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Heavy metal and pesticide content in commonly prescribed individual raw Chinese Herbal Medicines

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ABSTRACT

Heavy metal and pesticide contamination has previously been reported in Chinese Herbal Medicines (CHMs), in some cases at potentially toxic levels. This study was conducted to determine general patterns and toxicological significance of heavy metal and pesticide contamination in a broad sample of raw CHMs. Three-hundred-thirty-four samples representing 126 species of CHMs were collected throughout China and examined for arsenic, cadmium, chromium, lead, and mercury. Of the total, 294 samples representing 112 species were also tested for 162 pesticides. At least 1 metal was detected in all 334 samples (100%) and 115 samples (34%) had detectable levels of all metals. Forty-two different pesticides were detected in 108 samples (36.7%), with 1 to 9 pesticides per sample. Contaminant levels were compared to toxicological reference values in the context of different exposure scenarios. According to a likely scenario of CHM consumption, only 3 samples (1%) with heavy metals and 14 samples (5%) with pesticides were found with concentrations that could contribute to elevated background levels of contaminant exposure. According to the most conservative scenario of CHM consumption, 231 samples (69%) with heavy metals and 81 samples (28%) with pesticides had contaminants that could contribute to elevated levels of exposure. Wild collected plants had higher contaminant levels than cultivated samples. Cadmium, chromium, lead, and chlorpyrifos contamination showed weak correlations with geographic location. Based on our assumptions of the likely mode of consumption of raw CHMs, the vast majority (95%) of the 334 samples in this study contained levels of heavy metals or pesticides that would be of negligible concern. However, given the number of samples with detectable contaminants and the range between the more likely and more conservative scenarios of contaminant exposure, more research and monitoring of heavy metals (especially cadmium and chromium) and pesticide residues (especially chlorpyrifos) in raw CHMs are advised.

1. Introduction

Chinese Herbal Medicines (CHMs) are used throughout the world and their use is growing (Li et al., 2009). In the United States, a recent national survey indicated that approximately 14.8 billion USD were spent in 2007 on non-mineral, non-vitamin natural products, most of which consisted of herbal medicines (Nahin et al., 2009), up from an estimated total of 6.6 billion USD spent ten years previously (Eisenberg et al., 1998). While the herbal supplement market in the United States continues to expand (Cavaliere et al., 2010), the United States remains a modest market for Chinese herbs. For example, about 3 of the 10 most commonly used herbs in the United States are from Chinese Medicine (Cavaliere et al., 2010).

Several studies have shown that CHMs and other botanical supplements may be contaminated with heavy metals, and in some cases at toxic levels (Ernst, 2002; Ernst and Coon, 2001; Lin et al., 2010). Much of what has been reported regarding potentially worrisome contamination in herbal medicines relates to patent or proprietary medicines (Ang et al., 2003; Au et al., 2000; Cooper et al., 2007; Dolan et al., 2003; Ernst, 2002; Ko, 1998; Koh and Woo, 2000;

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Martena et al., 2010; Raman et al., 2004; Saper et al., 2004), which differ from raw herbs in that they are frequently a mix of different substances (e.g., plant, mineral, animal) in either pill or extract form (Yee et al., 2005). Patent herbal medicines may contain heavy metals that were intentionally added, such as arsenic (Liu et al., 2008a), mercury (Liu et al., 2008b), and lead (Saper et al., 2008). Heavy metals have also been found in raw CHMs (e.g., Han et al., 2008; Lu et al., 2009; Rai et al., 2001; Wong et al., 1993; Wu et al., 2008), and some CHM plant species are known to be heavy metal hyper-accumulators (e.g., Imahara et al., 1992; Lai and Chen, 2005; Pollard et al., 2002; Turan and Bringu, 2007; Wei et al., 2008).

Pesticides have also been reported in CHMs (Leung et al., 2005; Wong et al., 2007; Xue et al., 2008; Zuin and Vilegas, 2000). A recent study of over-the-counter herbal dietary supplements sold in the United States found detectable levels of heavy metals and pesticide residues in some samples, although the FDA and EPA officials who reviewed the data did not express concern about immediate negative health consequences (US GAO, 2010).

Most CHMs in the United States are typically covered under the Dietary Supplements Health and Education Act (DSHEA) of 1994 (Frankos et al., 2010), and as such, lack official limits for regulation of heavy metals or pesticides. Some guidelines for maximum levels of heavy metals and pesticides in raw CHMs have been published at the international (e.g., WHO, 1998) or national level (e.g., CPC, 2005), but considerable variation exists in the proposed standards (Zhao et al., 2007), and in most cases regulated limits apply to only a small subset of contaminants or CHMs.

