https://doi.org/10.31925/farmacia.2021.2.18 **ORIGINAL ARTICLE**

DIETARY SUPPLEMENTS AS ADDITIONAL SOURCES OF ZINC IN THE HUMAN ORGANISM

AGNIESZKA FISCHER [1], BARBARA BRODZIAK-DOPIERAŁA [1]*, IZABELA MOŃKA [2], KRZYSZTOF LOSKA [3], JERZY STOJKO [1]

[1]*Medical University of Silesia, School of Pharmacy with the Division of Laboratory Medicine, Department of Toxicology and Bioanalysis, 4 Jagiellonska Street, 41-200 Sosnowiec, Poland*
[2]*Magnolia Pharmacy, 14 Listopadowa Street, Praszka, Poland*
[3]*Silesian University of Technology, Institute of Water and Wastewater Engineering, 18 Konarskiego Street, 44-100 Gliwice, Poland*

**corresponding author: bbrodziak@sum.edu.pl*

Manuscript received: April 2020

Abstract

Zinc is an important oligoelement of the body. It is a component of all biological systems and it is required for the proper function of many enzymes. Important physiological role in combination with the relatively frequent insufficient supply means that this element is often recommended for additional supplementation. The aim of the study was to assess the zinc concentration in the popular dietary supplements available in Poland. Zinc content in supplements was determined and compared with the declared characteristics on the package. Zn concentration was detected in samples of 42 different multinutrient dietary supplements by the flame atomic absorption spectrometry method. Declared zinc varied from 0.5 to 15.6 mg *per* tablet. The obtained results showed that the determined concentration of zinc is not always compatible with its content indicated by manufacturer. In general, zinc content for all tested products was lower than declared. Both excess and deficiencies in the concentration of metals can lead to adverse health effects. For ensuring a good quality, the supplements need regulation of their composition. Considering the results of our research and the fact that both excess and deficiencies of zinc may lead to adverse health disorders, the composition of dietary supplements should be carefully controlled.

Rezumat

Zincul, element esențial al organismului, este o componentă a tuturor sistemelor biologice și este necesar pentru buna funcționare a multor enzime. Carența acestuia din organism coroborată cu rolul său fiziologic, fac necesară suplimentarea aportului. Scopul studiului a fost de a evalua concentrația de zinc din suplimentele alimentare disponibile în Polonia. Conținutul de zinc din suplimente a fost determinat prin spectrometrie de absorbție atomică și comparat cu concentrația declarată pe ambalaj, folosind 42 de suplimente alimentare. Având în vedere rezultatele cercetărilor întreprinse și faptul că atât excesul, cât și deficitul de zinc pot conduce la efecte adverse asupra sănătății, compoziția suplimentelor alimentare ar trebui controlată riguros înainte de a fi puse pe piața farmaceutică.

Keywords: dietary supplements, zinc, atomic absorption spectrometry

Introduction

Nutrients supplied to the body should satisfy the demand for quality and quantity. The varying living conditions, polluted environment, food modification processes make that their amount in diet not to be equal to the quality. High availability of drugs, dietary supplements and special products made the supplementation of nutrients and enriching the diet with additional substances to become very popular [1].

It has been estimated that the growth of the dietary supplements (DS) market in Poland will amount to 8% annually by 2020 and will reach an estimated value of 5.04 billion polish zloty (PLN) [2].

Supplementation is recommended in the prevention of illnesses or increased body demands [3, 4, 5]. However, the estimated data indicate that nearly 50% of the society uses nutrient supplements [6]. This applies to persons of various age (infants, youth, adults) and in most cases is not related to medical recommendations [6-9].

