product as a whole. In this article we delineate three crucial stages: total nickel uptake, its release from digested food and ultimately—its adsorption. Each of them is relevant to developing allergic response.

2. Materials and methods

2.1. Food sample preparation

Food samples were either purchased commercially or donated unconditionally by manufacturers. They were kept and transported in disposable metal-free containers. Food portions were manually ground in a ceramic mortar with porcelain pestle until homogenous. Three or more individual weighted samples (max. 0.3 g) were collected and mineralized, each in 5 ml 65% nitric acid (Merck, Suprapur®, Darmstadt, Germany, #100441) for complete decomposition in a microwave digester (Berghof Speedwave2, Eningen, Germany, #5305000). For quality control, analytical blanks and certified reference materials were included. Sole 5 ml mineralized nitric acid accounted for blanks, while certified wheat flour NCS ZC73009 (LCG Standards, Beijing, China, #NCS ZC73009) was mineralized as certified reference material. Reference standards were used for trace element recovery and method validations. Signal recovery in nickel detection was well in line with theoretical concentration range reported by the manufacturer, 0.06 ± 0.02 mg/kg. Analytes were diluted 4-fold in ultrapure water (HLP5 demineralizer, Hydrolab, Wislina, Poland, #DH-0005-00) to decrease their acidity.

2.2. Simulated digestion

Weighted food portions analogous to those from Section 2.1 were subjected to simulated digestion procedure. The process was conducted

according to the procedures previously described and validated (Berti, Trovato, Bardella, & Forlani, 2003). Briefly, the maximum weight of 0.3 g homogenous analyte samples was in each case suspended in 2 ml 36% hydrochloric acid (Merck, Tracepur®, Darmstadt, Germany #1151861000) prior diluted to a final concentration of 0.1 M. Pepsin from porcine gastric mucosa (Sigma-Aldrich, Schnellendorf, Germany, #P7012) was added at the ratio of 1/30 relative to analyte weight. Test tubes were placed in a water bath shaker and incubated at 37 °C for 3 h. Afterwards, 4 ml sodium bicarbonate (POCH, Gliwice, Poland, #810530115) saturated solution was added to ensure alkaline pH. Pancreatin (Abbott, Lipase 10,000 PhEur units, Warsaw, Poland, #1076615) was added at the ratio of 1/30 relative to analyte weight and incubation continued for another 2 h in 37 °C. Enzymes were heat-inactivated through 10 min incubation in a water bath set to 100 °C. Extract was centrifuged at 6000 rpm for 10 min. Undigested residue was discarded.

2.3. Serum sample collection and preparation

Blood samples, 7 ml each, were collected from 30 randomly chosen, healthy students of our university, aged 20–25. They gave their written consent to take part in this study. The group was made up of 15 male and 15 female participants. Twenty of these participants further continued collaboration by completing the task described in Section 2.5. The experiments took place in early autumn. All participants were mostly fit, their BMI was normal, i.e. within the range of 20–25.

Blood collection was carried out via venous puncture in a sterile environment at a local hospital. The study obtained ethical approval. The samples were collected into S-Monovette® vacuum blood collection system coated with lithium–heparin (Sarstedt S-Monovette 7.5 ml, Nümbrecht, Germany, #01.1604.400) for further serum separation. The serum was prepared by centrifuging the blood samples at 5000 rpm for 5 min. Serum samples, 1 ml each, were subjected to mineralization with 5 ml 65% nitric acid in a microwave digester until completely decomposed. Each sample was analyzed on a Graphite Furnace Atomic Absorption Spectrometer (Thermo Scientific SOLAAR M Series AA, Waltham, MA, USA) following 4-fold dilution in ultrapure water. For quality control, analytical blanks and certified reference materials were included. Sole 5 ml mineralized nitric acid + 1 ml ultrapure water accounted for blanks, while certified serum (LCG Standards, Seronorm™ Trace Elements Serum L-2, Billingstad, Norway) was mineralized as certified reference material. Reference standards were used for trace element recovery and method validations. Signal recovery in nickel detection was well in line with theoretical concentration range reported by the manufacturer, 8.6–11.0 µg/l (147–187 nmol/l).

