Review

Investigation on Presence & Determination of Metal Contaminants in Dietary Supplements

Mehri Aliasgharpour1*

1. Member of Biochemistry Laboratory Faculty, Reference Health Laboratory, Iran Ministry of Health & Medical Education, Tehran, Iran.

***Correspondence Author**: **Mehri Aliasgharpour**. Member of Biochemistry Laboratory Faculty, Reference Health Laboratory, Iran Ministry of Health & Medical Education, Tehran, Iran. Email: mehri9@gmail.com. ORCID: https://orcid.org/0000-0003-4906-2715.

Abstract

Introduction: Dietary supplements (DS) are preparations intended to deliver nutrients that may not be consumed in sufficient quantities in the diet. They improve health and are popular in different populations and age groups. Nevertheless, this popularity and most of the time using them without health professional advice expose consumers to the ingestion of different harmful contaminants that may lead to deleterious effects on human health.

Methods: A comprehensive literature search was performed during years 1994-2020. Many medical and scientific literatures on the authors opinion regarding presence of metal contaminants in DS and the analytical methods were collected.

Results: In different categories of DS metal contamination might occur as a consequence of a single factor or as a combination of sources. For determination purposes many analytical techniques have been developed. However, selection of a technique depends on the elements, concentration in the digested sample, detection limits, interference, accuracy, precision, linear range, and etc.

Conclusion: Various authors emphasized on applying proper quality control in different steps of dietary supplements production and quality assurance of all manufacturing phases to ensures that packaging materials and final products conform to the established criteria's of the country. It is hoped besides proper quality control and use of reference materials as a critical step , the knowledge of consumers toward the use of DS be increased by holding health care communication programs and these products consumed under medical advice.

Keywords: Dietary supplements, Contaminants, Accuracy, Precision, Quality Assurance, Reference Material.

Submitted: 11 April 2021, Revised: 2 May 2021, Accepted: 29 May 2021

Introduction

The idea behind food or dietary supplements (DS), are preparations intended to deliver nutrients that may not be consumed in sufficient quantities in the diet. They can be vitamins, minerals, amino acids, fatty acids, and other substances delivered in the form of pills, tablets, capsules, liquid, and etc (1). They are prepared through laboratory synthesis or from natural products including different

[DOR: 20.1001.1.23222913.2021.10.2.2.8]

parts of plants and fish oil. They aren't intended to substitute for a balanced diet. However, they improve health and wellbeing, as well as prevent and control the age-associated disease occurrences (1-3). Based on recent years' surveys results, it was estimated that more than half of the adults in the USA (4) and European countries(5) use DS. The use of these products is also particularly prevalent among elderly (6-11). This population is especially vulnerable to micronutrient deficiency due to physiological changes in aging, to the use of chronic medication therapy, or both (12). Furthermore, the use of DS is more common in women (7-10) , highly educated people (8-10) ,those who are following a favorable lifestyle (6,8-10) ,healthy individuals(13-14) and different patients' groups (15-16). Nevertheless, this popularity and most of the time using them without health professional advice over long periods of time, and even sometimes being over dosed, expose consumers to the ingestion of different harmful contaminants along with (17-19). Mycotoxins, heavy metals, pesticide residues, and other environmental contaminants have been often detected and quantified in DS (17-19) . Studies indicated that transition metals act as catalysts in the oxidative reactions of biological macromolecules therefore, the toxicities associated with these metals might be due to oxidative tissue damage. Redox-active metals, such as iron, copper and chromium, undergo redox cycling whereas redox-inactive metals, such as lead, cadmium, mercury and others deplete cells major antioxidants (18) particularly thiol-containing antioxidants and enzymes. Either redox-active or redox-inactive metals may cause an increase in production of reactive oxygen species (ROS) such as hydroxyl radical (HO.), superoxide radical (O2.-) or hydrogen peroxide (H_2O_2). Enhanced generation of ROS can overwhelm cells intrinsic antioxidant defenses, and result in a condition known as "oxidative stress". Cells under oxidative stress display various dysfunctions due to lesions caused by ROS to lipids, proteins and DNA. Consequently, it is suggested that metal-induced oxidative stress in cells can be partially responsible for the toxic effects of heavy metals (18). It has been shown that the use of DS does not contribute significantly to the total exposure to harmful metal contaminants (20). However, prolonged and/or combined exposure to the contaminants from DS may lead to deleterious effects on human health. This issue has been addresses by different authorities in the recent years (21-24).

Methods

The present paper reviewed different authors opinion on the presence of metal contaminants in samples of DS and the analytical methods used for their analysis. For this purpose a comprehensive medical and scientific literature search was performed during years 1994-2020 and relevant papers were collected.

