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Heavy Metals (Cu, Fe, Ni and Zn) in Traditional Chinese Herbal Medicines Bought from Selected Shops from Peninsular Malaysia

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Research Article

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Abstract

A total of 20 Traditional Chinese Herbal Medicine (TCHM) was bought randomly from shops in three states of Peninsular Malaysia. All of these samples were analyzed for Cu, Fe, Ni and Zn concentrations. Based on samples collected from selected shops in Peninsular Malaysia, the levels of Cu, Fe, Ni and Zn in the TCHM samples were comparable to reported studies of TCHM products in the literature. The levels of essential Fe and Zn were found to be higher than the levels of the essential Ni and Cu. The present levels of the 20 TCHM products from Malaysia can serve as important baseline information for future reference in the establishment of MRLs of the four less common heavy metals in Malaysia as well as in this region. Therefore, it is difficult to conclude whether the TCHM products are safe from contamination of Cu, Fe, Ni and Zn since the MRLs for Cu, Fe, Ni and Zn have not been recommended by WHO. Future regular monitoring, quality control and adequate regulatory measures of TCHM products for heavy metals are necessary.

Keywords: Heavy metals; Traditional Chinese Herbal Medicines; Malaysia

Introduction

Tradition Chinese Herbal Medicines (TCHMs) are currently used by large sections of the population. Because they are not regulated as medicines and are freely available to everyone, serious safety concerns might be associated with these Herbal Medicines (HMs) [1]. According to Rao and Galib (2011) [2], WHO has emphasized the need for quality assurance of herbal products, including testing of heavy metals? Ernest (2002) concluded from a review paper that evidence suggesting that some Asian HMs containing toxic heavy metals or undeclared prescription drugs. Evidence from various countries implies that toxic heavy metals and undeclared prescription drugs in Asian HMs might constitute a serious health problem. However, the

majority of the data is anecdotal and insufficient to define prevalence figures. Ways ought to be found to maximize consumer safety.

According to Donkin, et al. the common industrial uses of Ni are coins, jewellery, alloy, plating and batteries while the principal toxic effect is dermatitis in human. For Zn, the common industrial uses are batteries, alloys, galvanizing, dyes, and pharmaceuticals batteries while the principal toxic effects are gastrointestinal effects and anemia in human, According to Chan, et al. (1993) [3], the regulation of heavy metal contents in TCHM products has been an international concern. The increasing incidence of severe and fatal metal poisoning in the public has somewhat tarnished the overall image of TCHM products. Therefore, there is a need to screen the heavy metal levels in the TCHM in Malaysia since these TCHM products that is available in the market are imported where the safety consumption of these products were generally unknown. The safety issue of TCHM is an essential scientific subject of interest Ernst (1999) [4] which revolve the potential toxicity, risk and benefit of the TCHM product [5]. Many studies can be found in the literature regarding the toxic Hg, Cd and Pb levels in HMs but less in number for Cu, Fe, Ni and Zn. However, there is a growing concern on the levels of Cu, Fe, Ni and Zn in the TCHM products/ For example, Wang, et al. (1999) [6] analyzed four heavy metals including Ni and Zn in seven TCHM products purchased locally.

We previously reported the toxic Cd and Pb contents in the TCHM sold in Malaysian markets [7] but the levels of Cu, Fe, Ni and Zn have not been published. Therefore, the objective of the present study was to determine the background concentrations of Cu, Fe, Ni and Zn in the TCHM products sold from several markets in Kuala Lumpur, Selangor and Johore, from Peninsular Malaysia.

Materials and Methods

A total of 20 TCHM samples of different therapeutic effects were bought from several markets in Kuala Lumpur, Selangor and Johore between April and July 2005. All the samples were randomly purchased and selected. All these TCHM products are commonly used by many Malaysians. Samples bought were taken back to the laboratory and stored at room temperature. Ingredients and medicinal properties for the collected samples are presented in Table 1 [7].