Zinc is a mineral with important and versatile physiological functions [10, 11]. It plays catalytic, structural and modulatory functions in the tissues. Zinc finger transcription factors are characterized by finger-like DNA binding domains that require one or more zinc ions to stabilize the structure; they play an important role in many biological processes [12]. It plays an important role in the production of hormones (such as the growth hormone and insulin), is an ingredient of many enzymes (such as carbide anhydrase) or their activators (such as enolases, arginases) and maintains the stability of biological membranes [13]. It is involved in the metabolism of xenobiotics, activates the synthesis of metallothionein which binds toxic metals [14-16]. Zinc determines protective, antioxidant effects [17]. It is involved in the structure of superoxide dismutase,

an enzyme responsible for neutralizing the superoxide radical. What is more, a number of other mechanisms has been identified, through which zinc ions interfere with the oxidative status of cells: the inhibition of NMDA receptors, the modulation of intracellular calcium levels that regulates the activity of enzymes such as NDPH oxidase or nitric oxide synthase. Another intermediate mechanism of regulating the redox balance is the inhibition of the lipid peroxidation that depends on iron or copper ions [18]. The role played in the body is so versatile that this element is involved at least partially in all biological processes [19-25].

For ensuring the physiological role, the recommended zinc supply is 6.5 to 14 mg/day [26]. This amount varies depending on factors such as: age, sex, nourishment, co-presence of diseases or a period of increased physiological body demand, such as pregnancy, lactation or convalescence.

Zinc is present in many food products, however, its absorption is variable, with much higher amount in animal products than vegetable ones [27, 28]. Also other ingredients, such as the proteins in the diet may affect zinc bioavailability in the body [29].

Despite high zinc availability, relatively often its deficit in the body can be detected. It is estimated that a low supply of zinc from diet may be a problem of about 20% to even 40% of population [11, 30].

Body support products may be available as drugs or supplements. Supplements, in contrast to drugs, are not subjected to restrictive quality regulations. The Federal Food, Drug, and Cosmetic Act requires that producers who wish to market dietary supplements that contain "new dietary ingredients" to notify the competent authorities [33].

The legal regulations specify that the packaging must include the term "dietary supplement" and the ingredients included. The quantity list of ingredients should be given as calculated into the daily dose of product recommended for consumption and should contain the information on the percentage content in relation to the recommended daily consumption. The manufacturer is also required to place the warning on the package related to not exceeding the daily portion recommended for consumption [34].

The amounts of individual product ingredients are based on the basic product analysis of the manufacturer. The legal regulations do not specify the process of inspection and verification of the actual content of product ingredients. The guidelines determine only the tolerance limit for the declared content of nutrients. According to this limit, the bottom tolerance level for vitamins and minerals is 20% and the upper limit is 50% for vitamins and 45% for minerals [30, 35-39].

The aim of the present study was to assess the zinc concentration in the popular dietary supplements available in Poland. Zinc content in supplements was determined and compared with the declared characteristics on the package.

Materials and Methods

The study covered 42 different dietary supplements. These were generally available products in the sales points (pharmacies, stores) and commonly used by consumers. The products were acquired from 36 different manufacturers. Almost all were complex products containing other substances in addition to zinc, mainly vitamins, minerals and plant extracts. The products were recommended mainly for adults, some had annotation that they may be taken by children > 12 years old. The recommendation to use the products was various, both general (products recommended to improve health, supporting in periods of higher demand for nutrients) and special, such as anti-ageing, improvement of eye-vision, recommended during pregnancy and lactation. The products were in the form of pills.

Two packages of each dietary supplements were used for the study. Two pieces were chosen from each package and weighed (analytic balance RADWAG AS 220/C/2, Poland).

Each sample was crushed and homogenized to a mass of about 0.3 g. The samples were submitted to micro-wave mineralization: 65% HNO_3 (Supra pure, Merck, Dormstadt, Germany), mineralizer Magnum, ERTEC, Poland. Mineralized samples were filled up in calibrated flasks up to 25 cm^3 with purified water (Millipore SAS, Molsheim, France). The zinc concentration was determined in the samples with atomic absorption spectrometry (AAS) in the acetylene-air flame (Spectr-AA 880Z VARIAN). In order to verify the accuracy of the used method, the analysis of a reference material was performed using Mixed Polish Herbs (INCT-MPH-2), Institute of Nuclear Chemistry and Technology Department of Analytical Chemistry, Warsaw (results from six repetitions of assays: Zn: 32.2 ± 0.6 mg/kg (certified value 33.5 ± 2.1 mg/kg, recovery 93.9 - 97.6%).