Results

1- Presence of metal contaminants in different dietary supplements

In different categories of DS metal contamination might occur as a consequence of a single factor or as a combination of sources. According to Smichowski P et al (25) for plant based supplements, the chemical composition of the soil, the characteristics of plants, and its growing conditions as well as other aspects related to lack of purity, extraction techniques, and formulation/manufacturing, transport, and storage conditions can be responsible for the contamination and DS may contain a wide variety of chemical elements. Most of these factors can also contribute to metal contamination observed in other types of supplements. Some research articles provided analytical data regarding single metals/metalloids while others reported the concentrations of multiple metals ; including not only toxic but also essential elements (26-31). Metals such as aluminum (Al), cobalt(Co), chromium(Cr), copper(Cu), iron(Fe), manganese(Mn), nickel (Ni) and zinc (Zn) are essential plant nutrients; however, they may become toxic at higher concentrations and represent a health hazard for humans (26). From toxicological concern common toxic elements; lead(Pb), mercury(Hg), arsenic(As), and cadmium(Cd) are particularly worrying in view of their presence in DS. Korfali et al (27) in Lebanon has reported that in analyzed DS samples concentration of Cr, Hg, and Pb were below allowable limits and daily exposure. Whereas, 30% of analyzed samples had levels of Cd above allowable levels. Similarly 62% of the samples had levels of As above allowable limits. In other case, Dolan et al (28) has reported that the concentrations of As and Cd measured were considered below the tolerable limits. The same study also found that in 11 products estimated exposures of Pb exceeded the provisional tolerable intake of Pb defined for sensitive populations (e.g. children and women of childbearing age, especially if pregnant). Moreover, another study reported that the most abundant elements in dietary supplements were Cu and Zn , followed by Pb , Cd , and Hg . The estimated daily intakes of metals were below those recommended by WHO and the Institute of Medicine showing that little risk from heavy metals is associated with the consumption of the dietary supplements analyzed. However, some products presented more than 10% of the tolerable daily intake of Pb(29-30). In 30 widely used vitamins and herbal preparations, several analyzed formulations had metal levels above the maximum allowable limits (Pb: one honey-based product and one medicinal herb-based product; Cr: one product containing vitamins; Ni: two products containing vitamins and one product of animal origin) (31). In regard to calcium supplements, Whiting (32) has reported that while no evidence for in vivo toxicity has emerged, chronic use of these supplements may constitute unnecessary metal exposure. In another study, Ni and Pb were present in 10.1% (17/168) and 6.5% (11/168) of DS, at a mean ± SD content of 0.06 ± 0.01 and 0.07 ± 0.02 mg/single unit dose, respectively. In these cases, daily use of a single unit dose by a 70 kg adult would represent 30.6% of tolerable weekly intake (TWI) for Ni and 28% of provisional tolerable weekly intake (PTWI) for Pb. All DS that contained detectable levels of Pb had exceeded a maximum allowance level (3.0 mg kg-1) set by the European Commission with two products exceeding it by as much as 11.1-fold and 16.9-fold (30).

2- Analytical methods employed for dietary supplements metal contaminants analysis

Many analytical techniques have been developed for the determination of metal toxicological concentrations in DS. The selection of a technique depends on the element/elements, number of them to determine, concentration in the digested sample, detection limits, interference (spectral & matrix), accuracy and precision, linear range, skill level, instrument cost, and operating and maintenance cost of the instrument (25). The instrumental analytical techniques that have been employed for this purpose are ion–exchange chromatography (IC), flame atomic absorption spectrometry (FAAS), electrothermal atomic absorption spectrometry (ETAAS), atomic fluorescence spectrometry (AFS), X–ray fluorescence (XRF), and inductively coupled plasma–mass spectrometry (ICP–MS). FAAS has good accuracy and an adequate precision (0.1–1%) for minor and major elements determination. In spite of this, FAAS presents the disadvantage of single element operation capability. ETAAS is an important instrument for the accurate determination of trace metal content in DS. This technique is especially useful when a low mass or low volumes are available, owing to its low detection limit (<5 mg L−1), precision (0.5–5%), accuracy and selectivity. It is a very

[DOR: 20.1001.1.23222913.2021.10.2.2.8]

sensitive technique and for this reason requires very clean reagents to avoid blank problems (25). In all methods to avoid contamination from reagents, vessels, etc usually supplements are digested using acid mixtures, a key step in the analysis. However, this general procedure is time consuming and can increase the loss of volatile elements. To avoid/minimize sample preparation and dissolution, other authors adopted the alternative of coupling laser ablation (LA) to ICP–MS (LA–ICP–MS). Briefly, LA introduces solid samples, as ablated particles and vapor, to an ICP–MS instrument where signal intensities from isotopes of elements can be measured and quantified. Furthermore, the variations in the matrix composition of different supplements are important in choosing an analytical technique(25). In the past decade, EDXRF technique (Energy dispersive XRF, using X-ray tubes as an excitation source) have gained widespread strength for the samples that have toxic metal concentrations greater than 10 ppm(25). Better detection limits and more elements would be obtained using X-ray tubes as excitation sources (33).

