

## IMPORTANCE OF PUBLIC HEALTH CONTROL OF METALS AS CHEMICAL RISKS IN DIETARY SUPPLEMENTS

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**Abstract:** Popularity and use of dietary supplements are constantly growing. Dietary supplements are food products intended to supplement the usual diet and are concentrated source of nutrients or other substances with nutritional or physiological effect. The purpose of the Paper is to determine frequency of presence of cadmium, lead and mercury metals in dietary supplements based on protein and amino acids that were analyzed during 2018 and 2019 at the Public Health Institute of Republic of Srpska in Banja Luka. Content of metal was determined by the Atomic Absorption Spectrophotometry method. No health defective samples were identified by public health control, but due to modern frequent use of dietary supplements in various population groups (children, adolescents, pregnant women, athletes, etc.), the aim of the Paper is to raise people's awareness of the risks, such as heavy metals and artificial sweeteners, colors, prohormones and other chemical risks from dietary supplements since they may be associated with chronic health risks.

**Keywords:** public health control, chemical risks, dietary supplements, health risks.

### INTRODUCTION

Dietary supplements are food products intended to supplement the usual diet and are concentrated source of nutrients (vitamins and minerals) or other substances with nutritional or physiological effects, individually or in combination - amino acids, essential fatty acids, fibers, microorganisms, edible fungi, algae, bees products, raw materials of plant origin - bioflavonoids, carotenoids, isoflavones, glucosinolates and the like. (Food Additive Regulations, 2018). Dietary supplements are marketed in a dosage form such as capsules, lozenges, tablets, pills, ampoules with liquid, dropper vials and other similar forms for use in metered small quantities.

The beginning of dietary supplements use is associated with Japan, when, in the eighties of the 20<sup>th</sup> century, began the use of food products for special nutritional purposes (Eng. Foods for special dietary uses - FOSHU). By using dietary supplements, consumers want to improve their overall health, "neutralize" the impact of malnutrition, or delay the onset of disease. Expertly justified reasons for use of dietary supplements are prevention of nutritional deficits in age-specific population groups, persons with poor absorption syndrome, hepato-biliary and metabolic disorders, after surgical interventions in the gastrointestinal tract and long-term medicamentous therapy with corticosteroids and other medications (Torović et al., 2014).

Food is harmful to human health if it contains chemical risks above the maximum approved levels (Food Law, 2008; Regulation on maximum levels for certain contaminants in food, 2012), and presence of metals can occur as by-product of operations during production, processing, transport or storing food.

The goals of the paper are:

1. Determine the incidence of cadmium, lead and mercury in dietary supplements in Republika Srpska analyzed during 2018 and 2019;
2. Indicate the public health importance of the presence of heavy metals in dietary supplementation patterns due to possible health consequences;

3. Point out the need for monitoring and other chemical risks potentially present in dietary supplements, ie artificial sweeteners, colors and prohormones as health risks.

Lead, cadmium and mercury represent persistent chemical risks to human health due to acute toxic and chronic cumulative effects on human body (Environmental Protection Agency US, 2005). Mercury shows teratogenic, spermotoxic and neurotoxic effects. Cadmium, due to its incorporation into bone instead of calcium, leads to osteomalacia and bone fractures, and, by affecting zinc metabolism, it represents risk for heart disease (Norberg et al., 2007). The International Agency for Research on Cancer (IARC) classifies lead in Group 2B of human carcinogens and cadmium in Group 1 in human carcinogens because there is sufficient evidence of carcinogenic effect on humans (WHO/IARC, 2006).

## MATERIAL AND METHODS

The study was conducted as retrospective study on 90 samples of dietary supplements based on protein and amino acids submitted for registration to the Public Health Institute in Republic of Srpska in 2018 and 2019. The metal content was determined by the Atomic Absorption Spectrophotometry method (Atomic Absorption Spectrophotometry; AAS) on the "UNICAM" England device, a flame technique for lead and cadmium analysis. The mercury content of the samples was determined by method of amalgamation by atomic absorption spectrophotometry using direct mercury analyzer (DMA-80). Elemental mercury analyzers, also known as automatic and direct analyzers, with atomic absorption and atomic fluorescence detection methods are very sensitive and are designed for direct mercury detection in solid and liquid samples without previous sample preparation. Working principle of the instrument is based on thermal degradation, catalytic conversion, amalgamation and atomic absorption spectrophotometry. Descriptive statistics indicators (number of samples, minimum and maximum concentrations) were used for lead, cadmium and mercury content. Statistical analysis of mercury content of dietary supplementation samples (arithmetic mean, standard deviation) was performed. Determination of health safety of the samples was carried out in accordance with food safety regulations that were in force during the study period (Food Law, 2008).

