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Determination of Selected Trace Elements in Dietary Supplements Containing Plant Materials

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The need for analytical methods enabling determining trace metals concentration in herbal medicinal products and dietary supplements has increased in recent years due to the globalisation of international market and also due to the risk of using herbs contaminated by heavy metals. To this end, an analytical method was developed and validated for the accurate determination of trace elements (As, Cd, Co, Cr, Cu, Mn, Pb, Sr, Zn) in products in the form of tablets or capsules, herbal teas and their aqueous infusions. The validation of described procedure of digestion samples and determination metals by ICP-MS method, shows its usability in determination of trace elements in herbal products. Recovery percentage based on CRMs ranged from 90.1% to 110.7%, and the precision of the method was below 3%.

Out of all microelements determined, the highest concentration was found for Mn in herbal teas. The daily intake of Mn with infusions accounted for 53.3% and 126.4%, which corresponded to 41.7% and 98.9% of the AI values for adult women and men, respectively. The method was also used for quality control of the labelled level of chromium and zinc. In all analysed samples, the concentrations of cadmium and lead were below the EC maximum levels stipulated for Cd and Pb in dietary supplements.

INTRODUCTION

Traditional medicines, including Chinese medicines and Indian Ayurvedic medicines, have become more popular as alternative and supplementary remedies in recent years [Chan, 2003; Ożarowski *et al.*, 2005; Schilter *et al.*, 2003]. Toxic metals or metalloids such as lead, mercury, and arsenic, are frequently found in traditional medicines, justifiably raising public concerns. For therapeutic purposes, some traditional medicinal recipes used metals, such as mineral arsenicals and chromials, for hundreds of years as intentional additives, either as the presumed main active ingredient or as an auxiliary agent to assist the efficacy of the given recipes. However, arsenic is a known multi-site human carcinogen and has many other profound toxic effects following both acute and chronic exposure. Depending on its oxidation state chromium can be also a highly toxic substance. Hexavalent chromium compounds are more toxic than trivalent.

Dietary supplements are also more and more frequently used for body mass reduction. These kinds of products contain plant material and/or microelements which are increasing the metabolism and causing the reduction of fat tissue. Most often used to this end are: *Garcina cambogia*, green tea, Java tea, red tea, guarana and *Opuntia humifusa* [Mojska *et al*., 2003]. *Garcinia cambogia* is a small fruit that resembles a miniature pumpkin. It is indigenous to India and parts of Asia, and an extract from its fruit and rind is popular in many natural slimming products. The hydroxycitric acid (HCA) which was found in the extract is claimed to suppress appetite and enhance fat-burning. Animal research supports these claims, but subsequent human trials have been equivocal. The theory behind *Garcinia cambogia* is that HCA inhibits an enzyme called citrate lyase that helps turn excess carbohydrates into fat. Epicatechin gallate, a component of green tea (*Camelia sinensis* (L.) Kuntze), is being researched as well because *in-vitro* experiments have shown that it can influence the catabolism of lipids in the liver [Sobolewska & Podolak, 2006].

Effects on health of some organic compounds present in herbal products are not well known. The plant products or their extracts are characterised by high contents of vitamins, macro- and microelements but also of some metals for which international standard levels have been established. The World Health Organization (WHO) has stipulated maximum levels of cadmium (0.3 mg/kg) and lead (10 mg/kg) in medicinal plant materials. Arsenic is abundantly found in nature and its presence in herbs and herbal medicines should be no different to its wide occurrence in foods [WHO, 2005]. The growing location and condi-

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tions, accumulation of some metals and also environmental pollution influence the element's concentration in a plant [Baranowska *et al*., 2002; Gasser *et al*., 2009; Kabata-Pendias, 2004]. Considering the rising concern with respect to metals in traditional medicines among the general public, this paper is intended to offer a platform to discuss the pharmacology and toxicology of metals in traditional medicines. The discussion is intended to be candid and open with the aim of driving a science-based regulatory approach for comprehensive safety evaluation and optimal risk assessment for metals in traditional medicines. This topic will also be of interest to others engaged in wider aspects of metal toxicology, neurotoxicology, cancer research, risk assessment, clinical intervention, safety evaluation and regulatory affairs. Commission Regulation (EC) No 629/2008 of 2 July 2008, amending Regulation (EC) No 1881/2006 set maximum levels for certain metals in food supplements: lead (3.0 mg/kg); cadmium (1.0 mg/kg); mercury (0.10 mg/kg).