2.4. Calibration and quantitative measurements

Atomic Absorption Spectrometer was used for nickel determination in liquid samples. Ultrapure water was used for preparation of working reagents and for sample dilution. The glassware was cleaned and treated with 65% nitric acid for 24 h. Teflon beakers were treated with 65% nitric acid and washed with ultrapure water. To prepare the final standard stock solution, 1 ml standard nickel solution at 1000 mg/l was transferred in its entirety into 1 ml 65% extra pure nitric acid and mixed with ultrapure water up to 100 ml. The volume of 1 ml of this solution was added to 1 ml 65% nitric acid and again diluted up to 100 ml. Final concentration of 20 µg/l was obtained by diluting 20 ml of the solution in 1 ml 65% HNO₃ and ultrapure water up to the volume of 100 ml. This concentration corresponds to the highest one used for calibration curve. Consecutive solutions were prepared by diluting 20 µg/l solution right before the readings were taken. Calibration curve was then used as a reference for quantitative nickel analyses. Samples described in Sections 2.1–2.3 were subject to spectroscopic analysis.

2.5. Questionnaire

Twenty randomly chosen students of our University, aged 20–25, were asked to fill out a thorough survey. In addition, nine senior researchers, aged 40–50, were asked to supply their own surveys. They were asked to note down everything they would consume throughout their day, over a week's time. This included recording what exactly the meal was, its quantity and its volume/weight. The survey was based on recall recording. Participants filled out the survey in real-time or shortly after consumption. Questionnaires were used as a reference for subsequent literature research, which was thought to assign nickel content to each declared consumption. This way we could estimate daily and weekly nickel uptakes. The results obtained from students were further correlated with the average concentration of this element determined in serum for both genres separately.

2.6. Statistical analysis

The samples were prepared and analyzed in triplicate or in larger quantities (up to 5), if available. All data was analyzed statistically. The results were expressed as mean values $\pm$ standard deviation. One-Way analysis of variance was used as statistical method. Average values were considered statistically significant when $p \leq 0.05$.

3. Results and discussion

3.1. Total uptake of food-borne nickel—questionnaire study

Nickel content within edible biomass is an aggregate of natural bioaccumulation aptitude, chemical pressure from breeding environment and anthropogenic industrial processing. As with all other heavy metals (Kim et al., 2008), its excessive presence in foodstuffs is not desired. The questionnaire was to enable precise estimation of daily nickel uptake rate. Our study encompassed 20 healthy students and 9 senior researchers, enquired about their eating habits. The results are consistent with the figures reported for most other European nations (Pizzutelli, 2011). They point to the average daily consumption at $227 \pm 70 \mu\text{g/day}$ for students and $161 \pm 60 \mu\text{g/day}$ for senior staff (Tables 1 and 2). These numbers correspond to the total amount of nickel introduced into the human system.

There were a few significant differences between the two groups in regard of their preference for nickel-rich products. Students reported consumption of chocolate, processed meat and cheap marine fish much more frequently. Senior researchers exhibited preference for freshwater fish, consumed relatively less meat and much less sweets in general. This is mostly the reason for a discrepancy between young and older participants of the study.

The Tolerable Upper Intake Level (UL) is defined as the highest level of daily nutrient intake that is likely to pose no risk of adverse health effects. It is determined at 1.0 mg of soluble nickel salts per day for a person over 19 years old (Dietary Reference Intakes for Vitamin A et al., 2001). This means the average uptake in our study is at least 4-fold lower than UL and thereby considered safe.

3.2. Release of nickel ions during digestion—food sample analysis

Only a part of an incoming amount of nickel per day is processed in the gastrointestinal tract. Large dose of the consumed food is excreted and lost together with potentially viable nutrients. To have an insight into the proportions of this process, we closely analyzed a series of food samples.

It was our intention to analyze products that exhibit different characteristics of composition and various extent of elaboration involved in the manufacturing process. We picked from the array of the so-called nickel-rich products, such as chocolate, herbal spices, nuts and popular edible materials of fruit/vegetable origin. They were

Table 1
Nickel uptake, as concluded from questionnaire study conducted among students.

