Review article

Nickel – the use and influence on living organisms

Lidia Mielcarz,* Beata Smolińska

Institute of General Food Chemistry, Faculty of Biotechnology and Food Science, Lodz University of Technology, Stefanowskiego 4/10
90-924 Lodz, Poland

*800835@edu.p.lodz.pl

Abstract: *Regardless the form, nickel is an element commonly used. Its numerous advantages make it irreplaceable in many industries. The widespread use of this element in different branches leads to increasing nickel penetration to the environment and its pollution. Furthermore, the contamination of environment results in affecting the living organisms, including both plants that are directly exposed to Ni in soil, water or air, and humans whose exposition to Ni is direct (e.g. contaminated air) and/or indirect (e.g. food with high amount of Ni). Therefore, the exposition of living organisms to Ni may constitute a threat. This paper constitutes the short review of nickel as an environmental contaminant with characterization of its main sources in the environment. The nickel nanoparticles have been also studied. The influence of Ni and its nanoparticles on living organisms with emphasizing its allergenicity of human has been described.*

Keywords: *nickel, nanoparticles of nickel, ecotoxicity, use of nickel, food allergy for nickel, allergenicity.*

Introduction

Nickel is a trace element, that is important for proper functioning of organisms, mostly plants. It influence on the enzymes activity. The excess of nickel is very dangerous, it can even lead to cell death. Due to its characteristics and chemical properties, this element is widely used in different industrial branches.

Nowadays, nickel is often used in the form of nanoparticles. In this form, the properties of nickel are similar to the bulk element but nickel nanoparticles are more wide activities in relation to their volume. Unfortunately, their impact on the environment and living organisms is not known.

Properties of nickel and its uses

Nickel, as a silvery, glistening metal, is hardly corrosive and resistant to abrasion. Nickel is also resistant to weathering, seawater, mineral and organic acids. The most important nickel minerals are: millerite, nickeline, chloanthite, pyrite, iron- nickel and garnierite [1, 2]. Nickel has a catalytic capability and often creates complex compounds with other elements. Its compounds have generally intensive color [3].

Nickel is used for the production of nickel cast iron (coins, tools and electrical equipment), stainless steel and dentures. Moreover, this metal is used as a component of both the nickel-cadmium alkaline batteries and the household equipment. Its usage has also been known in jewelry, but due to high allergic properties its application in this branch has been limited. Nowadays, nickel is used in surgical steel, sterling silver and solders [1, 4-6].

The dominant forms of nickel that are in common use in food processing industries, metallurgy and dyeing are nickel alloys [7]. The group of nickel alloys includes monel, invar, kovar and permalloy. Monel is a flexible nickel alloy, enriched by cooper, iron and manganese. It shows high mechanic strength and resistance to corrosion. Monel is used for production of tanks, elements of chemical equipment as well as for the springs and surgical tools. The other mentioned nickel alloy is invar, which mainly consists of nickel and iron. Sometimes its chemical composition includes chromium and manganese. Invar is often used in the manufacture of precision mechanisms (clocks, valves, motors), and in bimetal thermometers. Kovar, as another nickel alloy, consists of nickel and cobalt. It is often used in hermetic seals, diodes, ceramic materials and in vacuum tubes, microwaves tubes. Permalloy is nickel alloy with the addition of iron. Its unusual properties are connected with its high permeability. The use of this alloy is found in devices operating at constant field, mainly in radio engineering and telecommunications [5, 8].

Nickel is often used for surface coating to protect the objects against corrosion. The nickel-plating can be carried out in two ways: nickel elektroplating (using electricity) and chemical nickel plating (phosphorus additive, without electricity). Chemical nickel-plating bath is based on objects in the salts and other solutions. Its advantage is the good plasticity and adhesion to the device, a uniform distribution over the entire surface of the items. Nickel-plating has three purposes: safety, aesthetic and preparing for subsequent processes [9].

Nowadays, nickel is also used in the form of- nanoparticles. Nanoparticles are small particles (below 100 nm) having a large surface to volume ratio. They are characterized by high chemical reactivity, dislocation of atoms and propensity to aggregate. Nanoparticles are quickly transported by the environment through and as a small compounds, contact easily with living organisms [10]. Nickel nanoparticles are currently used in processes of removal of toxic molecules and remediation [11]. They are also widely used as a components of batteries, diesel fuels and magnetic sensors. Their increasing application in different industrial branches lead to their spreading into environment where they may be a potential threat to the living organisms including humans [12].