The results of the zinc content determinations were analysed based on the mean content of this element in four tested samples. The determined and declared content were compared by calculating the relative deviation according to the following formula:

$$\Delta C = \frac{C_d - C_{declared}}{C_{declared}} * 100,$$

where: ΔC – relative deviation from declared zinc content [%], C_d – mean determined zinc content [mg], $C_{declared}$ – declared zinc content [mg].

The results analysis was conducted with Statistica 13 (StatSoft, PL) and Microsoft Excel. $p < 0.05$ was assumed to be statistically significant.

Results and Discussion

Table I shows the general characteristics of the tested products. The mass of the tested tablets ranged from 0.2 g to about 5 g, with average mass of 0.96 g. The

relative standard deviation from tested product mass varied between 0.2 to 2.72%, on average 1.2%. The result indicates that the difference between the mass of individual tested samples showed low variability.

Table I

Characteristics of tested dietary supplements

No.	Indications	Other ingredients	Weight		Zn [mg]	
			mean [mg]	RSD %	declared	determined
1	hair, skin, nails	taurine, catechin	0.68	0.2	7.5	8.0
2	hair, skin, nails	Fe, vit: A, B1, B2, B5, B6, B11, C, E, PP, H	0.95	1.2	7.3	10.9
3	body	Mg, Fe, Cu, Cr, Mo, Se, Mn, vit: C, E	1.38	1.0	5	4.9
4	liver	vit: C, E, extract of artichoke, mint, turmeric, rosemary	0.63	0.5	15	12.7
5	hair, skin, nails	vit: A, C, E, B1, B2, B6, PP, H, extract of horsetail and nettle	0.41	1.3	0.71	0.7
6	eyes	Se, vit: C, lutein, taurine	0.43	4.3	7.5	6.7
7	body	Mg, Fe, Cr, Mo, Se, Mn, Ca, I, vit: A, C, E, B1, B2, B5, B6, B11, B12, H, PP	1.37	2.6	10	10.5
8	body	I, lutein, vit: A, D3, E, B1, B2, B6, B12, C, PP, biotin, folic acid, pantothenic acid	1.44	0.4	7.5	9.3
9	body	vit: A, E, C, K, B1, B2, B6, B12, D, lutein, biotin, folic acid, niacin, pantothenic acid, P, I	1.26	0.4	5	5.2
10	body	Fe, Mg, Cu, Mo, Mn, Se, I, vit: A, C, D, E, B1, B2, B5, B6, B11, B12, PP, H, ginseng	0.92	1.4	10	12.3
11	hair, skin, nails	vit: A, C, B1, B2, B5, B6, H	0.48	1.4	7.5	8.0
12	body	Fe, Mg, Cu, Se, Mn, I, vit: A, C, D, E, B1, B2, B5, B6, B11, B12, H	0.37	0.5	5	4.9
13	eyes	Cu, Se, vit: C, E, extract of *Tagetes sp.*, green tea, blueberry fruit	0.46	0.7	7.5	6.4