Day	Amount of Ni [μg] within food consumed by 20 students																			
	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13	#14	#15	#16	#17	#18	#19	#20
Mon	313.6	107.2	632.5	120.8	491	208	137.6	355	168.8	260.1	231.3	152.8	274.3	208	133.9	185.2	194.9	200.2	283.2	238.3
Tue	304.9	221.3	651	162.1	245.4	363.2	65.6	211.9	63.28	125.8	138.2	113	362.7	174.3	167.2	240.3	210.2	84.1	238.2	88.6
Wed	243.9	166.6	516.4	122.5	427.8	376.6	177	257.9	129.4	134.7	156.9	120.7	216.1	240.2	92.54	211.4	366.2	224.2	310.5	352.5
Thu	272.1	216.3	945.9	56.34	143.7	171.6	224.4	94.66	122.7	163.1	130.2	230.4	163.8	210	165.7	120.6	358.3	250.3	280.9	320.9
Fri	295.2	160	514.5	189.5	192.1	225.5	65.28	49.03	212.2	117.5	286.4	150.4	269.2	176.3	180.5	150	233.4	316.7	305.7	417.2
Sat	297.2	185.3	653.9	48.91	331.1	249.2	136.6	169.8	79.57	164.6	205.8	135.7	235.2	190.4	174.5	202.8	70.8	190.6	214.8	213.4
Sun	279.7	200.4	456	158.4	123.1	279.5	102.3	363.7	287.6	70.38	186.8	149.1	208.4	193.1	166.46	139.2	353.3	242.4	227.3	381.6
Total	2006	1257	4370	858.5	1954	1873	908.8	1501	1063	1036	1335	1052	1729	1392	1080	1249	1787	1508	1860	2012
Avg.	286.6	179.6	624.3	122.6	279.2	267.7	129.8	214.6	151.9	148	190.8	150.3	247.1	198.9	154.4	178.5	255.3	215.5	265.8	287.5
SD	23.54	39.46	161.8	53.45	142.1	77.5	58.32	120.9	78.29	58.73	55.69	38.52	63.42	22.85	31.01	43.29	110.1	71.15	38.66	114.4

Table 2

Nickel uptake, as concluded from questionnaire study conducted among senior researchers.

Day	Amount of Ni [µg] within food consumed by 9 senior researchers								
	#1	#2	#3	#4	#5	#6	#7	#8	#9
Mon	202.7	93.43	171.4	179.5	176.8	88.73	163.7	106.2	129
Tue	277.3	132.8	80.27	206.8	204.3	176.9	173.4	196.8	34.84
Wed	116.6	134.3	106.8	107.3	309.1	94.40	94.54	68.44	60.47
Thu	439.5	191.9	203.8	161.5	275.5	133.6	156	237.6	185.7
Fri	130.7	208.3	130.7	182.6	165.5	90.75	45.23	264.6	153.9
Sat	135.9	91.3	161.7	107.8	265.3	104.9	173.8	218	166.9
Sun	267.9	122	174.3	165.4	388.9	81.51	82.11	187.6	50.37
Total	1570	974	1029	1111	1785	770.9	888.9	1279	781.3
Avg.	224.4	139.1	147	158.7	255.1	110.1	126.9	182.7	111.6
SD	115.2	45.28	43.07	37.86	79.66	34.02	52.11	70.81	61.79

subjected to simulated digestion study, thought to mimic processes that occur in the human gastrointestinal tract. This gave us an idea about the rate at which nickel is released from foods, when subjected to metabolic conditions. We were willing to find out what the interplay is between the consumed amount of nickel and its part that successfully underwent digestion. The latter would now be free from matrix and potentially bioavailable for absorption. Resultant nickel release rate is not synonymous to the absorption rate at which the element is assimilated from food. It is, however, an important feature that allows better characterization for each dietary product.

Also, we took a chance to explore the profile of nickel contamination in samples used for analyses. We were particularly interested in how commodities acquire their share of metal.

First, we tested popular plant products that are often used as additives for bakeries (Table 3). Some of them represent a group of leguminous plants, which are considered as particularly high in nickel.