Nickel in the environment

Nickel is one of many trace elements widely distributed in the environment, being released from both natural sources and anthropogenic activity, with input from both stationary and mobile sources [13]. It is present in the air, water, soil and biological materials [13]. Natural sources of nickel include weathering of soils and rocks, forest fires and volcanic eruptions. Otherwise, nickel gets to environment through anthropogenic activity. Nickel enters environment as a result of the pouring out of sewage, combustion of coal and fuel oils. In addition, the other anthropogenic sources include the discharges of industrial wastewater, precipitation with high concentrations of heavy metals and surface run off from areas with heavy traffic [13].

Nickel concentrations in ambient air vary considerably and the highest values have been reported from highly industrialized areas [13]. In aquatic ecosystems natural concentrations of nickel are low, however, the constant inflow of pollutants, like domestic wastewater effluents and non-ferrous metal smelters, increase its concentrations in lakes, rivers and oceans [13]. In soil nickel is generally distributed uniformly through the soil profile but typically accumulates at the surface from deposition by industrial and agricultural activities [13].

Increasing use of nickel in the form of nanoparticles becomes an environmental problem. The scale of production of nanoparticles entails their unavoidable influx to various elements of environment, including soils [14].

Regardless of the form of nickel, this element is easily accumulated in the biota, especially in the ecosystems which are highly contaminated. Although this element is an essential micronutrient for plant growth and development, its high concentrations becames toxic [2, 3, 13, 15].

Effect of nickel on living organisms

Microorganisms

Prokaryotes have a lot of systems to maintain homeostasis, use and storage of nickel and regulate the gene expression. The mechanisms by which microorganisms cope with nickel are: binding intra- and extracellular transport outside of the cell, reducing the permeability of the cell covers, enzymatic detoxification or decrease the sensitivity of cells to heavy metals [16]. Nickel allows bacteria to adapt and defend against pathogens. However, in high concentrations it is toxic. Nickel causes malfunction due to non-specific protein binding with this element, therefore bacteria have to work out some solutions to cope with excess of nickel in environment. For example studies on response of *Saccharomyces cerevisiae* on increasing concentrations of nickel have shown that in such conditions the yeast`s proteins are enable to maintain homeostasis and transport of metal ions to their cells. On the other hand, some gram-negative bacteria, e.g., *H. pylori* have developed the transport proteins in the outer membrane that are responsible for active transport of nickel [17, 18].

The tests described by Boros, Wyszkowska and Kucharski (2007) revealed that the most sensitive to the concentration of nickel are bacteries, the fungi are the most resistant. Both nickel chloride and the nickel sulphate had a negative impact on the growth of all tested microorganisms (eg *Azotobacter* ssp., *Rhizobium leguminosarum* bv. *Streptomyces intermedius, Streptomyces fumosus, viciae, Penicillium* spp.). However, bacteria reacted strongly to nickel chloride, nickel sulfate on actinomycetes, and fungi growth depend on the concentration of the compound and not on nickel sources [19].

Plants

Nickel is an important element in the functioning of many enzymes of plants. Its main role is related with functioning of enzymes like ureases, acetylo – S – CoA synthase, glyoxalase I and hydrogenases. Loss of certain plants, like beans, access to nickel can even lead to their death. Nickel affects the process of biological degradation of the molecular nitrogen from the air and contributes to its dislocation to the aerial parts of plants [3, 20, 21, 22]. Nickel is critical to some plants, and its salts have a beneficial effect on their development. This mineral is easily absorbed by plants, characterized by a long migration in the tissue. Download the intensity of nickel by the plants depends on the type and degree of contamination of soils. Plants growing on soils contaminated with nickel usually absorb larger quantity, until it reaches toxic. The most common results of nickel excess are inhibition of seed germination, growth reduction, chlorosis, metabolic disorders and affecting the reduction of transpiration and photosynthesis [2].