14	body	Mg, Fe, Cu, Cr, Mn, Se, Ca, P, I, vit: A, C, D, E, B1, B2, B5, B6, B11, B12, PP, H, ginseng	1.09	2.1	10	10.8
15	body	Cu, Cr, Mo, Mn, Se, I, vit: A, D, E, B1, B2, B5, B6, B11, B12, PP, lutein	0.22	0.6	10	7.5
16	body	Mg, Fe, Se, Ca, I, vit: A, C, E, B1, B2, B5, B6, B11, B12, PP, H	0.94	1.0	9.4	8.8
17	hair, skin, nails	Fe, vit: A, C, E, B1, B2, B6, H, horsetail and nettle extract, chicory inulin	0.42	2.7	3.6	3.2
18	skin	extract of the herb of a tricolour violet	0.35	1.1	5	3.9
19	hair, skin, nails	vit: C, B1, H, extract of the horsetail and nettle	0.51	0.2	4.95	3.6
20	eyes	Cu, Se, Mn, vit: C, E, B1, B2, B6, B12, PP, troxerutin, lutein, omega-3 fatty acids	0.84	1.1	10	10.2
21	hair, skin, nails	Fe, I, vit: A, C, E, B1, B2, B5, B6, B11, B12, PP, L-cysteine, β-carotene, horsetail extract	0.97	0.8	2.25	2.2
22	hair, skin, nails	Cu, vit: B6, theanine, taurine, inositol, acetylcarnitine	0.50	1.2	6	6.6
23	hair, skin, nails	Cu, I, vit: A, C, E, B1, B2, B5, B6, B11, B12, PP	0.95	2.5	7.3	7.7
24	body	Mg, Fe, Cu, Mo, Mn, Ca, Se, I, vit: A, C, D, E, B1, B2, B5, B6, B11, B12, PP	0.92	0.9	15	12.7
25	fresh breath	none	0.71	0.5	7	7.3
26	body	Fe, I, vit: C, E, B1, B2, B5, B6, B11, B12, PP, routine, lutein	0.53	1.7	10.6	10.2
27	skin	vit: B6, PP, lactoferrin, dandelion root extract, green tea, violet herb	0.63	2.1	15	13.9
28	immunity	Se, vit: C, rutoside, citrus biflavonoids	0.40	1.9	2	1.8
29	immunity	Se, vit: C, rutoside, citrus biflavonoids	0.21	0.4	1	0.9
30	hair, skin, nails	Cu, Se, Mn, Si, I, vit: A, C, B1, B2, B5, B6, B11, B12, PP, H, horsetail and nettle extract	0.76	0.8	5	2.1
31	body	Mg, Cr, Mo, Se, Ca, P, K, vit: A, C, D, E, K, B1, B2, B5, B6, B11, B12, PP, lutein	1.31	0.0	5	5.0
32	eyes	Cu, vit: C, E, lutein, zeaxanthin, omega-3 acids	0.67	0.9	10	9.9
33	anti-allergic	Ca, quercetin	4.56	0.2	5	8.1
34	body	Mg, Fe, Cu, Se, Mn, I, vit: C, E, B1, B2, B5, B6, B11, B12, PP	4.96	1.1	7.5	9.9
35	body	Mg, Fe, Cu, Cr, Mo, Mn, Se, Ca, I, vit: A, C, D, E, B1, B2, B5, B6, B11, B12, PP, H	4.36	1.2	10	9.5
36	body	Mg, Fe, Cr, K, vit: B6, B12	1.64	1.9	5	4.9
37	eyes	Cu, Se, vit: E, lutein, zeaxanthin	0.82	0.1	10	9.5
38	eyes	Cr, vit: A, C, E, B2, lutein, zeaxanthin, anthocyanins, resveratrol	0.41	2.9	5	4.0
39	body weight	Cr, vit: B6, PP, inuline	0.46	2.5	10	7.5
40	pregnancy and lactation	Mg, Fe, Cu, Mn, I, vit: A, C, D, E, B1, B2, B5, B6, B11, B12, PP, H	0.80	1.2	15	15.6