Microelements, including: Co, Cr, Cu, F, Fe, I, Mn, Mo, Se, Zn, are necessary for the proper functioning of living organisms. For the trace elements the safety limit between essential and toxic doses is thin. Therefore, the Estimated Average Requirement (EAR), Recommended Dietary Allowances (RDA) and Adequate Intake (AI) were established [Expert Group…2003; Gawęcki, 2010; Martindale, 2007].

The dietary supplements used for body mass reduction contain mostly chromium and zinc. Chromium is an essential trace element needed for maintenance of normal carbohydrate metabolism. Chromium trichloride has been given as a chromium supplement in total parenteral nutrition. Over the past decades, chromium supplementation has been established to be beneficial in individuals with metabolic syndrome, impaired glucose tolerance or type 2 diabetes. Increased lean body mass and decreased total body fat have been attributed to trivalent chromium and chromium compounds that had been used to enhance weight loss. However, the more recently reported studies, suggest that patient selection may be an important factor in determining clinical response to chromium [Wang & Cefalu, 2010].

Zinc is an essential trace mineral that is a component of over 200 enzymes, and have a function of enzymes activator [Expert Group…2003; Martindale, 2007]. Zinc is necessary for cell division, synthesis and degradation of carbohydrates, lipids and proteins. Zinc salts are readily absorbed in the upper small intestine and zinc is stored in the liver, pancreas, kidney, bones, voluntary muscles, parts of the eyes, prostate gland, sperm, skin, hair, and fingernails. However, because of the small intestine only absorbs what is currently needed, it is important that zinc is constantly replaced.

Other elements also have a role in the metabolic process, such as: cobalt (an integral component of Vitamin B12 (cyanocobalamin)), copper (transports oxygen through the body, and influences the metabolism of lipids), manganese (bone development and maintenance of strong bones, utilisation of thiamine, support in the activation of enzymes that are necessary for the body's proper use of biotin, B1 and vitamin C) and strontium (behaves similarly to calcium, although it is not homeostatically controlled, *i.e.*, the body does not actively regulate levels within the cells) [WHO, 1996].

The health risk caused by micro- and macroelements consumed with herbs and their infusions is strongly determined by the form of the element involved [Blicharska *et al*., 2007; Leśniewicz *et al.*, 2006; Łozak *et al*., 2002].

In risk assessment, oral exposures are typically stated in terms of the external dose or intake. For this reason it is important to validate appropriate analytical procedure to control the labelled level of added elements (Cr and Zn) and also to determine the content of other elements in medicinal products and in herbal teas infusions.

The aim of this research was, therefore, to validate a procedure for trace element determination based on micro-wave digestion and inductively-coupled plasma mass spectrometry (ICP-MS) method. The validated method was used for the determination of selected elements in herbal products and herbal tea infusions.

MATERIAL AND METHODS

Instrumentation

All ICP-MS measurements were carried out with an ICP mass spectrometer Thermo Electron X Series II (Thermo Electron Corporation, USA). The plant material was ground with the use of a vibration mill Testchem - S (Testchem, Pszów, Poland) made of corundum. Sample decomposition was performed in a microwave decomposition unit UniClever (Plazmatronika-Service, Wroclaw, Poland).

Standards and reagents

Basic stock solutions containing 1.0 mg/mL (Merck, Darmstadt, Germany) of elements (As, Cd, Co, Cr, Cu, Mn, Pb, Sr and Zn) were used for the preparation of a diluted standard solution. Digestion was done using concentrated nitric acid for ICP-MS (Merck). The indium and caesium stock solution containing 1.0 mg/mL was obtained from Merck. Distilled deionised water (Nanopure Deionization System, Barnstead, Boston, MA, USA) was used for the preparation of all solutions. Argon of 99.995% purity was supplied by BOC GAZY (Warsaw, Poland).

Samples and sample preparation

The method's accuracy was validated using the following certified reference materials (CRM): Tea Leaves (INCT-TL-1), Mixed Polish Herbs (INCT-MPH-2) [Dybczyński *et al.*, 2004] and Tea (NCS ZC 73014, China National Analysis Center for Iron and Steel, Beijing, China).

