Review

Investigation on Presence & Determination of Metal Contaminants in Dietary Supplements

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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**.**

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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

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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),

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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

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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

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