Certain plant seeds exhibited relatively high inherent nickel content, ranging from 1 to 4 µg/g. As regards the poor reputation of leguminous plants, we have found that its level in this group is diverse. Nickel-rich peas and soy largely considered as indigestible due to their oligosaccharide content exhibited fairly high nickel release. So did nickel-scarce plum. On the other hand, corn with its thick, hard to digest skin, as well as equally stodgy beans displayed substantially lower nickel release. Baguette, by comparison, had little nickel as well, but most of it was free. Plotting total nickel against its release rate in the context of assayed group as a whole suggests no potential correlation between the two characteristics. Also, nickel release seems uncoupled from overall digestibility profile commonly ascribed to individual commodities.

Cocoa is enlisted as a peak among highly nickel-rich products, suggesting chocolate as potentially contaminated commodity. As seen in Table 4, we have found that nickel content indeed changed in proportion to the cocoa percentage. Since all three chocolates were manufactured in the same company and represented a consistent line of commercial items, we anticipated that everything other than cocoa level would be identical in their chemical composition. Analogous matrix

would in turn imply similar nickel release rates, which is roughly the case and yields $50 \pm 6\%$.

Results from Tables 3 and 4 highlight that sole fact of high nickel uptake should not be considered in isolation from specific food characteristics. When it comes to total nickel content, sunflower seeds were on par with 70% cocoa chocolate, both indicating ca. 3 µg/g nickel. Nickel release from sunflower seeds occurs at the rate of 85%, whereas it is only 55% for chocolate. The seeds are responsible for delivering 30% more nickel into the human system. If a link exists between adsorption rate and abundance of nickel available after digestion, then quite possibly both products would yield different extent of allergenicity. Clinical and dietetic reports would not accord if detailed food characteristics were omitted. This is particularly crucial when patients are encouraged to take up nickel-free diet. Most of these diets rely on quantitative results and are therefore to an extent misleading.

Spices turn out to be highly heterogeneous group when it comes to nickel management. With its content varying from 0.1 to 2.4 µg/g, they also exhibited dramatic differences in nickel release during simulated digestion (Table 5). Total content was in no way correlated with how much nickel was released. Still, for a commodity that had little direct contamination, most herbal spices appear as something to avoid if one develops oral intolerance. This is particularly true for oregano and caraway. In this case 100 g portion releases over 0.1 mg nickel. This would correspond to 1/2 of the average total daily nickel uptake.

In the case of nut samples we cannot draw decisive conclusions whether or not industrial processing is a prevalent source of nickel. Two of the processed samples exhibit less amount of nickel than raw hazelnuts. Then again, two of the raw samples are below all of the processed ones (Table 6). That said, we can only assume that natural nickel uptake processes in plants are no more relevant than anthropological ones.

Invasive food processing can potentially impact food characteristics, enough so to affect nutrient absorption in the gastrointestinal tract. It was not the case in our examinations. Roasting and frying did not significantly alter nickel release from nut samples. It did increase the absolute content of this microelement, though. This means that processed nuts pose much more threat to nickel sensitive consumer than as a raw product. Nickel release occurs irrespective of its absolute content and is probably specific to the food matrix profile. Roasted and fried meals

Table 3

Content of nickel determined in baguette and edible plant product samples before and after simulated digestion.

No.	Baguette and additives	Total nickel content [ng/g]		Nickel [ng/g] after simulated digestion		Release rate [%]
		Mean	SD	Mean	SD	
1.	Baguette	30.81	10.47	27.87	6.53	90.46
2.	Soy	4384	748.1	3434	93.49	78.34
3.	Pumpkin	2786	215.6	2325	138.3	83.46
4.	Sunflower	3032	3.01	2594	74.48	85.56
5.	Green peas	1146	94.07	827.9	51.80	72.22
6.	Corn	148.1	46.8	57.17	7.06	38.60
7.	Red bean	188.4	17.92	94.05	15.33	49.92
8.	Plum	599.4	314.2	291.2	113.5	77.20

Table 4

Content of nickel determined in chocolate samples before and after simulated digestion.