Samples of: (1) Slim Figura 1 Burning (lot S-63-L, content: pu-erh tea, mate leaf, guarana seed, chamomile flower, peppermint leaf, *Garcinia cambogia* fruit extract, fennel and aniseed), daily dose: 3 bags for the tea preparation; (2) Slim Figura 2 Cleaning (lot S-21-L, content: red-sorrel flower, green tea, dandelion root, nettle leaf, verbenae herba, guarana seed, licorice root, chicory root), daily dose: 3 bags for the tea preparation; (3) Slim Figura 3 Stabilisation (lot S-14-l, content: mate leaf, apple, licorice root, guarana seed, ginseng root, L-carnitine, daily dose: 3 bags for the tea preparation; (4) Figurella capsules (lot 4168, content: green tea extract, birch leaf, green mate, coleus forskohlli, 4–5 capsules daily; (5) Chrom tablets (lot 25.04.2006, con-

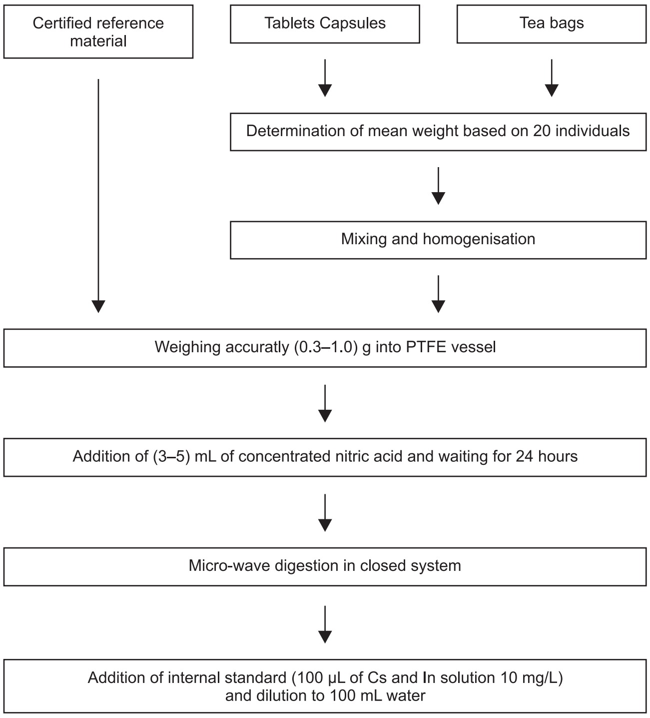

FIGURE 1. Solid samples preparation procedure before the ICP-MS determination.

tent: 30 μg chromium (as chromium chloride), 9 mg zinc (as zinc gluconate), green tea extract and vitamin B6, 1 tablet daily; and (6) Bio-Chrom tablets (lot 0600787, content: 50 μg of chromium produced by yeast, 1 tablet daily, were analysed in the study.

The method of solid sample preparation prior to ICP-MS determination is presented in Figure 1. For preparation of the tea infusion 100 mL of boiling water were poured onto a tea bag in a glass beaker and the beaker was then covered. After 10 min the bag was removed and, after cooling down to room temperature, the solution was transferred into a 100 mL volumetric flask. After addition of internal standard the samples were diluted with water to a final volume of 100 mL. The internal standard of In was used to eliminate interferences in determination of As, Co, Cr, Cu, Mn, Sr and Zn while the Cs internal standard was used to correct Cd and Pb results.

Determination of total content of elements

The ICP-MS measurement were performed using the following parameters: R.f. power 1380 W, background line <0.5 counts/s, Ar flow: plasma: 12.5–12.6 L/min; support: 0.78–0.79 L/min, nebulizer: 0.81–0.84 L/min, proportion of double charged ions $^{137}Ba^{+2}/^{137}Ba$ less than 3.0%, proportion of oxide ions $^{156}CeO/^{140}Ce$ less than 2.0%; $^{115}In/^{220}Bkg$ >800 000; acquisition time for 3 replicates 24 s.