High concentration of heavy metals, including nickel in plant tissues can be used to protect tissues. Plants defend themselves in this way from both pathogens and herbivores. In wheat nickel salts prevent fungal infections of leaves and stems. Also for plant of the genus *Alyssum* higher nickel concentration is fungicidal. Accumulation of nickel in the tissues is protected from snails. However, the stress caused by an excess of nickel can cause a shortage of micro- and macronutrients. A higher concentration of nickel reduces the amount of calcium, manganese and iron. Furthermore, Ni is a potential inhibitor of growth of meristematic cells of *Allium cepa* root. Plant exposition to high concentration of Ni results in both reduced quantum yield of primary photochemistry and reduced chlorophyll contents. Metals accumulation mechanism is not fully understood. This process involves several transport proteins and the membrane that is involved in collecting ingredients from the soil, vacuoles, and many others. The highest concentration of nickel is usually observed in the underground plant tissues [23].

Toxic effect of the high concentration of nickel on plant tissues was described in many articles. For example Snigh and Prasad (2015), as well as Molas (2002) tested the effect of Ni on *Brasica oleracea Raphanus sativus* or *Zea mays*. According to mentioned authors, tests on *Brasica oleracea* showed a decrease in growth and quality of the biomass in a high concentration of nickel. Moreover, studies on *Raphanus sativus* response on increasing concentrations of nickel resulted in deterioration of the functioning of the metabolism of plant tissues, and exhibited the ability to accumulate Ni in cells [29, 30]. High concentrations of Ni decreased the enzyme activity in the roots of cereal (*Alyssum bertolonii, Nicotana tabacum*) [26, 27].

The impact of nickel nanoparticles on the plant is two-fold and it depends on the nickel concentrations. Literature data points out that high concentrations of nickel nanoparticles are potentially as harmful as nickel compounds and have similar effects on plants [28]. The positive effect of nickel nanoparticles is connected with its protection role against herbivores and disease. In addition, low concentrations of nanoparticles stimulate the ability of plants to cope with stressful environmental conditions. The mechanism of action of nickel nanoparticles remains unknown [28]. The high concentrations of nickel nanoparticles in the environment show negative influence of these compounds on the plants. Nickel nanoparticles, similarly to nickel molecules, cause the formation of reactive oxygen (ROS), which leads to damage to the structure of DNA and proteins. They stimulate the formation of free radicals, which in turn affects the function of plant enzymes and biochemical processes related to functioning of plant cells [10].

Animals

Due to lack of detail information about specific influence of Ni on human, some tests have been provided on animals. The impact of nickel on higher organisms has being studied extensively on rabbits and rats. Seńczuk (2005) has studied the influence of Ni on rabbits. The tests were conducted for five days, after 3 hours a day the rabbits were subjected to the action of dust of particulate nickel (100 mg/m^3) by inhalation. After this time, they detected in these changes in the nasal mucosa and emphysema. 4 weekly exposure of rabbits on the nickel concentration of 0.5-2 mg/m^3 caused a reduction in lung weight. Exposure to a concentration of 0.1 mg Ni/m^3 of air per 8 months resulted in a decrease in lung concentrations of lysosomes. In rats exposed to nickel in an amount of 25 or 50 mg/kg of body weight per day for 6 weeks was observed reduction of weight gain and reduced levels of alkaline phosphatase and hemoglobin. At lower concentrations of nickel changes in clinical trials was not observed. In the case of long-term exposure of rats to nickel (5, 50 and 125 mg/kg of body weight per day for 2 years), there was a decrease in liver weight and increased heart weight. However, due to the low survival rate of rats in both the test and control, result cannot clearly determine the effect of nickel on these changes. After the two-year study in dogs treated with nickel at doses of 0, 2.5, 25 and 62.5 mg/kg body weight was observed less appetite, weight loss and the bigger weight of kidneys and liver. In addition, histological lesions were found in the lungs. Also, they studied the effect of nickel on the reproductive capabilities of selected species. Administration of 12 mg nickel/kg body weight of the mice resulted in a decrease in motility of spermatozoa, but such effect was not observed for a dose of 8 mg nickel/kg body weight. A one-nickel dose of 16 mg nickel/kg body weight of rats resulted in decreased fetal body weight and result in higher fetal mortality [1, 3, 29, 30].

Humans

Nickel constitutes the threat for humans. Based on animal studies are set permitted nickel content in products for humans (for example, indicators TUIL, TDI). TUIL is a Tolerable Upper Intake Levels for vitamins and minerals. This indicator said what is a pose which is no risk for health for a daily nutrient intake. The highest concentration of nickel is in cocoa (8.2-12 mg/kg), next in soya beans (4.7-5.9 mg/kg) and oatmeal (0.33-4.8 mg/kg). All nickel in human tissues should not exceed 0.5 mg, in human blood – 1-5 µg/L. Above this value, nickel is accumulated in lungs, adrenals and other organs [31].