No.	Indications	Other ingredients	Weight		Zn [mg]	
			mean [mg]	RSD %	declared	determined
41	brain	Cu, vit: A, E, lecithin, salmon oil	1.66	0.8	2.5	2.7
42	hair, skin, nails	Mg, Ca, P, K, vit: B1, B2, yeast, bee pollen	0.57	0.7	0.5	0.5

The declared Zn content in the tested products was between 0.5 to 15 mg. For example, the zinc content in products recommended for improving eye-vision was 5 to 10 mg. The highest concentration of this element was in products recommended during pregnancy and lactation. Zn content of 15 mg occurred also in products for general support and antioxidative action. The lowest Zn content, 0.5 g, was present in the product based on the yeast extract enriched with minerals.

Table I shows the zinc content determined through our tests and also declared by the manufacturers. The determined zinc content varied between 0.5 to 15.6 mg. In 55% of the tested products, the determined Zn content was lower than the amount indicated on the package. Figure 1 illustrates the percentage deviation of Zn content found versus the amount declared by the manufacturers. The deviations between the declared and the determined zinc content were between 27.5% - 61.4%.

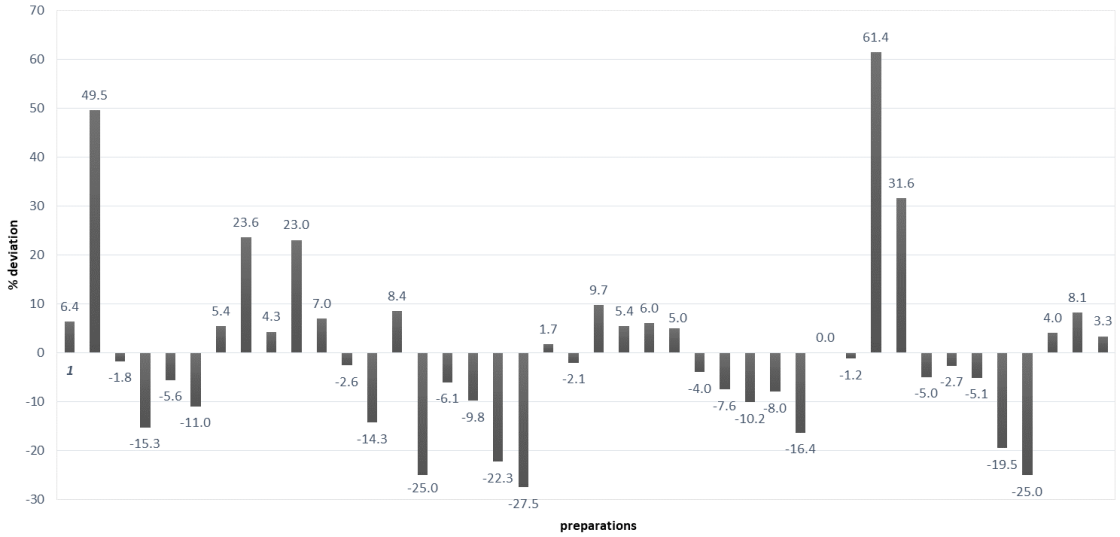

Figure 1.
Deviation from the declared content of Zn in dietary supplements [%]

Dietary supplements are a source of concentrated nutrients which counterbalance the deficits in the diet. In contrast to drugs, dietary supplements are not intended to treat diseases. They are also subject to a separate legal regulation [34, 39-41].

The literature on dietary supplements mainly refers to methods and techniques of preparation analysis [42-44]. Publications concerning composition most often refer to the content of toxic components, including metals, e.g. mercury [45-47].

The analysis of Zn content in the tested samples of supplementation products indicated that in most products [48, 49], the concentration of this element deviated from the amount declared by the manufacturer, which indicates that the amount of minerals supplied to the body deviates from the data on the package. Studies of other authors [37, 38, 50] also show the discrepancy between the declared content and the determined content. In the light of literature, also the excessive zinc supply may lead to pathological changes in the body [48].

In the light of the already published data, the supplements may often have a reduced Zn content as compared to the declared one. The current standards allow a possible reduction of minerals in products by 20% [28, 35, 36]. The above allowable limit is maintained in most of the tested products. For 4 products, zinc concentration was reduced by more than 20%. Using products with lower content of minerals to supplement the diet reduces their nutrient value and efficiency assumed by the consumers.

Efficiency and reliability of supplement products is very important especially for the persons whose physiological diet only partially satisfies body demand for zinc and minerals. As an example, the recommendation for long-term zinc supplementation covers persons on plant based diet which provide much lower zinc absorption than the rich-amine animal products [36, 39]. Higher Zn dosage of about 15 mg should be supplied to the body in certain conditions, such as pregnancy and lactation and for body regeneration. The extra and well-informed diet supplementation in

these periods is very important. The dietary Zn intake for pregnant women in Poland is 10.5 mg/day, while zinc consumption from diet and supplements is 12.7 mg/day, as previously reported [5].

In the light of literature, the excessive zinc supply may also lead to pathological changes in the body. These are mainly disorders related to the absorption of other minerals (mainly copper and iron). The excessive and permanent zinc supplementation may lead to improper oligoelements homeostasis. Higher metal content may be also a carcinogenic factor [11, 31, 32]. In our study, all tested products did not exceed the safe quantity *per* day of 40 mg Zn [49].