No.	Dark chocolate	Total nickel content [ng/g]		Nickel [ng/g] after simulated digestion		Release rate [%]
		Mean	SD	Mean	SD	
1.	Chocolate 70% cocoa	3097	202.5	1701	80.14	54.94
2.	Chocolate 85% cocoa	4776	60.79	2675	70.17	56.01
3.	Chocolate 90% cocoa	4706	869.7	2140	221.7	45.48

Table 5

Content of nickel determined in herbal spice samples before and after simulated digestion.

No.	Herbal spices	Total nickel content [ng/g]		Nickel [ng/g] after simulated digestion		Release rate [%]
		Mean	SD	Mean	SD	
1.	Sesame <i>Sesamum indicum</i>	696.3	79.39	351.4	13.90	50.46
2.	Basil <i>Ocimum basilicum</i>	811.5	57.83	290.4	40.33	35.78
3.	Oregano <i>Origanum vulgare</i>	2431	72.49	1583	136.9	65.12
4.	Nutmeg <i>Myristica fragrans</i>	750.9	64.50	269.4	23.24	35.87
5.	Sweet paprika <i>Capsicum annuum</i>	1474	166.6	571.1	115.7	38.72
6.	Caraway <i>Carum carvi</i>	2022	109.9	1873	147.7	92.58
7.	Clove <i>Syzygium aromaticum</i>	380.5	169.6	86.28	35.62	22.67
8.	Cinnamon <i>Cinnamomum zeylanicum</i>	166	77.72	–	–	–
9.	Ginger <i>Zingiber officinale</i>	333.3	58.64	138.1	8.32	50.46

are considered as more stodgy. Again, judging from nut samples analyzed, reduced digestibility did not tackle nickel from being released as it would normally be. In a related article, researchers (Ramírez-Cárdenas, Leonel, Costa, & Reis, 2010) concluded that zinc bioavailability does not change due to cooking. Neither processing, nor improved digestibility did affect the amount of available zinc, which in the end was equally adsorbed in rats.

3.3. Nickel absorbed during digestion—quantitative determinations

We already established that consumption of 1 g fried salty almonds would introduce approximately 1 µg nickel into our system. Half of this would account for a bioavailable nickel dose released from the food matrix. In an attempt to cover the cycle of our examinations, we explored the actual level of nickel assimilability from the gastrointestinal tract based on the results obtained from the group of students in their early 20s.

Absorbed amount of nickel becomes a component of blood serum. It circulates conjugated to the carrier proteins, mainly albumin, until ions are filtered out and excreted in the form of low-molecular compounds. Excretion occurs through every possible route including saliva, tears, milk, bile, deposition in hair and most notably sweat and urine. Despite this fact, nickel blood level remains rather constant due to the equilibrium formed between excretion and constantly incoming dietary doses. To have it determined, we collected blood samples from 15 male and 15 female student volunteers without reported illnesses.

Table 6

Content of nickel determined in raw and processed nut samples before and after simulated digestion.

No.	Nut products	Total nickel content [ng/g]		Nickel [ng/g] after simulated digestion		Release rate [%]
		Mean	SD	Mean	SD	
Raw nuts						
1.	Walnuts	304.8	24.96	137.2	24.95	45.01
2.	Almonds	758.9	1.96	488.2	116.9	64.32
3.	Hazelnuts	1668	62.58	911.9	64.66	54.64
Processed nuts						
4.	Fried salty almonds	1057	191.6	611.1	52.13	57.81
5.	Peanuts fried in skin	1238	132.5	696.6	95.41	56.23
6.	Fried salty peanuts	7429	117.4	4526	226.4	60.93
7.	Roasted peanuts	10,865	1670.4	4726	135.6	43.50

Mean nickel concentration determined for men was 7.8 ± 0.23 µg/l, whereas for women it was 13.7 ± 0.38 µg/l. Overall average value equals 10.75 ± 0.305 µg/l.