## RESULTS AND DISCUSSION

Results regarding number of dietary supplements samples analyzed for metals in 2018 and 2019 are shown in the Table 1.

**Table 1:** Number of dietary supplements samples analyzed for metals in 2018 and 2019

Year	2018	2019	TOTAL
Total	62	28	90
Contaminated	0	0	0

Table 2 shows data on types of metals that were analyzed in dietary supplements (lead, cadmium and mercury) in 2018 and 2019, as well as their minimum and maximum concentrations. In all dietary supplements samples, lead concentrations were found to be  $<0.01\text{mg/kg}$  and cadmium  $<0.03\text{mg/kg}$ . Mercury concentrations ranged from  $0.008\text{--}0.10\text{mg/kg}$  (Table 2). The reference allowed values for lead content in dietary supplements are  $\leq 3.0\text{mg/kg}$ , for cadmium  $\leq 1.0\text{mg/kg}$  and for mercury  $\leq 0.10\text{mg/kg}$ .

**Table 2:** Types and concentrations of analyzed metals in dietary supplements in 2018 and 2019

Type of metal	No. of Analyzed samples	Unit measure	Minimum concentration	Maximum concentration
Lead	90	mg/kg	< 0.01	< 0.01
Cadmium	90	mg/kg	< 0.03	< 0.03
Mercury	90	mg/kg	0.008	< 0.10

The results of the study of lead, cadmium and mercury at the Institute of Public Health in 2018 and 2019 indicate that no health defective food samples were determined for the tested characteristics - lead, cadmium and mercury, that is, all determined concentrations of metals were below the legally prescribed maximum allowed concentration (MDC). The lead and cadmium concentrations found in all dietary supplement samples were below the detection limit. A statistical analysis of the mercury content is presented in a table in dietary supplementation samples, ie concentration range, arithmetic mean and standard deviation (Table 3).

**Table 3:** Mercury concentrations in protein and amino acid based dietary supplementation samples- sports supplements

Type of metal	N	Unit measure	Range (a)	Mean (b)	SD (c)
Mercury	90	mg/kg	0.008 - 0.010	0.0095	0.0007

N –Number of samples

(a) Range concentration

(b) Arithmetic mean

(c) Standard deviation

The mercury content (as well as lead and cadmium) were analyzed in protein and amino acid based dietary supplements, which were submitted for registration to the Institute of Public Health of Republika Srpska during 2018 and 2019, and due to the representativeness of the sample (N = 90 samples). this type of dietary supplement.

The mercury study reduced the number of samples compared to the study presented, in West Africa (Ghana), consensus results were obtained because no health-safe dietary supplementation patterns were identified. All established concentrations of mercury in ten omega-3 acid supplement products from different manufacturers were within acceptable limits. There are frequent use of omega-3 acid supplements in cardiovascular patients and pregnant women as these supplements are recommended as a measure to prevent cardiovascular disease and enhance intrauterine fetal development (Akwasi et al, 2014).

Consistent results as in the present study were confirmed by studying of small number of dietary supplements samples (n = 10) in BiH (Bosnia and Herzegovina) during 2019 and no health defective food samples were identified (Food Safety Agency, 2019).

The authors (Costa et al, 2019) investigate metals but also other contaminants (toxins, pesticides, dioxins and PCBs) as chemical risks in dietary supplements, highlighting the frequent preventive use of dietary supplements as a strategy to combat oxidative stress and aging, but despite the popularity of dietary supplements, there are concerns about their safety. The variety of nutritional supplements and the presence of potential metal contaminants (lead, mercury, arsenic and cadmium), each of which has a variety of toxic effects, undoubtedly adds to the complexity of the safety issues to be considered given the additional harmful chemicals from other products and their possible toxicological interactions with toxic metals. Although

the presence of a contaminant does not necessarily mean that their concentrations exceed the maximum allowable concentrations or that the intake of dietary supplements poses a risk to human health, it does warn of the need to continue monitoring the safety of dietary supplements.

