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The role of analytical techniques in the determination of metals and metalloids in dietary supplements: A review

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ABSTRACT

This review is focused to cover the application of different analytical techniques for the determination of metals and metalloids in different categories of dietary supplements. Atomic spectrometric methods based on flame atomic absorption spectrometry, electrothermal atomic absorption spectrometry, atomic fluorescence spectrometry, X–ray fluorescence spectrometry and plasma–based techniques such as inductively coupled plasma optical emission spectrometry and inductively coupled plasma–mass spectrometry are reviewed because a considerable amount of research is presently performed in this field. Even when much less reported in the literature, the application of neutron activation analysis, isotope dilution mass spectrometry and hyphenated methodologies for speciation studies based on the use of separative techniques in combination with specific detectors are also discussed. This survey contains 46 references and covers mainly the literature published over the last fifteen years.

1. Introduction and general considerations

Dietary supplements (DS) are products that intend to supplement the diet, which contains vitamins, minerals, herbs, botanicals, biofortified yeasts, ayurvedic formulations, amino acids, or any combination of the above ingredients [1]. They are prepared through laboratory synthesis or from natural products including different part of plants and fish oil [2]. Dietary supplements can be found in the market in different forms such as gel, pills, caps, oils, capsules and tablets. We can say that DS are on a gray zone between drugs and nutrients.

The marketing and the current frantic pace are some of the reasons that have caused a significantly increase in DS consumption in the last 15 years, especially in countries with greater purchasing power. The consumers are attracted to these alternative products for a variety of reasons such as:

(i). to compensate the lack of nutrients/compensate the diet,
(ii). relatively low cost,
(iii). easy access,
(iv). supposed to be preventive of numerous diseases and disorders,
(v). supposed to be natural, safe, without adverse effects,
(vi). massive advertising campaigns,
(vii). considered as alternative medicines without side effects,
(viii). promise to be the elixir of youth, health and vitality.

Regrettably, many consumers have limited information on this topic and they are often not able to evaluate the health claims and possible health risks of these products. The situation is more worrying when they are consumed during extended periods of time without medical supervision or without proper control.

Medicinal plants products are very used as therapeutic medicines. In the same direction, the consumption of herbals supplements (HS) has expanded rapidly. According to Kowalski and Frankowski [3], it is estimated that 25% of the prescribed drugs are from plant origin with 121 active substances used in their formulation. They may content a single herb or a combination of herbs in an extract, powder, pill or tablet. The botanicals used in the manufacturer of these supplements use different parts of the plants from whole plant to fruits, roots, rhizomes, flowers, seeds, bark, stem and leaves. For this reason, these HS may contain a wide variety of chemical elements. Metals such as Al, Co, Cr, Cu, Fe, Mn, Ni and Zn are essential plant nutrients; however, they may become toxic at higher concentrations [4]. Contrary to chemically synthetic drugs, herbal medicines are classified as non–prescriptions and are not required to undergo strict approval procedures [5]. The Food and Drugs Administration (FDA) established in 2007 a rule to ensure the quality of HS and DS available to the public [6]. Respect to ayurvedic formulations, in USA they are regulated by the Dietary Supplements Health and Education Act but no proofs of safety are required [7]. In the

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European Union, ayurvedic medicines are market as DS, which are regulated under a specific legislation for traditional medicines [7,8].

Even when DS are, in many cases, assumed as beneficial for health and without side effects, many studies performed worldwide report the presence of heavy metals, bacteria, pesticides, etc. [9–13]. Respect to heavy metals, commercial supplements contains a variable type and amount of metals and metalloids that can be essential and non–essential elements. Some of them are introduced into the environment through industrial activities and vehicular traffic (especially those derived for plants). In addition, recognized toxic metals such as As, Cd, Ni, Pb, Sb can naturally occur in the environment, due to weathering, biological and volcanic activities.

In DS, pharmaceuticals and food products in general, especial attention should be paid to those that represent a health hazard such as As, Cd, Cr, Hg, Pb, etc. Metals and metalloids may be introduced in different ways, especially for botanical products, and depends on:

(i). natural or anthropogenic environmental contamination,
(ii). geochemical characteristics of the soil,
(iii). growing conditions of the plants,
(iv). ability of the plants to selectively accumulate specific elements,
(v). purity of the raw materials,
(vi). extraction process,
(vii). formulation,
(viii). manufacturing process,
(ix). transport,
(x). inappropriate storage.

The FDA published regulations hold supplements manufacturer or distributors for the content of the DS, which should only contain what is declared in the label and not any harmful or undesirable substances including pesticides and heavy metals [14]. This is a key point because researchers involved in the characterization of the elemental composition of these nutritionals know that, in general terms, they contain much more elements that those declared in the labels and studies documenting this fact have been reported [11,15].