If we assume the total blood volume at 4.7 l and the overall concentration of assimilated nickel at 7.8 ± 0.23 µg/l and 13.7 ± 0.38 µg/l, we see that the amount effectively introduced into the system equals 36.6 ± 1.52 µg and 64.39 ± 2.52 µg, for men and women respectively. In order to evaluate the extent of nickel assimilation, the average theoretical uptake concluded from survey study was juxtaposed with the mean nickel content determined in human serum. Assuming an input value, expressed as daily nickel consumption at 227 µg, and an output value, expressed as micrograms of assimilated nickel calculated above, we can determine the assimilability rate for men at approximately 16%. In the case of increased nickel content in women's sera, chances are that the result is affected by exposure routes other than oral. Piercing as well as cutaneous metal penetration from jewelry are associated with consistent release of nickel ions into an organism (Brandao, Gontijo, Girundi, & de Castro, 2010; Fors, Stenberg, Stenlund, & Persson, 2012). This is why drawing a direct analogy between food-borne nickel assimilability and its content in human serum would be far-fetched in the case women group, much more inclined for exposure.

Digestion provokes release of some of the microelements from the food mass, facilitating their rapid absorption. Most authors estimate nickel adsorption rate at 1–10%, but reportedly up to 15% total nickel consumed with food and up to 50% nickel introduced with drinking water is absorbed in the gastrointestinal tract, as quoted in WHO's air quality guidelines for Europe in 2000 (WHO, 2000). Our findings indicate that the general rate of nickel absorption from diet is approximately 16%, which is concurrent with the overall borderline values.

The average nickel release could be drawn up for samples similar in their regard of their homogeneity, such as chocolate or nuts. In both cases approximately 50% nickel ions are free, while the rest remains in undigested solid remnants. The whole absorbed content originates from the bioavailable pool. Thus, in the case of the assayed products we can calculate the *corrected* absorption rate, expressed as a relation of general absorption rate to the food-specific nickel release rate. Assuming general adsorption close to 15%, obtained value corresponds to $15\%/50\% = 30\%$. The ratio expresses capacity of the human system to assimilate nutrients, irrespective of the efficiency in performing their decomposition.

Occasionally, reports briefly mention cases of severe allergic response to products whose nickel level is not particularly high, like beer, juice, certain fruits and vegetables (Falagiani et al., 2008). These

seemingly contradictory observations were questioned (Pizzutelli, 2011) and partly explainable by the fact of steel utensils being vulnerable to wear and localized corrosion (Jellesen et al., 2006; Kamerud, Hobbie, & Anderson, 2013). This answer does not exhaust a subject, though, because it does not address high allergenicity observed in products where little processing is involved.

We could speculate if nickel release and its subsequent absorption could be somewhat correlated. It seems logical that if a great deal of microelements remains accumulated in the food mass, their overall adsorption is reduced. It needs to be explored if the opposite thesis would also be true. If so, food matrices prone to release single ions from their mass (Stecka, Greda, & Pohl, 2012) would be particularly threatening to the allergic. Also, facts of low uptake/low nickel content would not be as significant as its potential release.

It would be challenging to provide a direct, point-blank verification of nickel release and absorption rates possibly being correlated. Multiple individual foods would have to be broken down into groups exhibiting either high or low nickel release. Diet promoting higher nickel release could possibly result in higher concentrations determined in blood serum. There is also a need for future research where target group assayed for nickel assimilability would be composed exclusively of hypersensitive individuals. Absorption processes could well be distorted in a system afflicted with immunological responsiveness. This could be a direct relation associated with pathologic physiology. Alternatively, it could be a secondary aftermath resulting from adherence to a specific diet (Kies & Harms, 1989), whose components inhibit nickel adsorption.

4. Conclusions

Medical setback caused by nickel exposure largely depends on the food matrix that either favors or confines its availability for human digestive enzymes. In our study we examined the whole dietary path—starting from nutrient uptake, through their release during digestion and ending with absorption. We determined the possible tendencies in food-borne nickel release from individual products. We have found that this feature is consistent and reproducible between analogous samples, characteristic to the food matrix composition and independent of exhibited total nickel content, or commonly assumed level of digestibility. Hampered nickel assimilability as an ascribed food characteristic could potentially complement criteria for product selection. In the same way, processing operations could be identified that affect nickel bioavailability for the human digestive system. More conscious risk management in this field would allow less constraining diet and thereby more diverse nutrition.

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