There are studies where health defective dietary supplements samples were identified when analyzed for metals. The content of arsenic, cadmium, mercury and lead was analyzed in 95 dietary supplements and the measured concentrations of arsenic and cadmium were below the permitted limits, with only one dietary supplement having unacceptable mercury values. Nonetheless, the authors argued that this concern could be reduced in some way if part of the total determined concentration of mercury corresponds to the inorganic form of mercury rather than methyl mercury (Dolan et al. 2003).

The dietary supplements market in Poland is growing rapidly and number of registered products and their consumption is constantly increasing. Among the most popular supplements and those that are easily available are herbal supplements, available at any supermarket. During the study, 24 dietary supplements available on the Polish market and containing one or more herbal ingredients were tested. The mercury content in concentration higher than allowed was found in preparations - the bamboo shoots and in algae *Chlorella pyrenoidosa*. The studies have shown that mercury is present in every herbal supplement tested, and its content in two preparations (with bamboo and algae) exceeds the allowed limit of 0.10 mg/kg. Statistically significant differences were found in occurrence of mercury depending on plant ingredient in the supplement. The lowest content was found in preparation with *Tanacetum parthenia*, and the highest in bamboo shoots. The mercury content of the tested herbal supplements was statistically significant in the form of supplements - tablets and capsules. Calculation of daily, weekly, monthly and annual consumption of mercury with the tested dietary supplements was performed - results did not exceed PTWI - temporary intolerable weekly mercury intake (Brodziak-Dopierała et al., 2018).

Study in Lebanon shows that consumption of dietary supplements is widespread and on the rise. Dietary supplements are generally used without prescription, proper counseling or awareness of their health risk. The study aimed to analyze metals in 33 samples of imported dietary supplements, which were frequently consumed by the Lebanese population, to ensure safety and increase citizens' awareness of dietary supplements. It was found that all dietary supplements contained mercury and lead concentrations below the allowed limits, as well as daily exposure, while 30% of the analyzed samples had cadmium levels above the allowed limits but they statistically correlated with essential minerals calcium and zinc. For dietary supplements consumed as basic nutrients, it has been emphasized that their calcium, zinc, iron and manganese content should be monitored for the level of toxic metals and their natural geochemical association with these parent metals to ensure safe allowed levels for consumers (Korfali et al., 2013).

Public health control of harmful substances in dietary supplements is important for consumer safety given the increasing frequency of use of dietary supplements in all population groups, especially specific age groups such as infants, young children, pregnant and lactating women, menopausal women and elderly persons. Many studies show the frequent use of dietary supplements in various countries.

In the United States, a study conducted by the FDA (Food and drug administration) in 2002 found that as many as 73% of the population used dietary supplements and considered them natural and safe to use (Timbo et al., 2006). According to the study conducted by the NHANES (National Health and Nutrition Examination Survey) in 1999-2002 period, over 60% of the population with coronary artery disease, hypertension, or hypercholesterolemia take one or more dietary supplements (Buettner et al., 2007). The study on use of non-vitamin /non-mineral dietary supplements such as amino acids, herbs and herbal products, conducted in early 2000, shows that 6.0% of respondents use these dietary supplements every day (Millen et al., 2004).

Study of the Canadian Institute has shown that more than 50% of people combine the use of at least one dietary supplement with medications they use, where an interaction was noticed in 28% of people, one-third of whom had moderate or severe clinical consequences (Singh and Levine, 2004).

Risk control in dietary supplements is important especially in sensitive population groups such as children, as exposure of children to chemical risks in food can have adverse effects on children's health (WHO, 2009).

Due to the use of additives in the production of dietary supplements, colors and artificial sweeteners (acesulfame K, Na-saccharin, aspartame and Na-cyclamate) as chemical risks, there is possibility of chronic health risks (EFSA, 2006).

