

A review on Medication Heavy Metals and Current Assay Methods

Sidra Waheed, Jamal Kafaee¹

College of Medical Science, University of Hyderabad, India

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Abstract

Traditional medicine (TM) has been used since ages, during the past few decades there was a notable global increase in TM usage. According to the World Health Organization (WHO) around 70% of world population relies on traditional healing system for their basic health care needs. The broad use of TM has highlighted many issues subjected to the efficacy and safety of such products. Some TM products contain toxic materials such as heavy metals. Exposure to heavy metals such as arsenic (As), cadmium (Cd), lead (Pb), nickel (Ni), zinc (Zn) and iron (Fe) can cause adverse health effects and toxicity. This article explains, several possibilities for the presence of heavy metals in TM, the toxicity of some heavy metals and a number of reported clinical cases regarding to heavy metals toxicity due to the consumption of TM products from different parts of the world.

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1. Introduction

Traditional medicine is the earliest healthcare system known to humanity. Different plants/herbs and animal parts have been used since ages to treat various illness [1]. The use of TM has grown and evolved over centuries [2]. Currently TM is widely used in the developing countries as a prime health care system due to its affordability, accessibility and availability [3]. Meanwhile the consumption of TM has increased in some developed countries as well, for the reason that herbal medicines are originated from natural sources and thus they are more likely to be safe compared to the modern medicine which are made of synthetic substances [4]. As a result, there was a global vast growth in the popularity of traditional healing modalities, mainly herbal remedies during the later part of the twentieth century [5].

The rapid growing worldwide is evident by the estimated value of the global TM market which was about US\$ 60 billion annually in 2008². The global

wide diffusion of TM had highlighted the issues of safety, efficacy and quality control of such products to be an important concern from certain global health authorities such as the WHO and Food and Drug Administration (FDA) [6]. Herbal/TM must be used cautiously; some TM products may cause negative health impact and even toxicity due to many reasons such as the adulteration with conventional medicine and contamination with heavy metals and other toxic substances [7].

1.1 Heavy metals contamination in TM products

In general, heavy metals can be defined as elements with metallic properties and an atomic number higher than 20, they are natural components of the earth's crust and ubiquitous in trace concentrations [8]. It has been reported that some herbal products contain heavy metals [9]. The presence of heavy metals in herbal/TM products is attributed to several possibilities. The environmental factors are probably contributed in the contamination of such products. It includes the contamination of the

¹ Corresponding Author E-mail: j.kafaee.mika@hotmail.com

agricultural soils and irrigation water as a result of the industrial waste disposal, mining activities and the usage of certain types fertilizers [10].

Heavy metals may also introduce during the preparation of the raw materials for TM products which covers many steps such as cultivation, harvesting, collecting, cleaning and drying of the medicinal plants [11]. The other possibility is the accidental contamination during the manufacturing process such as grinding, mixing and the exposure to heavy metals from metal releasing equipment which might be used in different steps of the processing part [12]. The intentional addition of heavy metals during the preparation as part of the ingredients for a curative purpose constitutes another source of TM contamination with heavy metals [13]. Figure 1 shows a diagram of different sources of heavy metals contamination in TM products.

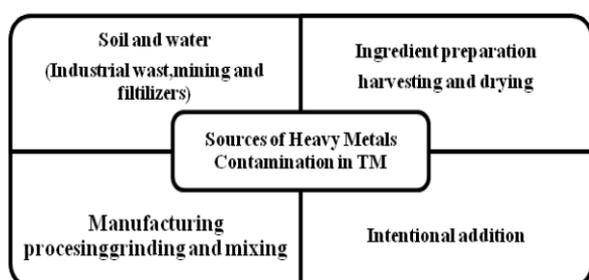


Figure 1. Diagram of different sources of heavy metals contamination in TM products

1.2 Toxicity of heavy metals

Arsenic (As), cadmium (Cd), lead (Pb), nickel (Ni), zinc (Zn) and iron (Fe) are often reported to be found in TM. Prolong exposure to heavy metals may cause adverse health effect and toxicity due to the capability of heavy metals to bioaccumulate and disrupt the functions of vital organs in the human body such as brain, kidneys and liver [14]. Some heavy metals are essential as trace amounts such as zinc and iron however, they are dangerous if present in a higher concentration [15]. This article aims to provide a summary of the obtained information regarding the toxicity and other negative health impacts due to the exposure to some heavy metals. In addition of revealing various clinical cases of heavy metal toxicity associated with the consumption of some TM products and to consider some of the reported studies on the subject of heavy metals detection in TM products which have been published in different parts of the world.

1.3 Arsenic (As)

Arsenic is a toxic heavy metal which may be present in some herbal products. It can penetrate in to the plant through the contaminated soil and water

using the same mechanism to gain the essential micronutrients [16].

Exposure to As causes acute and chronic adverse health effects, including cancer. Acute toxic effects include abdominal cramping, chronic arsenic toxicity is mostly manifested in weight loss and a capricious appetite [17]. The most significant consequence of chronic exposure to arsenic is the occurrence of cancers in various organs especially in the skin and lungs [18].