RESULTS AND DISCUSSION

Before the procedure for element determination in different slimming products by ICP-MS was used, a validation of some parameters was done (calibration curve, linearity range, accuracy, precision, detection and determination limit). For quality assurance, the Standard Reference Material, Tea (NCS ZC 73014) was used (Table 1). To confirm measurement accuracy use was made of three CRMs: Tea Leaves (INCT-TL-1), Mixed Polish Herbs (INCT-MPH-2) and Tea (NCS ZC 73014). The results obtained (Table 2) demonstrate that the range of accuracy was between 94% and 100% for As, 100% and 106% for Cd, 93% and 104% for Co, 94% and 98% for Cr, 98% and 102% for Cu, 100% and 106% for Mn, 94% and 111% for Pb, 90% and 104% for Sr, 100% and 106% for Zn. A good consistency between the determined and certified values for all elements indicates that the described procedure can be used for elements determination in plant materials. Additionally, to verify the digestion procedure and measurement accuracy of tablet and capsule samples, the recovery analysis was carried out by adding the standard. The recovery analysis was conducted for four elements (Cd, Cr, Pb, Zn). Contents of Cr and Zn were labelled by the producer. Cd and Pb were limited by the EC. The range of recovery was between 97% and 105% for Cr, 87% and 106% for Zn, 101% and 103% for Cd, 87% and 104% for Pb.

In the Chrom and Bio-Chrom products the labelled value for chromium was 30 and 50 μg per tablet, respectively. Concentrations of chromium found by ICP-MS measurements in both samples (Table 3) do not demonstrate significantly different values. Also the concentration of Zn found in Chrom tablets is very close to the labelled value of 9 mg. Comparing to the AI values of 25 and 35 μg/day for adult women and men, the daily intake values of Cr represent 126% and 90%

TABLE 1. Validation parameters for element determination in CRM Tea (NCS ZC 73014).

Element	Range (μg/L)	Linear equation	Correlation coefficient	Precision (n=6) (RSD %)	LOD (ng/L)	LOQ (ng/L)
^{52}Cr	0.5–10.0	Y=18738X+2660	0.9999	0.69	11	34
^{55}Mn	0.5–20.0	Y=30957X+1746	0.9999	0.73	17	50
^{59}Co	0.5–6.0	Y=20823X+295	0.9999	1.27	2	7
^{65}Cu	0.5–10.0	Y=5190X+2138	0.9997	0.50	57	173
^{66}Zn	1.0–15.0	Y=7410X+3990	1.0000	0.34	69	209
^{75}As	0.5–2.5	Y=3151X–2	0.9993	1.20	4	13
^{88}Sr	0.5–10.0	Y=30722X+2573	0.9999	0.50	7	21
^{111}Cd	0.1–2.5	Y=10514X+82	0.9999	0.69	2	5
^{208}Pb	2.0–20.0	Y=30139X+76275	0.9996	0.84	198	599

TABLE 2. Element determination in CRMs by the applied procedure (n (digestion) = 4, m (measurement from each digestion) = 3).

Element	As	Cd	Co	Cr	Cu	Mn	Pb	Sr	Zn
INCT-TL-1									
Certified value	(ng/g) 85–131	(ng/g) 26.2–34.2	(ng/g) 345–429	(mg/kg) 1.69–2.13	(mg/kg) 18.9–21.9	(%) 0.141–0.168	(mg/kg) 1.54–2.02	(mg/kg) 19.1–22.5	(mg/kg) 32.0–37.4
Determined value	100±7	32.0±0.5	367±18	1.80±0.08	20.6 ±0.6	0.166±0.002	1.68±0.12	21.4±0.3	36.5±1.0
RSD (%)	2.50	0.86	2.56	2.63	1.55	0.55	3.90	0.52	0.89
INCT-MPH-2									
Certified value	(ng/g) 168–214	(ng/g) 184–214	(ng/g) 185–235	(mg/kg) 1.56–1.82	(mg/kg) 7.24–8.30	(mg/kg) 179–203	(mg/kg) 1.93–2.39	(mg/kg) 34.9–40.3	(mg/kg) 31.4–35.6
Determined value	183±8	200±3	196±11	1.65±0.03	7.92±0.03	199±1	2.24±0.11	39.3±0.3	33.4±0.1
RSD (%)	3.84	1.44	3.93	1.83	0.36	0.26	4.36	0.63	0.30
NCS ZC 73014									
Certified value	(mg/kg) 0.08–0.10	(ng/g) 58–66	(mg/kg) 0.20–0.24	(mg/kg) 0.35–0.55	(mg/kg) 17.9–19.3	(mg/kg) 480–520	(mg/kg) 1.3–1.7	(mg/kg) 7.9–10.3	(mg/kg) 49–53
Determined value	0.09±0.01	62±7	0.23±0.01	0.43±0.02	18.3±0.2	501±5	1.66±0.04	8.2±0.3	51±1
RSD (%)	0	5.37	1.90	2.85	0.47	0.51	0.28	1.82	0.97