It needs to be indicated as well that a health promoting or curative effect of a product is determined by dose, which is not defined for many products. The discrepancies that arise make that the same product may be a dietary supplement in some countries while in other countries it is registered as a drug [49].

Zn content determined in the tested products was higher than the declared amount by 2 to 61%. The standards allow for the upper tolerance limit of up to 50% of the content. Based on this assumption, almost all (except one) tested products were within the limit. However, the limit allowing for the increase of minerals content up to 50% combined with a different concentration of these ingredients than the declared one, may contribute to the fact that the dietary supplements may supply the body with very different doses of elements.

Qualifying dietary supplements as food products makes them available not only in the pharmacies but also in stores which undoubtedly increases their distribution. The wide availability of all products endorses their use in uncontrolled amounts and in various forms. The results of surveys indicate that the consumers very often use different products at the same time [51]. The important issue is the possible interactions of supplementation products taken together with the drugs [52].

The question is whether supplementing the standard with Zn products that exceed recommended dosages may produce an excess amount of zinc in the body.

An excessive consumption of vitamins and minerals may affect the balance of other nutrients and cause side effects. Therefore, it is so important that the minerals are taken in specific doses and ratios. The daily dosage should allow for upper safe level for the nutrients based on generally accepted scientific data [49].

Incomplete analysis of authorized dietary supplements does not confirm the efficiency and safety of its use, therefore the consumers choice is on own responsibility.

Conclusions

The tests performed on zinc dietary supplements showed the differences between the determined and declared content in its composition.

In general, zinc content for all tested products was lower than the declared one. The differences were on average of 10%. The lack of studies on the dietary supplements in respect with the safety and the possibility of unwanted effects and interactions make that the consumers use them with risks.

Conflict of interest

The authors declare no conflict of interest.

References

1. Garcia-Cazarin ML, Wambogo EA, Regan KS, Davis CD, Dietary supplement research portfolio at the NIH 2009-2011. *J Nutr.*, 2014; 144(4): 414-418.
2. Brodziak-Dopierała B, Fischer A, Szczelina W, Stojko J, The content of mercury in herbal dietary supplements. *Biol Trace Elem Res.*, 2018; 185(1): 236-243.
3. Jia HX, Han JH, Li HZ, Liang D, Deng TT, Chang SY, Mineral intake in urban pregnant women from base diet, fortified foods, and food supplements: focus on calcium, iron, and zinc. *Biomed Environ Sci.*, 2016; 29(12): 898-901.
4. Pereira PTVT, Reis AD, Diniz RR, Lima FA, Leite RD, da Silva MCP, Guerra RNM, de Moraes Vieira ÉB, Garcia JBS. Dietary supplements and fatigue in patients with breast cancer: a systematic review. *Breast Cancer Res Treat.*, 2018; 171(3): 515-526.
5. Kocyłowski R, Lewicka I, Grzesiak M, Gaj Z, Sobańska A, Poznaniak J, von Kaisenberg C, Suliburska J, Assessment of dietary intake and mineral status in pregnant women. *Arch Gynecol Obstet.*, 2018; 297(6): 1433-1440.
6. Dickinson A, MacKay D, Health habits and other characteristics of dietary supplement users: a review. *Nutr J.*, 2014; 13: 14: 1-8.
7. Bailey RL, Catellier DJ, Jun S, Dwyer JT, Jacquier EF, Anater AS, Eldridge AL, Total usual nutrient intakes of US children (under 48 months): findings from the feeding infants and toddlers study (FITS) 2016. *J Nutr.*, 2018; 1: 148: 1557-1566.
8. Del Balzo V, Vitiello V, Germani A, Donini LM, Poggiogalle E, Pinto A, A cross-sectional survey on dietary supplements consumption among Italian teen-agers. *PLoS One.*, 2014; 2: 9(7): e100508: 1-6.
9. O'Dea JA, Consumption of nutritional supplements among adolescents: usage and perceived benefits. *Health Educ Res.*, 2003; 18: 98-107.
10. Kabata-Pendias A, Mukherjee AB, Trace elements from soil to human. Springer Science & Business Media, 2007.
11. Sandstead HH, Au W, Zinc. In: Nordberg GF, Fowler BA, Nordberg M, Friberg LT, Handbook on the toxicology of metals. London: Elsevier; 2008.
12. Huang M, Chen Y, Han D, Lei Z, Chu X, Role of the zinc finger and SCAN domain-containing transcription factors in cancer. *Am J Cancer Res.*, 2019; 9(5): 816-836.