Discussion &Conclusion

Food or dietary supplements are products that are used because of imbalances in diets. They are prepared through laboratory synthesis or from natural products including different part of plants and fish oil(1-3). They are widely used in many populations and in different age categories(1,29). Regardless of self administration of dietary supplements, their use is widespread not only in healthy people (13-14) but also among different patients' groups (15-16). It has also been indicated that consumers especially those who take significant amounts of DS may ingest high doses of different contaminants including toxic metals, especially when they are consumed over long periods of time (25). Even sometimes essential (34) and probably essential metals (35) can be regarded as metal contaminants in some types of DS (26). Many analytical techniques have been developed for their determination purposes and it is demonstrated that relatively low concentrations of metal contents could be accurately measured in complex DS matrices (25).

Various authors (18,25,36) emphasized on applying proper quality control in different steps of dietary supplements production and quality assurance of all manufacturing phases to ensures that packaging materials and final products conform to the established criteria's of the country. It is hoped besides proper quality control and use of reference materials as a critical step , the knowledge of consumers toward the use of DS be increased by holding health care communication programs and these products consumed under medical advice.

Conflict of Interest

None.

Abbreviations list

AFS-Atomic Fluorescence Spectrometry

DS- Dietary Supplements

EDXRF- Energy Dispersive X-ray Fluorescence

ETAAS-Electro Thermal Atomic Absorption Spectrometry

FAAS- Flame Atomic Absorption Spectrometry

IC-Ion-exchange Chromatography

ICP-MS- Inductively Coupled Plasma Mass Spectrometry

LA-ICP-MS- Laser Ablation Inductively Coupled Plasma Mass Spectrometry

ROS-Reactive Oxygen Species

XRF-X-ray Fluorescence

References

[DOR: 20.1001.1.23222913.2021.10.2.2.8]

1- Camire ME . Kantor MA. Dietary supplements: nutritional and legal considerations,
Food Technol. 1999; 53 : 87–96.

2-Pokladnikova J. Selke-Krulichova I. The use of complementary and alternative medicine by the general population in the Czech Republic: a follow-up study. Complement Med Res. 2018;25(3):159–166.

3- Frey A. Hoffmann I. Heuer T. Characterization of vitamin and mineral supplement users differentiated according to their motives for using supplements: results of the German National Nutrition Monitoring (NEMONIT). Public Health Nutr. 2017;20 (12):2173–2182.

4- Kantor ED. Rehm CD. Du . et al. Trends in dietary supplement use among US adults from 1999–2012. JAMA. 2016; 316 (14):1464–1474.

5- Garcia-Alvarez A. Egan B. de Klein S. et al. Usage of plant food supplements across six European countries: findings from the Plant LIBRA consumer survey. PLoS One. 2014;9(3):e92265.

6- Li K. Kaaks R. Linseisen J.et al. Consistency of vitamin and/or mineral supplement use and demographic, lifestyle and health-status predictors: findings from the European Prospective Investigation into Cancer and Nutrition (EPIC)-Heidelberg cohort. Br J Nutr. 2010;104(7):1058–1064.

7- Bruce N. Amesa. Prolonging healthy aging: Longevity vitamins and proteins. PNAS 115(43).2018

8- Schwab S. Heier M. Schneider A. et al. The use of dietary supplements among older persons in Southern Germany – results from the KORA-age study. J Nutr Health Aging. 2014;18(5):510–519.

9- Kofoed CLF. Christensen J. Dragsted LO. et al. Determinants of dietary supplement use – healthy individuals use dietary supplements. Br J Nutr. 2015; 113(12):1993–2000.

10- Rovira MA. Grau M. Casta~ner O.et al. Dietary supplement use and health-related behaviors in a Mediterranean population. J Nutr Educ Behav. 2013; 45(5):386–391.

11- Peklar J. Henman MC. Richardson K. et al. Food supplement use in the community dwelling population
aged 50 and over in the Republic of Ireland. Medicine. 2013; 21(4):333–341.

12-Marra MV. Bailey RL. Position of the Academy of Nutrition and Dietetics: micronutrient supplementation. J Acad Nutr Diet. 2018; 118 (11):2162–2173.

13-Sadowska J. Bruszkowska M. Estimation of dietary supplements intake in a selected group of women over 50 and the risk assessment of interactions between the ingredients of dietary supplements and drugs. Rocz Panstw Zakl Hig. 2016; 67(4):391–397.