The widespread use of dietary supplements also points to other types of chemical and biological risks. The European Food Safety Authority (EFSA) has been asked for scientific advice on safety of hydroxanthracene derivatives and on daily intake that does not raise concerns about adverse health effects. Based on currently available data, the EFSA commission concluded that hydroxanthracene derivatives such as emodin, aloe-emodin and structurally related substance danthron showed *in vitro* genotoxicity. Aloe extracts have also shown to be genotoxic *in vitro*, possibly due to the presence of hydroxanthracene derivatives in the extract, as well as that aloe-emodin is genotoxic *in vivo* and that aloe extract and structural analog danthron are carcinogenic. Epidemiological data suggest an increased risk of colorectal cancer associated with general use of laxatives, some of which contain hydroxanthracene derivatives. Considering possible presence of aloe-emodin and emodin in extracts, the commission concluded that there were concerns about extracts containing hydroxanthracene derivatives that could be considered genotoxic and carcinogenic unless the opposite specific data existed. The Commission has been unable to advise on daily intake of hydroxanthracene derivatives that would not raise concerns about adverse health effects (EFSA, 2018).

EFSA was asked to provide scientific advice on safety of green tea catechins from food products sources, including dietary supplements. Most polyphenols in green tea are made up of catechins. The EFSA Commission considered the possible link between (-) - epigallocatechin-3-gallate (EGCG) consumption, the most relevant catechin in green tea, and hepatotoxicity. The Commission concluded that catechins from green tea infusions prepared in traditional way and reconstituted beverages of the same composition as traditional green tea infusions, are generally considered safe under presumption of safety approach, provided that intake corresponds to the reported intakes in the European member states. However, rare cases of the liver damage have been reported after consumption of green tea infusion, most likely due to an idiosyncratic reaction. On the basis of available data on potential adverse effects of catechins from green tea to the liver, the EFSA Commission concluded that there was evidence from clinical trials showing that intake of doses equal to or greater than 800 mg EGCG daily from dietary supplements induces statistically significant increase of serum transaminase in treated persons in comparison with control group (EFSA, 2018).

Lately, concerns have been growing regarding the use of dietary supplements, especially when used for treating certain disease. There is increasing number of reported side effects and interactions that are associated with them. Unfortunately, credibility and amount of clinical evidence continues to vary, and these data are largely based on reported side effects during administration of these preparations. One extreme example of side effect is the risk of heart attack, arrhythmia, and even death associated with use of dietary supplements containing ephedra, which led to the fact that those products lost the license in the United States territory in 2004 (Rogers et al., 2001).

EFSA delivers scientific opinion on assessing safety of using the ephedra plant and its preparations when used in dietary supplements. The ephedra plant contains biological alkaloids: ephedrine, pseu-



doephedrine, norephedrine, norpseudoephedrine (cathine), methylphedrine and methylpseudoephedrine. These alkaloids have a sympathomimetic effect, and some of them are also used as active ingredients in medicinal products. Use of ephedra plant in dietary supplements is banned in several European countries; however, supplements containing ephedra plant in combination with caffeine are marketed online. There are large differences in concentration of individual ephedra alkaloids in different dietary supplements containing ephedra. Due to the lack of adequate data on genotoxicity and reproductive toxicity, the EFSA Commission did not advise on daily intake of ephedra and its preparations that would not cause concern for adverse health effects. Consumption of ephedra dietary supplements may result in exposure to total ephedra alkaloids or ephedrine, which may exceed therapeutic doses for individual ephedra alkaloids or ephedrine in medications. Such exposure can lead to serious adverse effects that can be enhanced when combined with caffeine. The EFSA Commission concluded that the ephedra plant and its alkaloids used as dietary supplements represent significant concern for human safety at the level of estimated use (EFSA, 2013).