13. Zaporowska H, Micronutrients in the life of animals and humans. *UMCS Lublin*, 2002; 29-35: 49-53, (available in Polish).
14. Bonaventura P, Benedetti G, Albarède F, Miossec P, Zinc and its role in immunity and inflammation. *Autoimmun Rev.*, 2015; 14(4): 277-285.
15. Maywald M, Rink L, Zinc homeostasis and immunosenescence. *J Trace Elem Med Biol.*, 2015; 29: 24-30.
16. Mocchegiani E, Costarelli L, Giacconi R, Piacenza F, Basso A, Malavolta M, Zinc, metallothioneins and immunosenescence: effect of zinc supply as nutrigenomic approach. *Biogerontology.*, 2011; 12(5): 455-465.
17. Hojyo S, Fukada T, Zinc transporters and signaling in physiology and pathogenesis. *Arch Biochem Biophys.*, 2016; 611: 43-50.
18. Gapys B, Raszeja-Specht A, Bielarczyk H, Role of zinc in physiological and pathological processes of the body. *J Labor Diag.*, 2014; 50(1): 45-52.
19. Chabosseau P, Rutter GA, Zinc and diabetes. *Arch Biochem Biophys.*, 2016; 611: 79-85.
20. Song Y, Elias V, Loban A, Scrimgeour AG, Ho E, Marginal zinc deficiency increases oxidative DNA damage in the prostate after chronic exercise. *Free Radic Biol Med.*, 2010; 48: 82-88.
21. Bruno RS, Song Y, Leonard SW, Mustacich DJ, Taylor AW, Ho MG, Traber E, Dietary zinc restriction in rats alters antioxidant status and increases plasma F2 isoprostanes. *J Nutr Bioch.*, 2007; 18: 509-518.
22. Jenkins A, Lengyel I, Rutter GA, Lowe N, Shai I, Tirosh A, Petro T, Khamaisi M, Andrews S, Zmora N, Gross A, Maret W, Lewis EC, Moran A, Obesity, diabetes and zinc: A workshop promoting knowledge and collaboration between the UK and Israel, November 28-30, 2016 - Israel. *J Trace Elem Med Biol.*, 2018; 49: 79-85.
23. Chu DS, Zinc: A small molecule with a big impact on sperm function. *PLoS Biol*., 2018; 7: 16(6), e2006204: 1-6.
24. Orlov AP, Orlova MA, Trofimova TP, Kalmykov SN, Kuznetsov DA, The role of zinc and its compounds in leukemia. *J Biol Inorg Chem.*, 2018; 23(3): 347-362.
25. Maares M, Haase H, Zinc and immunity: An essential interrelation. *Arch Biochem Biophys.*, 2016; 611, 58-65.
26. https://www.nrv.gov.au/nutrients/zinc.
27. Jarosz M, Nutrition standards for the Polish population - amendment. Food and Nutrition Institute, Warsaw, 2012: 130-133, 140, 186-187, (available in Polish).
28. Journal of Laws from 2007 No. 196 item 1425. Regulation of the Minister of Health of October 9, 2007 on the composition and labeling of dietary supplements (in Polish).
29. Maret W, Zinc biochemistry, physiology, and homeostasis: recent insights and current. USA, Springer Science - Buisness Media, 2001.
30. Maret W, Sadstead HH, Zinc requirements and the risks and benefits of zinc supplementation. *J Trace Elem Med Biol*., 2006; 20: 3-18.
31. Plum LM, Rink L, Haase H, The essential toxin: impact of zinc on human health. *Int J Environ Res Public Health.*, 2010; 7: 1342-1365.
32. U.S. Environmental Protection Agency. Toxicological review of zinc and compounds. www.epa.gov/iris, 2005.
33. https://www.fda.gov/Food/DietarySupplements/NewDietaryIngredientsNotificationProcess/default.htm
34. Gęsiak K, Kondrat M; Stefańczyk-Kaczmarzyk J, The law of dietary supplements. Warsaw: Wolters Kluwer SA. 2012. (in Polish)