14- Pouchieu C. Andreeva VA. P_eneau S. et al. Sociodemographic, lifestyle and dietary correlates of dietary supplement use in a large sample of French adults: results from the NutriNet-Sant e cohort study. Br J Nutr. 2013;110 (8):1480–1491

15-Pouchieu C. Fassier P. Druesne-Pecollo N. et al. Dietary supplement use among cancer survivors of the NutriNet-Sant_e cohort study. Br J Nutr. 2015; 113(8):1319–1329.

16- Heller T. M€uller N. Kloos C. et al. Self medication and use of dietary supplements in adult patients with endocrine and metabolic disorders. Exp Clin Endocrinol Diabetes. 2012; 120(9):540–546.

17- da Silva EO. Bracarense APFL. Oswald IP. Mycotoxins and oxidative stress: where are we? World MycotoxinJ. 2018; 11(1):113–134.

[DOR: 20.1001.1.23222913.2021.10.2.2.8]

18- Ercal N. Gurer-Orhan H. Aykin-Burns N. Toxic metals and oxidative stress part I: mechanisms involved in metal-induced oxidative damage. Curr Top Medicinal Chem. 2001;1(6):529–539.

19- Abdollahi M. Ranjbar A. Shadnia S. et al. Pesticides and oxidative stress: a review. Med Sci Monit. 2004; 10(6):RA141–RA147.

20- Gil F. Hern_andez AF. Mart_ın-Domingo MC. Toxic contamination of nutraceuticals and food ingredients. In: Nutraceuticals. New York: Elsevier; 2016. p. 825–837.

21- Hedegaard RV. Rokkjær I. Sloth JJ. Total and inorganic arsenic in dietary supplements based on herbs, other botanicals and algae–a possible contributor to inorganic arsenic exposure. Anal Bioanal Chem. 2013; 405(13):4429–4435.

22- EFSA. Guidance on Safety assessment of botanicals and botanical preparations intended for use as ingredients in food supplements. EFSA J. 2009; 7:1249.

23- Raman P. Patino LC. Nair MG. Evaluation of metal and microbial contamination in botanical supplements. J Agric Food Chem. 2004;52(26):7822–7827.

24- Knutsen HK. Alexander J. Barregård L. et al. Risks for human health related to the presence of pyrrolizidine alkaloids in honey, tea, herbal infusions and food supplements. EFSA J. 2017;15:4908.

25- Smichowski P. Londonio A. The role of analytical techniques in the determination of metals and metalloids in dietary supplements: a review. Microchem J. 2018;136:113–120.

26- Filipiak–Szok A. Kurzawa M. Szłyk E. Determination of toxic metals by ICP–MS in Asiatic and European medicinal plants and dietary supplements, 2015. J. Trace Elem. Med. Biol. 30 54–58.

27-Korfali SI. Tamer Hawi and Mohamad Mroueh. Evaluation of heavy metals content in dietary supplements in Lebanon. Chemistry Central Journal. 2013,7:10.

28- Dolan SP. Nortrup DA. Bolger PM. et al. Analysis of dietary supplements for arsenic, cadmium, mercury, and lead using inductively coupled plasma mass spectrometry. J Agric Food Chem. 2003;51(5):1307–1312.

29- Leticia Garcı´a-Rico. Johanna Leyva-Perez. Martin E. Jara-Marini. Content and daily intake of copper, zinc, lead, cadmium, and mercury from dietary supplements in Mexico. Food and Chemical Toxicology.2007; 45 : 1599–1605.

30- Poniedziałek B. Niedzielski P. Kozak L. et al. Monitoring of essential and toxic elements in multi ingredient food supplements produced in European Union. J Consum Prot Food Saf. 2018;13(1):41–48.

31-Tumir H. Bo_snir J. Vedrina-Dragojevic I. et al. Monitoring of metal and metalloid content in dietary supplements on the Croatian market. Food Control. 2010;21(6):885–889.

32-Whiting SJ. Safety of some calcium supplements questioned. Nutr Rev. 1994;52(3):95-7.

33- Palmer PT. Jacobs R. Baker PE. Ferguson K. et al. Use of Field-Portable XRF analyzers for rapid screening of toxic elements in FDA-regulated products. J Agric Food Chem. 2009; 57:2605–2613.

34- Aliasgharpour M. Trace elements in human nutrition (II) – An update. Int J Prev Med 2020;11:2.

35- Aliasgharpour M. From Epsom salt to a beneficial mineral ; Magnesium. Int J Med Invest 2019; 8(4): 1-8.

36- Dwyer JT. Coates PM. Smith MJ. Dietary supplements: regulatory challenges and research resources. Nutrients.2018; 10(1):41.