The five-year study conducted by the “National Institute of Health” (NIH) in the USA, which included 295 344 men who did not suffer from cancer, examined association of prostate cancer with use of multivitamines as dietary supplements. These studies have shown higher incidence of moderate and severe prostate cancer forms in men who used the multivitamins seven or more times per week compared to men who did not take the multivitamins (Wood et al., 2003). In addition to this case, harmfulness of excessive intake of dietary supplements was also determined on an example of use of antioxidants for primary and secondary protection of the body against disease. Studies have shown that persons who have been taking beta-carotene, vitamin C, vitamin A, vitamin E, and selenium in excess quantities increased their mortality rate (by various factors which led to such outcome) compared with persons who did not take dietary supplements with antioxidant (Lanski et al., 2003).

Dietary supplements may contain substances that are not indicated on a declaration and may be due to expiration of the preparation or subsequent contamination of the product. According to the Food Law, declaration is segment of product quality and an inadequately declared product is food of inadequate quality.

Frequent use of dietary supplements in adolescents and athletes draws additional attention. The International Olympic Committee conducted a study which showed that 14.6% of dietary supplements intended for athletes contain prehormones which are not listed on a declaration (Geyer et al., 2006). The tennis player Guillermo Coria filed a lawsuit in 2003 against a company that produced dietary supplements, claiming that the multivitamin he used contained substances that led to his doping test being positive (Johnson, 2007). Two cases of severe liver damage in 2007 were reported by patients using dietary supplements containing anabolic androgenic steroids as adulterant (Kafrouni et al., 2007). Also in the USA, Joel Romero, a mixed martial arts fighter, filed a lawsuit in 2016 against the “Gold Star Performance Products“, which produced dietary supplements, claiming that he had failed the doping test because the dietary supplements he used contained ibutamoren. Romero received monetary compensation in May 2019 as he won a lawsuit against the said company (Bohn, 2019).

Dietary supplements should be taken as recommended by a healthcare professional. Data from the survey conducted by the “Health and Diet Survey” in the United States in 2002 indicated that among dietary supplement users who reported an adverse effect, 33% of them were taking these preparations on their own instead of medical device that they were prescribed for treatment of relevant disease, where only 54% of respondents discussed possible replacement of therapy with physician or other healthcare professional (Timbo et al., 2006).

Use of dietary supplements is becoming more frequent in persons with no nutritional deficiency who use dietary supplements to maintain health. An additional problem is that in public, through the media,

large amount of information about dietary supplements is disseminated, and there are many unsubstantiated claims about their action. Dietary supplements, for the purpose of informing consumers, labeling, advertising and presenting, in addition to requirements of the dietary supplement rulebook, should also meet requirements in terms of providing information to consumers about food and regulations on nutrition and health claims (Nutrition and Health Claims Regulation, 2018).

The following are examples of health claims that appear on dietary supplement declaration and which are not in compliance with applicable regulations because they are not on the approved health claims list:

- *“During exercise, it replaces lost water, electrolytes, carbohydrates and vitamins-minerals, necessary for proper metabolism during intense or prolonged training.”*
- *“L-carnitine stimulates and accelerates higher consumption of calories during exercise”*
- *“L-glutamine will ensure more effective and faster regeneration after exercise.”*
- *“Isotonic drinks are much better for adding energy, water and electrolytes than other beverages, and in addition they contribute to better durability. The drink is intended for athletes and other persons for long and enduring trainings.”*

In everyday laboratory practice, the original dietary supplement declaration in English language often contains health claims approved by the European Food Safety Authority (EFSA) which may accordingly be quoted on declaration in one of the languages which are in official use in RS.

## CONCLUSION

- During 2018 and 2019, a total of 90 samples of dietary supplements submitted for registration to the Public Health Institute in the Republic of Srpska were analyzed for lead, cadmium and mercury presence.
- No health defective samples were identified during the study in terms of metal content, but early identification of chemical risks (metals, artificial sweeteners, colors, prohormones...) and other risks from dietary supplements has the public health significance for maintaining health of population considering the increasing frequency of use of dietary supplements in all population groups, especially specific age groups such as infants, young children, pregnant and lactating women, menopausal women and the elderly persons.
- Long-term exposure even to the allowed concentrations of chemical risks can lead to chronic health risks (allergic reactions, potentially toxic effects and other adverse effects).
- On the dietary supplement declaration, only approved health claims shall be stated.
- - In order to increase the consumer safety, it is necessary to conduct further public health studies on dietary supplements and exercise stricter dietary supplements control.

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