35. Guidance document for competent authorities for the control of compliance with EU legislation on: Regulation (EU) No 1169/2011 of the European Parliament and of the Council of 25 October 2011 on the provision of food information to consumers.
36. Jarosz M, Dietary supplements and health. Warsaw: PZWL 2008; 15-23: 137-180 (in Polish).
37. Poniedziałek B, Niedzielski P, Kozak L, Rzymski P, Wachelka M, Rzymska I, Karczewski J, Rzymski P, Monitoring of essential and toxic elements in multi-ingredient food supplements produced in European Union. *J Consum Protec Food Safe.*, 2018; 13: 41-48.
38. Garcia-Rico L, Leyva-Perez J, Jara-Marini ME, Content and daily intake of copper, zinc, lead, cadmium and mercury from dietary supplements in Mexico. *Food Chem Toxicol.*, 2007; 45: 1599-1605.
39. Wawer I, Supplements for you. Vector publishing house. Warsaw, 2009, (available in Polish).
40. Journal of Laws from 2006 No. 171 item 1225. Act of August 25, 2006 on food and nutrition safety (in Polish).
41. Journal of Laws from 2007 No. 137 item 966. Dz.U. 2007 nr 137 poz. 966. Regulation of the Minister of Agriculture and Rural Development of 10 July 2007 on labeling foodstuffs (in Polish).
42. Krawczyk M, Determination of macro and trace elements in multi vitamin dietary supplements by high-resolution continuum source graphite furnace atomic absorption spectrometry with slurry sampling. *J Pharma Biomed Anal.*, 2014, 88: 377-384.
43. Smichowski P, Londonioa A, The role of analytical techniques in the determination of metals and metalloids in dietary supplements: A review. *Microchem J.*, 2018, 136: 113-120.
44. Blicharska E, Szczęsna B, Kocjan R, Gumieniczek A, Łukasz K, Analysis of dissolution profiles of iron, zinc, and manganese from complex dietary supplements by ion chromatography and chemometrics. *J Liq Chromatogr Related Techno.*, 2015; 39: 1: 30-34.
45. Filipiak-Szok A, Kurzawa M, Szłyk E, Determination of toxic metals by ICP-MS in Asiatic and European medicinal plants and dietary supplements. *J Trace Elem Med Biol.*, 2015; 30: 54-58.
46. Udousoroa I, Ikemb A, Akinboc OT, Content and daily intake of essential and potentially toxic elements from dietary supplements marketed in Nigeria. *J Food Compos Anal.*, 2017; 62: 23-34.
47. Brodziak-Dopierała B, Fischer A, Szczelina W, Stojko J, The content of mercury in herbal dietary supplements. *Biol Trace Elem Res.*, 2018; 185(1): 236-243.
48. Korfali SI, Hawi T, Mroueh M, Evaluation of heavy metals content in dietary supplements in Lebanon. *Chem Central J.*, 2013; 7: 10: 1-13.
49. Kransowska G, Sikora T, Dietary supplements vs consumer safety. *Żywność Nauka Technologia Jakość.*, 2011; 4(77): 5-23, (in Polish).
50. Tumir H, Bošnir J, Dragun Z, Tomić S, Puntarić D, Jurak G, Monitoring metal and metalloid content in

dietary supplements on the Croatian market. *Food Control.*, 2010; 21: 885-889.

51. Lim K, Booth A, Szymlek-Gay EA, Gibson RS, Bailey K, Irving D, Nowson C, Riddell L, Associations between dietary iron and zinc intakes, and between biochemical iron and zinc status in women. *Nutrients*, 2015; 7: 2983-2999.
52. Mocchegiani E, Romeo J, Malavolta M, Costarelli L, Giacconi R, Diaz LE, Marcos A, Zinc: dietary intake and impact of supplementation on immune function in elderly. *Age*, 2013; 35: 839-860.