TABLE 3. Element content (in μg/tablet and μg/capsule) in Chrom (mean tablet weight: 0.250 g), Bio-Chrom (mean tablet weight: 0.460 g), Figurella (mean capsule content: 0.415 g) and daily intake in compliance with a daily dose indicated on the product's label; determined by ICP-MS (n = 4).

Element	Chrom		Bio-Chrom		Figurella		
	Content (μg), equivalent to daily intake	RSD (%)	Content (μg), equivalent to daily intake	RSD (%)	Content (μg)	RSD (%)	Daily intake (μg)
As	0.012±0.003	12.0	0.014±0.002	8.75	0.042±0.002	2.92	0.21
Cd	0.106±0.001	0.67	0.030±0.002	4.97	0.019±0.001	2.25	0.095
Co	0.010±0.001	4.76	0.278±0.004	0.82	0.047±0.002	2.13	0.235
Cr	31.4±0.1 (labeled with 30 μg)	0.26	47.7±0.5 (labeled with 50 μg)	0.54	0.329±0.015	2.44	1.645
Cu	0.316±0.015	2.66	1.280±0.033	1.41	2.18±0.01	0.29	10.9
Mn	0.844±0.034	2.18	1.12±0.01	0.53	133±3	1.24	665
Pb	0.294±0.033	6.14	0.372±0.037	5.35	0.042±0.010	13.6	0.21
Sr	0.052±0.009	9.12	2.14±0.01	0.34	1.68±0.02	0.51	8.4
Zn (content mg)	9.17±0.45 (labeled with 9 μg)	2.65	23.84±0.29	0.66	15.4±0.5	1.90	77

for Chrom tablets, as well as 191% and 136% for Bio-Chrom tablets, respectively. The daily intake of Zn in Chrom tablets represents 115% RDA value for adult women (which means 8 mg/day) and 83% RDA value for adult men (which means 11 mg/day). Figurella is a product based on plant extracts and has no added chromium. The concentration of Cr was 0.329 μg in one capsule, which corresponds to 1.645 μg Cr in a daily dose. It means 7% and 5% of AI values for women and men, respectively. A significantly higher content of Mn was determined in Figurella (133 μg/capsule) in comparison to Bio-Chrom (1.12 μg/tablet) and Chrom (0.844 μg/tablet) products. The daily intake of Mn with prescribed Figurella dosage was 37% and 29% of the AI values of 1800 and 2300 μg/day for adult women and adult men, respectively.

The concentrations of As, Co, Cu, Mn and Zn in samples of System Slim Figura 1 Burning, System Slim Figura 2 Cleaning and System Slim Figura 3 Stabilisation (Figure 2) demonstrate that there are no significant differences in elements content between all the plant materials including the CRM Tea. Out of all determined microelements, the highest concentration was found for Mn, namely 741.1, 277.1 and 614.3 μg/g in Slim Figura 1, Slim Figura 2 and Slim Figura 3, respectively. The daily Mn intake from infusions obtained from the examined products represented 74.2% and 58%, 53.3% and 41.7%, 126.4% and 98.9% of the AI values for adult women and men, respectively. The lowest contents were recorded for As, Cd and Pb. The daily intake of these toxic elements was at a significantly lower level, ac-

TABLE 4. Element content (μg/g) in Slim Figura products and daily intake with infusion (μg/daily dose); determined by ICP-MS (n = 4).