TDI – Tolerable Daily Intake – is the another indicator. Its value is similar to TUIL. This indicator is controlled by EFSA – European Food Safe Authority According to EFSA, daily intake should be lower than 500 µg [32].

The low concentration of nickel is required for proper functioning of living organisms. Nickel is normally present in human tissues. However, the exposition to high concentrations of Ni may lead to significant increase of this element in human body. In general, the health effect of nickel is depend on the route of exposure (inhalation, oral or dermal) and physicochemical form of this element [13, 33]. Contributions of Ni to the body can differ. Body exposition to the Ni in the air and in drinking water is usually less important than its dietary intake [38]. Nickel shows its neurotoxic and carcinogenic properties. A high concentration of nickel, like for example the oral doses in weight of 73 mg elemental Ni results nausea, headache, cough, diarrhea, decreased pulse. Nickel supplied to the body from food is poorly absorbed and eliminated. A particular threat is skin contact and inhalation. Nickel which is inhaled with air is accumulated and damages the mucous membranes [1, 3, 34, 35].

The chemical form of nickel affects its fate in human body. For instance, the water-soluble forms of this element are more readily absorbed than others [13]. Nickel is easily absorbed in the ionic form. However, even less soluble compounds of this element can be phagocytized. Nickel is transported and distributed through out the body in the form of its complex compounds. It is usually bound to proteins or amino acids. The changes in human body functions are noticed when nickel interacts with other elements, like zinc, magnesium and calcium [33]. These connections can suppress or modify the toxic or cancerogenic effects of nickel [13]. Nickel deficiency causes a reduction in the level of hemoglobin in the blood, fat accumulation in the liver and skin changes. The most important function of this element is to activate dehydrogenases [2].

The influence of nickel in the form of its nanoparticles to the human is related to increasing concentration of ROS. There are studies with indicate that cells exposed to the presence of nickel nanoparticles increased their activity of caspase-3, which suggests increase the risk of apoptosis of these cells. Particularly vulnerable organ to the nickel nanoparticles are the lungs [36]. Moreover, the research indicated that nickel nanoparticles show their genotoxicity and impair the mechanism of degradation of lipids in the liver and can interfere ion transport in mitochondria [10]. However, the studies on nickel nanoparticles effect on humans are still conducted.

Threat of nickel

The most widespread threat of use nickel are allergies. It is estimated that the sensitized to this metal is high: 17% of adults and 8% of children. Nickel allergy can manifest itself as allergic contact dermatitis, conjunctivitis, asthma and rhinitis. Nickel allergy can also cause rejection of orthopedic and dental implants [3, 6].

Nickel ions are too small to independently trigger an allergic reaction. However, since nickel readily binds to proteins, such as larger particles can induce an immune response and cause the production of antibodies. The binding of the metal to the native protein results in antibodies inability to recognize the protein. The cells recognize such a complex molecule as foreign and begin to fight them [13, 33].

The problem of nickel allergy caused heated discussion in the design of euro coins. Coins highest denominations (one euro and two euros) are made of cupronickel. Fortunately, contact with coins is frequent, but short-lived. As with the keys, tools and utensils they are made of too small amounts of nickel ions, to be able to cause a nickel allergy [3].

Nickel is also used in the production of implants and prostheses. Implants are materials with special physico-chemical properties that may include beside of nickel, also other elements like chromium, cobalt, titanium, molybdenum or vanadium. For example, the material of cemented hip prosthesis is stainless steel chrome-nickel. It has been shown that very slow damaged prosthesis (fluids have a strong corrosiveness) can release ions of nickel, chromium and cobalt. This may cause loosening of implants and prostheses, because of the body's response – to attack the surface of implants by tissues and fluids [37, 38].

In addition to induction of allergy, nickel has a neurotoxic and carcinogenic properties for both animals and humans. For people high concentration of nickel (oral doses, 325 mg nickel sulfate = 73 mg elemental Ni) results in nausea, headache, cough, diarrhea, decreased pulse.