This study was conducted as part of a larger project initiated to evaluate more than 200 species of commonly used raw CHMs for their bioactivity and potential for drug discovery (Eisenberg et al., 2011). A unique aspect of the study was that a large number of CHMs were collected and each collection was from a single sampling location, as opposed to being a mixture from different collection sites, which is what is usually available on the market. Moreover, each sample was processed using traditional methods, authenticated according to visual, microscopic, and chemical characteristics, and was accompanied by detailed collection information, including photographs, video, and GPS coordinates. As part of the project, all samples were examined for heavy metals and pesticide residues.

It was hypothesized that because raw CHMs are typically free of substances that are added in patent medicines, they would contain relatively low levels of heavy metals. Furthermore, because roughly two-thirds of medicinal plants are collected from the wild and cultivation is typically on a small scale (Canter et al., 2005), it would be expected that the pesticide content in raw CHMs, particularly those collected from the wild, would be low. The goals of this study were to: summarize patterns of heavy metal and pesticide content observed in a large sample of CHMs collected throughout China and compare observed levels to established limits; examine the association between heavy metal and pesticide contamination, collection location in China, and cultivation status; assess the contribution of contaminant levels found in the CHMs to background levels of exposure; and discuss implications of these findings for policy makers and researchers in the field of herbal medicine.

2. Methods

2.1. Sample collection

A total of 334 samples representing 126 species of commonly used CHMs were collected for examination of heavy metal content (Fig. 1). Of those, 210 samples (62.9%) were collected from cultivated locations and 124 samples (37.1%) were collected from the wild. Of the total samples, 294 samples representing 112 species were also examined for 162 pesticide residues. Species of CHMs used in this study were chosen only if they were listed in the 2005 edition of the Chinese Pharmacopoeia (CPC, 2005) and were not endangered (CITES, 2010). Each species was collected between 2006 and 2009 from 1 to 3 different sampling locations (species listed in Supplementary data, Table S1). Sampling locations were chosen according to areas of traditional production of the CHM, without regard to possible pollution sources. Collection site information, including photographs, video, and GPS data, was obtained for all samples. Each collection consisted of a bulk sample of 10 kg dry weight of the medicinal part of the plant (e.g., root) and an accompanying voucher sample for botanical authentication. Each bulk sample was harvested, cleaned, and processed according to traditional methods, then authenticated by Chinese medicine experts according to visual, microscopic, and chemical characteristics (Eisenberg et al., 2011). As part of the authentication process, all samples were tested for purity according to total water and ash content (CPC, 2005). The test of ash content provided information on the presence of impurities such as soil. Samples that did not meet the Chinese Pharmacopoeia standards of any authentication test were removed from the study. Following authentication, 250 g were separated for heavy metal and pesticide testing. The 250 g sample was first ground into a powder using an IKA grinder (Model A11 B21; IKA Works, Inc., Wilmington, NC). Sample preparation time varied according to the quality and consistency of the samples. For example, leaf material required less grinding than root material.

2.2. Examination of heavy metals

Samples were tested for the total concentration of arsenic, cadmium, chromium, lead, and mercury. These five metals were chosen since they are most commonly associated with possible toxicity in dietary supplements (WHO, 1998) and/or are specified in the NSF International (NSF) and American National Standards Institute (ANSI) Standard 173 for dietary supplements (NSF International, 2008). Metal concentrations were measured as the total, unspeciated amounts. Approximately 0.5 g of ground sample was first microwave digested for 40 min in concentrated nitric acid (HNO_3) and 30% hydrogen peroxide (H_2O_2) in a quartz vessel. The resulting digestate was analyzed using a Thermo X-Series Inductively-Coupled Plasma Mass Spectrometer (ICP-MS) (Thermo Fisher Scientific, Waltham, MA). Heavy metal results from the ICP-MS were quantified against standard curves generated from 1 blank and at least 4 standard reference solutions (High-Purity Standards, Charleston, SC) run separately. Quality control was assessed by running a laboratory reagent blank after every 10 samples. The limit of detection achieved for each metal was 0.08 ppm for arsenic, 0.02 ppm for cadmium, 0.01 ppm for chromium, 0.04 ppm for lead, and 0.01 ppm for mercury. The detection limit was based on consideration of the blank runs, concentration of the low standard in the calibration curve, and the sample preparation procedure. Based on this method, the limit of detection was considered equivalent to the limit of quantitation.

2.3. Examination of pesticides

Samples were tested for the presence of 162 different pesticide residues. Information about pesticides applied to the CHMs or to neighboring areas of cultivation in this study was not always known. In addition, there are no international recommendations for specific pesticides that should be screened in medicinal plants (WHO, 1998), so for this project a broad, comprehensive test was employed. A modified QuEChERS method ("Quick, easy, cheap, effective, rugged, safe"; Anastassiades et al., 2003) was used for the preparation of the samples for pesticide analysis. Approximately 2 g of the ground sample was first extracted in acetonitrile. If required, some samples were cleaned with dispersive solid-phase extraction clean-up (dSPE, Supelclean ENVI-Carb II/PSA SPE Tube; Supelco, Bellefonte, PA). A portion of the dSPE eluted solution or original extract was then dried