Element	Slim Figura 1			Slim Figura 2			Slim Figura 3		
	Content (μg/g)	RSD (%)	Daily intake with infusion (μg/daily dose)	Content (μg/g)	RSD (%)	Daily intake with infusion (μg/daily dose)	Content (μg/g)	RSD (%)	Daily intake with infusion (μg/daily dose)
As	0.265±0.005	1.21	0.195	0.144±0.021	7.68	0.165	0.078±0.005	3.72	0.234
Cd	0.065±0.003	3.04	0.087	0.005±0.001	11.78	0.024	0.137±0.005	2.10	0.165
Co	0.349±0.034	5.33	0.585	0.335±0.022	3.55	0.879	0.085±0.012	7.27	0.189
Cr	1.325±0.055	2.30	1.461	0.648±0.029	2.47	1.197	0.404±0.003	0.45	1.857
Cu	15.36±0.11	1.22	14.00	8.700±0.040	0.27	11.66	7.404±0.355	2.61	25.41
Mn	741.9±14.0	1.04	1335	277.1±0.9	3.81	959	614.3±32.4	2.86	2275
Sr	25.11±0.17	0.39	24.51	65.83±0.39	0.31	126	44.73±0.10	1.18	29.15
Zn	50.85±3.06	3.29	80.22	27.23±0.99	1.99	64.17	30.44±1.61	2.87	55.38
Pb	0.169±0.014	4.71	*	0.067±0.026	21.20	*	0.359±0.069	10.33	*

* daily intake with infusion below the limit of determination (0.599 μg/L).

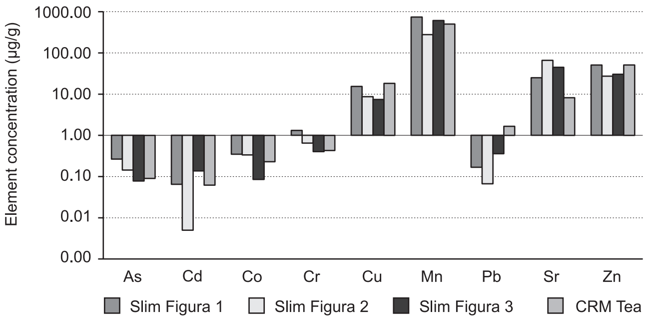

FIGURE 2. Comparison of element concentration pattern for different herbal products.

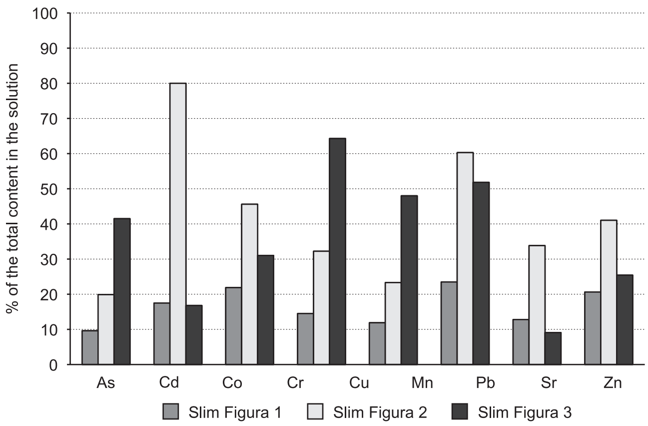

FIGURE 3. Extraction efficiency of determined elements from herbal teas.

cording to PTWI (Provisional Tolerable Weekly Intake) of arsenic (25 μg/kg BW/week), cadmium (7 μg/kg BW/week) and lead (25 μg/kg BW/week) [Gawęcki, 2010].

To estimate the content of elements extracted by hot water from the tea bags (Figure 3) some experiments were performed under different conditions. Extending the extraction time and keeping the extraction temperature constant at 100°C has no significant influence on elements concentration in the infusion. The highest extraction level of 80% was stated for Cd in Slim Figura 2.The extraction of over 50% was received in Slim Figura 2 and Slim Figura 3 for Cr and Mn. The lowest level of extraction, *i.e.* below 10%, was obtained in the case of As and Sr in Slim Figura 1 and Slim Figura 3. The extraction rate of lead was low, and in all infusions lead concentration in the solution was below the limit of quantification (0.599 μg/L) (see Table 4).

CONCLUSIONS

The data presented demonstrate that it is possible to use ICP-MS after microwave digestion to check the labelled values of some elements in dietary supplements. It is also possible to determine other elements important for risk assessment or health status. In all analysed samples, the concentrations of cadmium and lead were below the EC maximum level for Cd and Pb in dietary supplements.

The results are only applying to the products, that were tested in this study. This research can be a contribution to the further study on dietary supplements used for body mass reduction.

In the case of dietary supplements with the addition of chromium and zinc, due to the fact that the added amounts are close to the recommended daily intake, especially for chromium, it is important that the label should include this information.

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