Food allergy to nickel is very rare, because the nickel and its compounds in food usually occur in trace amounts. For this reason, the presence of this element in the everyday, average diet is considered to be safe for the average person. However, in people with contact allergy to nickel, nickel in the diet can cause systemic reactions. Such people need to control the consumed food for the content of nickel in it. An additional source of Ni in the diet is water. Both drinking water and used it for food preparation may contain nickel and cause difficult to estimate the increase of the number of ions and nickel compounds in food [13, 39, 40].

Conclusions

Nickel is an element that has found wide application in various industries. It is used to coat a variety of metal surfaces to protect them. However, this carries many risks. A large part of the population is allergic to nickel, which makes everyday objects dangerous for them. In addition, nickel gets into the environment, mainly due to waste water and corrosion of the pipes. Although small amounts of nickel are essential to living organisms (e.g., correspond to multiple roles in plants), its excess is extremely harmful and can interfere with to the tissues and enzymes. It also has a deleterious effect on the DNA strand and causes mutations.

Increasingly, people are also used nanoparticles of nickel. However, their impact on the environment is not fully understood. There are many indications to suggest a beneficial effect of nickel nanoparticles on plants, mainly in the field of defense and stimulating growth. At the same time, more and more research has deleterious effect of the excess of nickel nanoparticles, especially in the animal organisms, including human. However, the further investigations should be provided on influence of nickel nanoparticles to environment and living organisms.

References

1. Barceloux DG, Barceloux D. Nickel. J Toxicol Clin Toxicol **1999**, 37:239-258.
2. Kabata-Pendias A, Pendias H. Biogeochemia pierwiastków śladowych. Wyd. Naukowe PWN, Warszawa **1999**, 353-354.
3. Śpiewak R, Piętowska J. Nikiel - alergen wyjątkowy. Od struktury atomu do regulacji prawnych. Alergol Immun **2006**, 3:58-62.
4. Bielański A, Podstawy chemii nieorganicznej II. Wyd. Naukowe PWN, Warszawa **2002**, pp 938-940.
5. Warner JS, Sunderman FW Jr. Occupational exposure to airborne nickel in producing and using primary nickel products, Nickel in the Human Environment. Lyon: International Agency for Research in Cancer, **1984**, 419-437.
6. Gawk Rodger DJ, Lewis FM, Sham M. Contact sensitivity to nickel and other metals in jewelry reactors. J Am Acad Dermatol **2000**, 43:31-36.
7. Cempel M, Nikel G. Nickel: A Review of its Sources and Environmental Toxicology. Polish J of Environ Stud **2006**, 15:375-382.
8. Davis JR. Special-Purpose Nickel Alloys, ASM Specialty Handbook: Nickel, Cobalt, and Their Alloys **2000**, 106-123.
9. Parkinson R. Properties and applications of electroless nickel. Nickel Development Institute, 1-33. https://nickelinstitute.org/~/Media/Files/TechnicalLiterature/Propertiesandapplicationsofelectrolessnickel_10081_.pdf; entry 20.06.2016.
10. Łebkowska M, Załęska-Radziwiłł M. Występowanie i ekotoksyczność nanocząstek. Ochr Śr **2011**, 4:23-26.
11. Bystrzejewska-Pitrowska G, Golimowski J, Urban PL. Nanoparticles: their potential toxicity, waste and enviromental management. Waste Manage **2009**, 29:2587-2595.
12. Gong N, Shao K, Feng W, Lin Z, Liang C, Sun Y. Biotoxicity of nickel oxide nanoparticles and bio-remediation by microalgae *Chlorella vulgaris*. Chemosphere **2011**, 83:510-516.
13. Cempel M, Nikel G. Nickel: a review of its sources and environmental toxicology. Polish J of Environ Stud **2006**, 15:375-382.