The detection of arsenic in herbal products has been reported in different parts of the world. A study in India reported the results of arsenic concentration in 10 batches of herbal preparation "Septiloc". Arsenic was found in five samples, with a concentration range of 0.28 - 0.05 mg/kg [19]. In Nigeria, a study was carried out to investigate the concentration of toxic metals including arsenic in twenty brands of herbal products. The concentration of As was found in the range of 0.301-1.108 µg/g [20]. In California, a screening study of 251 Chinese medicines collected from herbal retail stores was conducted. It was found that 14% of the samples contained an average concentration of 14.6 ppm of As [13]. Another study in Boston USA, for a total of seventy TM samples were collected from different shops. Six samples had a high concentration range of As 37-8130 µg/g [21].

Arsenic toxicity due to the consumption of TM products had been reported, in Taiwan, 17 patients had cutaneous lesions related to chronic arsenicism, among them 14 patients had a history of traditional Chinese medicine (TCM) intake. Squamous cell carcinomas were developed in 11 of the 17 [22]. Another case of As toxicity was reported on a five-year-old Italian boy in August 1995, with congenital bilateral retinoblastoma. He had been given an Indian healer prescribed ethnic remedies. Signs of toxicity were nausea, fatigue, progressive weakness of lower limbs, and leucopenia. It was found that arsenic concentration in the remedy was 184 mg/kg and in the patient's hair was 6.6 mg/kg [13]. Which provided the evidence of As toxicity.

1.4 Cadmium (Cd)

Cadmium is a non-essential element, soluble in the biological systems [23]. It is known for its high toxicity and similar to other heavy metals it has a tendency to bioaccumulate and disrupts the functions of vital organs in the human body [14].

Both acute and chronic exposure to cadmium has a negative impact for human health. Cadmium may cause high blood pressure and destruction of red blood cells. Cadmium metal ion in the body's metallo-enzyme can easily replace another metal ion due to the chemical similarities and competition for binding stage therefore, Cd²⁺ can replace Zn²⁺ which in some dehydrogenating enzymes, causes

cadmium toxicity [24]. Studies have provided fundamental evidence that long-term exposure to low levels of cadmium is associated with increasing the risk of cancer [25].

Cadmium has been detected in TM in a number of studies conducted in various parts of the world. In Nigeria, a detection study of Cd content in herbal drugs was reported that Cd concentration was found in the range of 16.438 - 29.796 mg/g [26]. In Pakistan Cd was detected in twenty-five branded herbal products using atomic absorption spectroscopy (AAS) and the results showed that the tested samples contained Cd in a concentration range of 1.9-45.2 µg/g [9].

1.5 Lead (Pb)

Lead is one of the heavy metals which have been recognized for its undesirable effects on different body organs. Prolonged exposure to Pb decreases the performance of the nervous system and lowers renal clearance [27]. Lead poisoning is considered one of the significant environmental health threats for children even at low levels of exposure. It is associated with impairment of childhood cognitive function [28]. A high lead level during pregnancy is directly related to several outcomes such as spontaneous abortion, low birth weight and impaired neurodevelopment [29]. Lead poisoning occur when the concentration reach between 100-140 µg/L [30-31]. According to the international Agency for Research on cancer (IARC) inorganic lead is carcinogenic to human.

Many clinical cases had been reported regarding lead poisoning due the consumption of different types of traditional medicine. A lead poisoning case was reported in Auckland New Zealand. A 51-year-old man with 2-weeks history of colicky abdominal pain and background history of type two diabetes had been taking Ayurvedic Jambrulin tablets. The whole blood lead level was 375.2 µg/L. The analysis of his Ayurvedic tablets showed that each one contained approximately 10 mg of lead [32]. Another case of lead poisoning had been reported in Bangalore for a 45-years-old man, he was admitted twice to the hospital due to vomiting and abdominal pain. The patient's history revealed that he had been consuming 12 different Ayurvedic medicines for stress relief for the past 4 years. The patient's blood lead level (BLL) was 1224 µg/L, which confirmed lead poisoning. Analysis of the 12 Ayurvedic products revealed that 75% of the products contained high levels of lead, arsenic and mercury in concentration higher than the daily permissible limits [33].

Many studies were performed regarding the detection of lead in TM in different parts of the world. In Karachi Pakistan, herbal medicine samples were collected from three different parts of the city (southern, eastern and western) for the

determination of eight heavy metals including lead (Pb). Lead concentrations were found in the range of 3.26-30.46 µg/g and 71.4% of the samples were beyond the permissible limit [34]. In China different batches of four types of natural herbal medicines manufactured by local pharmaceutical factories, were analyzed for lead content, the results indicate that all samples contain lead in concentration range of 0.125-4.79 µg/g [35]. In Malaysia a study was performed to determine the concentration of lead in 100 products in various pharmaceutical dosage forms of tongkat Ali hitam herbal preparation, the results showed that 8% of the samples contained lead in a range 10.64-20.72 µg/g and therefore Pb concentration were more than the permissible limit [36].