Consumers, especially those that take significant amounts of DS, may ingest high doses, receiving in this way overloads of metals especially when DS are consumed over long periods of time. Unfortunately, national and international directives governing the regulation of these supplements, in terms of their safety and efficacy, are in flux [16]. These supplements should contain only what is declared on the label and should not contain any harmful or undesirable substance as toxic metals [17]. The question is: Is it true? Researchers involved in the elemental characterization of DS know that it is not true and that much more elements, even toxic elements, can be found that are not declared in the label [18].

This survey intends to provide information on the techniques used to investigate the elemental composition of DS and briefly discuss if declared concentrations in the labels agree with levels found. Due to the diversity of DS investigated and characterized in terms of metals and metalloids content, it is impracticable to cover all of these in this review. For this reason, the discussion is restricted to key components and the most used instrumental analytical techniques that have been employed, alone or hyphenated, that have played a crucial role in the analysis of DS. The research done in the 15 years in the field of DS analysis using ion–exchange chromatography (IC), flame atomic absorption spectrometry (FAAS), electrothermal atomic absorption spectrometry (ETAAS), atomic fluorescence spectrometry (AFS), X–ray fluorescence (XRF), neutron activation analysis and plasma–based techniques such as inductively coupled plasma optical emission spectrometry (ICP OES) and inductively coupled plasma–mass spectrometry (ICP–MS), is briefly described.

2. Sample preparation

In general terms, and according to the experience of the authors, the preparation of these samples for subsequent chemical analysis do not pose a significant difficulty. For this reason, only some lines have been included on this topic. Nevertheless, in analytical chemistry sample preparation is usually a key step affecting analytical results. In the case of DS analysis it is necessary to take into account the great variations in the matrix composition of different supplements including herbs, plants, oils, gelatin, proteins, fat, etc. Special attention should be paid to avoid contamination from reagents, vessels, mortar and pestle, etc.

The normal operation of atomic spectrometric and plasma–based techniques requires that samples be necessarily put in solution before being presented to the technique of choice for measurement. Most of these techniques use a nebulization system to introduce the sample. To this end, microwave (MW)–assisted digestion was mainly used to mineralize DS samples. The most used procedure for solid samples (e.g., tablets) is the trituration with mortar and pestle to reach a homogeneous sample. For capsules and liquid samples, they can be introduced directly into the polytetrafluoroethylene MW oven vessels. Other alternative is to empty the liquid content into the MW oven vessel.

Oxidizing acids with high degree of purity such as HNO_3, and non–oxidizing acids such as HCl and HF, as well as H_2O_2, have been used to digest these samples. Several possibilities of acids and mixtures of reagents have been reported: (i) HNO_3, (ii) HNO_3 + HCl, (iii) HNO_3 + HF, (iv) HNO_3 + H_2O_2. Nitric acid and H_2O_2 was the mixture most commonly used [6,7,11,17,18]. Nitric acid is an almost universal digestion reagent and it is intended to destroy organic compounds into H_2O and CO_2 and to oxidize metals. In addition, HNO_3 forms water–soluble salts with most elements and consequently precipitation not are expected. When ICP–MS is used for quantification, HNO_3 is recommended to digest the samples because H, N and O are present in the plasma [4,12,13]. Nitric acid can also be used together H_2O_2 and HCl to improve the performance of digestion. Hydrochloric acid is also employed for DS digestion because chlorides are in general terms soluble, excepting for Ag, Hg and Pb [3,14].

An alternative method such as cryogenic grinding was reported and employed to composite soft samples such as oil filled capsules and candy–like products such as gummies and jelly beans [19]. This methodology acts cooling or chilling a material and then reducing it into a small particle size.

3. The role of analytical techniques in dietary supplement analysis

Numerous analytical techniques and experimental approaches have been proposed in the last 15 years to identify and measure metals and metalloids aimed at obtaining reliable results and correct evaluations in the field of DS analysis. In this context, researchers are benefiting from developments of innovative analytical methodologies where atomic spectrometric and plasma–based techniques are important tools for element determination. The outstanding developments undergone by these techniques over the last years have marked a parallel and irreversible progress in the exploitation of such techniques from both the viewpoint of research activities, routine analysis and regulatory tasks.

The selection of a technique for DS analysis will depend on the element/elements, number of elements to determine, concentration in the digested sample, detection capability, interferences (spectral, matrix), accuracy and precision required, linear dynamic range, multielemental capability, possibility of isotopic analysis, skill level required, instrument cost, and operating and maintenance costs of the instrument.

The widespread use of atomic spectrometric and plasma–based techniques in the field of DS analysis is well–reflected by the number of papers, reports, books, and other scientific publications that have become available in recent years.

3.1. Atomic spectrometric techniques

Atomic spectrometric methods based on FAAS, ETAAS and in less extent AFS have been used to determine metals and metalloids in DS especially when the focus was put in the determination of specific elements of toxicological relevance.

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