14. Jośko I, Oleszczuk P, Futa B. The effect of inorganic nanoparticles (ZnO, Cr2O3, CuO and Ni) and their bulk counterparts on enzyme activities in different soils. Geoderma **2014**, 232-234:528-237.
15. Uruc Parlak K. Effect of nickel on growth and biochemical characteristics of wheat (*Triticum aestivum L.)* seedlings. NJAS-Wageningen J Life Sci **2016**, 76:1-5.
16. Jarosławiecka A., Piotrowska-Geget Z., Mechanizmy oporności na metale ciężkie u mikroorganizmów. **2006**, 231-238.
17. Cheng T, Li H, Xia W, Jin L, Sun H. Exploration into the nickel "microcosmos" in procariotes. Coordin Chem Rev **2016**, 311:24-37.
18. Sydor AM, Zamble DB. Nickel Metallomics: General Themes Guiding Nickel Homeostasis, Metallomics and the Cell **2013**, 375-416.
19. Boros E, Wyszkowska J, Kucharski J. Wpływ niklu na wzrost drobnoustrojów na podłożach stałych, J Elementol **2007**, 12:167-180.
20. Ragsdale SW, Wood HG, Morton TA, Ljungdahl LG, DerVartanian DV. Nickel in CO dehydrogenase. The bioinorganic chemistry of nickel. VCH Publishers, New York **1988**, 311-332.
21. Brown PH, Welch RM, Cary EE. Nickel: A micronutrient essential for higher plants. Plant Physiol **1987**, 85:801-803.
22. Karaś Z, Barałkiewicz D. Chrom, nikiel i kobalt w ekosystemie żywieniowym sojusznicy czy wrogowie? PTTŻ - Oddział Wielkopolski, Poznań **2000**, 35-124.
23. Shanying He, Zhenli He, Xiaoe Yangz, Virupax CB. Mechanisms of Nickel Uptake and Hyperaccumulation by Plants and Implications for Soil Remediation. Adv Agron **2012,** 117:117-189.
24. Snigh A, Prasad SM. A lucrative techniqe to reduce Ni toxicity in *Raphanus sativus* plant by phosphate amendment: Special reference to plant metabolism. Ecotox Environ Safe **2015**, 119:81-89.
25. Molas J. Changes in chloroplast ultrastructure and total chlorophyll concentration in cabbage leaves caused by excess of organic Ni (II) complex. Environ Exp Bot **2002**, 47:115-126.
26. Boominathan R, Doran PM. Ni-induced oxidative stress in roots of the Ni hyper-accumulator, *Alyssum bertolonii*. New Phytol **2002**, 156:205-215.
27. Gajewska E, Skłodowska M, Słaba M, Mazur J. Effect of nickel on antioxidative enzyme activities, proline and chlorophyll contents in wheat shoots. Biol Plantarium **2006**, 50:653-659.
28. Arruda SCC, Silva ALD, Galazzi RM, Azevedo RAA, Arruda MAZ. Nanopatricles applied to plant science: A review. Talanta **2015**, 131:693-705.
29. WHO/SDE/WSH/05.08/55.
30. Seńczuk W. praca zbiorowa, Toksykologia współczesna. Wyd. Lekarskie PZWL, Warszawa **2005**, 412- 417.
31. Scientific Committee on Food, Tolerable upper intake levels for vitamins and minerals. EFSA **2006**, 345-357.
32. European Food Safety Authority (EFSA), Scientific Opinion on the risks to public health related to the presence of nickel in food and drinking water. EFSA Journal **2015**, 13:1-202.
33. Das KK, Das SN, Dhundasi SA. Nickel its adverse effects and oxidative stress. Indian J Med Res **2008**, 128:412-425.

34. Reichrtova E, Takac L, Sulicowa L, Foltinova J. Biological monitoring of airborn metal particles originated from nickel refinery dump. Hazardous waste: detection, control, treatment, **1988**, 931-936.
35. Kasprzek KS, Sunderman NFW, Salnikow K. Nickel carcinogenesis. Mutat Res **2003**, 533:67-97.
36. Maqsood AS, Maqusood A, Javed A, Javed M, Abdulaziz A Al-Khedhairy, Salman A Alrokayan. Nickel oxide nanoparticles induce cytotoxicity, oxidative stress and apoptosis in cultured human cells that is abrogated by the dietary antioxidant curcumin. Food Chem Toxicol **2012**, 50:641-647.
37. Śpiewak R, Brewczyński PZ. Powikłania po stabilizacji płytą metalową złamania kości udowej u chorej z alergią kontaktową na chrom nikiel i kobalt. Pol Tyg Lek **1993**, 48:651-652.
38. Rahilly G, Price N. Nickel allergy and orthodontics. J Orthod **2003**, 30:171-174.
39. Duran A, Tuzen M, Soylak M. Trace metal contents in chewing gum and candy samples marketed in Turkey. Environ Monit Assess **2009**, 149:283-289.
40. Ščanča J, Zuliani T, Milačič R. Study of nickel content in Ni-rich food products in Slovenia. J. Food Compos Anal **2013**, 32:83-89.