1.6 Nickel (Ni)

Exposure to Ni may result in a variety of pathological effects. Oral exposure to large doses of nickel mainly targets the cardiovascular system [37]. The common adverse health effect of nickel in humans is allergic skin reaction in those who are sensitive to nickel [38]. Most of the toxicity of nickel might be attributed to its interference with the physiological processes of zinc and calcium [39]. According to the International Agency for Research on Cancer (IARC) and the United States Department of Health and Human Services, nickel compounds have been classified as human carcinogens. Carcinogenic nickel compounds have been shown to induce different types of tumors in experimental animal systems [40]. A clinical case of Ni toxicity had been reported for a 2-years old child who accidentally ingested nickel sulfate crystals rough estimate of 570 mg/kg of Ni. After few hours of the ingestion the child had cardiac arrest and he died 8 hours after the exposure [41].

Nickel poisoning cases were reported for a group of workers were exposed to nickel in an estimated dose of 7.1-35.7 mg/kg. The exposure was through drinking of fountain water contained nickel sulfate, nickel chloride, and boric acid. All workers reported symptoms included abdominal cramps nausea, vomiting and diarrhea [40].

A number of studies had been reported for Ni detection in TM. In Pakistan two studies had been reported for Ni determination in TM products. The first study was aimed to detect the concentration of different heavy metals including Ni in a group of branded herbal products using flame atomic absorption spectroscopy (FAAS). Nickel was found in concentration range of 0.256.3 µg/g [9]. The second study was conducted to determine eight heavy metals including Ni in a group of selected herbal products available in the local market in various places of Karachi city using AAS. The results showed that Ni was found in the range of 0.48-76.97 µg/g [34].

1.7 Zinc (Zn)

Zinc is an essential trace element. It exists in all types of tissues of the body and takes part in vital roles for cell growth and other physiological activities. Despite its important, it can be dangerous if exist in high concentration. Excessive oral zinc exposure could lead to Zn accumulation in different organs in the human body and subsequently cause an adverse health effects. High dose of zinc ingestion have a direct effect to the gastrointestinal tract before it is dispersed through the body⁴². Zinc may have effect on serum cholesterol balance as it causes increase of the low density lipoprotein (LDL) cholesterol and a decrease in high-density lipoprotein (HDL) cholesterol [43].

Several studies had been reported for Zn detection in TM in different parts of the world. A study to find out the concentrations of zinc and other heavy metals in branded herbal products in Pakistan using FAAS. Zinc was found in concentration range 5.1-1071 µg/g [9]. Another study was conducted in Pakistan for the detection of heavy metals including Zn in selected TM products purchased from different places in Karachi. The results showed that Zn was found in the range of 83.74-433.76 µg/g [34].

A clinical case of gastrointestinal disturbances after the consumption of zinc sulfate was reported in England. The girl was given 440 mg zinc sulfate/day (2.6 mg zinc/kg/day) in capsules as a medically prescribed treatment for acne. After taking each capsule, she experienced epigastric discomfort like abdominal cramps and diarrhea. After one week she had an indicated signs of gastrointestinal bleeding and later was treated in the hospital [44].

1.8 Iron (Fe)

It is an essential micronutrient as it plays a critical role in major biochemical activities, such as oxygen transport and electron transfer [45]. There are about 3-5 grams of iron (45-55 mg/kg) in human body, about 60-70% is utilized within hemoglobin in circulating red blood cells [46]. Although iron is very important it can be hazardous when exist in high concentration. Ingesting excessive doses of iron causes irritation of the gastrointestinal mucosa which increases the gastric discomfort symptoms like nausea, vomiting and diarrhea. It may also cause severe damage to the mucosal cells which leads to bleeding in the stomach and perforation of the gutwall [47]. Excess of iron disrupts the redox balance of the cell resulting in generation of chronic oxidative stress, which organized the signaling networks related to malignant transformation [48]. In humans, high concentration of iron storage has been shown to increase the risk of cancers, including breast cancer [49]. The possibility for Fe accumulation in human body is higher in contrast

with other heavy metals, because iron intake from various sources such as dietary and supplements is very high. This could subsequently lead to many health complications such as severe necrotizing gastritis with vomiting, hemorrhage and diarrhea [50].

Many studies conducted to determine heavy metal concentrations including Fe. A concentration range 8.6-2731.8 µg/g of Fe had been found in a selected group of branded herbal products in Pakistan in a study to detect the concentration range of several heavy metals including Fe [9]. Another study with a similar approach had been conducted and Fe concentration range was 65.68-1652.89 µg/g in different products of herbal medicine purchased from various places in Karachi city of Pakistan [34].

2. Conclusion

Traditional medicines products are consumed by a wide range of the world population. Some TM products contain toxic materials such as heavy metals. Exposure to heavy metals can cause health hazard and toxicity. The presence of heavy metals in these medications could expose the consumers to different adverse health effects. Therefore, a proper general awareness should be provided to consumers and producers to minimize this risk.

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