No.	Name of product/ samples	Ingredients	Medicinal properties
1	Herbal tea	Tea leaves, radix and *Mentha arvensis*	Sore throat, headache and fatigue
2	Ginseng Pills	American ginseng	Fatigue and blood pressure
3	Ban Kah Chai	Pepermint oil and pogostemonis	Stomachache and diarrhea
4	Li Chee Powder	*Pulsatilla chinensis* and *Paenial actiflora*	Mild diarrhea
5	Green Pills	Essential oil and radix	Fever
6	Bo Ji Wan	*Cordyceps sinensis*	Excessive sputum, cough and cold
7	Chee Ke Wan	Essential oil and radix	Diarrhea and flu
8	Chee Suat Tan	Radix and gypsum	Throat ulcer
9	Seng Lian Cough Pills	Radix and essential oil	Cough
10	Intamol	Essential oil and radix	Fever
11	Guan Ying Chian	Bark of "Guan Ying Chian"	Fatigue and blood pressure
12	Pang Nian Jin	Bark of "Pang Nian Jin"	Fatigue and relief cold
13	Cold Relief Pills	Rhizome Belancandae and essential oil	Cold relief
14	Flu Pills	Essential oil	Flu
15	Biau Leng San	*Artemisia*, malt and coptis	Woman stomachache
16	Oh Ouh Pau Chee San Medicated Powder	Mentha herb and *radix angelica*	Improving appetite
17	Stomachache Powder	Mentha herb and *radix angelica*	Stomachache and flatulence
18	Soo Hup Wan Tiny Pills	Essential oil and rhizome cymbopogon	Indigestion and vomiting
19	Tou Seah San (Baby)	*Poriacocos* and semen *Plantago asiatica*	Stomachache
20	Hung Lien Shang Ching Pien	Essential oil and ginseng	Reducing heat

Table 1: Chinese Herbal Medicines under investigation; name, ingredients and medicinal properties. Note: Information is gathered from the label of each Chinese Herbal Medicines [7].

The samples were cleaned and removed of any particulates that came with the herbal were removed. Samples were then dried at 105˚C for least 16 h until constant dry weight was achieved. Dried samples were shaken vigorously through a 0.5 mm stainless steel sieve to achieve homogeneity. Three replicates of each TCHM sample were analyzed for Cd and Pb.

Extraction of heavy metals from TCHM samples was performed by using the acid digestion method. Dried TCHM samples (1 gram each) were digested in a combination of concentrated nitric acid (69%) and perchloric acid (60%) at 4:1 ratio, at 40˚C for the first hour and 140˚C for the next 3 hours.

Digested samples were then diluted with double distilled water and filtered through Whatman No.1 filter paper before they were stored for metal determination later on. Determination of Cu, Fe, Ni and Zn in the digested samples was carried out by using an Atomic Absorption Spectrophotometer (AAS) Model AAnalyst 800. For quality control, all glass wares used were acid-washed to avoid contamination. In addition to that, the procedural blanks were analyzed together with the samples. The data from the AAS were verified by certified reference materials (IAEA Soil-5) and the recoveries for the two metals were of satisfactory (80-120%).

Results and Discussion

Fe

Fe levels ranged from 0.70 to 1873 mg/kg dry weight (dw) (Table 2) with the highest Fe level was found in Bo Ji Wan while Soo Hup Wan Tiny Pills, Biau Leng San, and Cold Relief Pills also exceeded 1000. However, maximum permissible/residue limits for Fe in herbal products have yet to be set at the global level [8], as reviewed by Sarma, et al. (2011) [9]. WHO does not recommend any maximum residue limit (MRL) for Fe [10].

Medicines	Cu	Fe	Ni	Zn
Herbal Tea	12.20 ± 5.76	660 ± 395	23.6 ± 36.4	35.4 ± 18.2
Ginseng Pills	3.04 ± 0.88	32.7 ± 3.05	0.97 ± 0.49	1.86 ± 0.54
Ban Kah Chai	13.1 ± 1.81	579 ± 39.2	3.07 ± 0.77	63.7 ± 4.65
Li Chee Powder	8.29 ± 0.62	384 ± 20.8	2.63 ± 1.22	25.7 ±1.59
Green Pills	3.42 ± 0.34	17.5 ± 5.81	BDL	1.25 ± 0.51
Bo Ji Wan	9.39 ± 0.25	1873 ± 57.8	BDL	27.3 ± 1.86
Chee Ke Wan	8.14 ± 0.65	668 ± 66.9	1.45 ± 1.31	31.8 ± 2.45
Chee Suat Tan	13.1 ± 1.81	579 ± 39.2	3.07 ± 0.77	63.7 ± 4.65
Seng Lian Cough Pills	8.07 ± 0.49	203 ± 66.9	12.1 ± 0.77	47.0 ± 1.32
Intamol	BDL	35.7 ± 25.2	0.95 ± 0.52	0.03 ± 0.73
Guan Ying Chian	4.11 ± 0.45	0.70 ± 0.21	54.5 ± 165	13.2 ± 3.05
Pang Nian Jin	1.60 ± 0.53	41.7 ± 8.88	0.93± 0.34	3.36 ± 0.09
Cold Relief Pills	6.56 ± 0.16	1041 ± 35.8	12.2 ± 1.00	20.0 ± 0.47
Flu Pills	0.22 ± 0.19	45.9 ± 9.73	2.96 ± 0.53	1.53 ± 0.67
Biau Leng San	22.2 ± 3.78	1026 ± 25.0	12.9 ± 9.13	61.2 ± 6.52
Oh Ouh Pau Chee San Medicated Powder	9.77 ± 2.26	449 ± 23.6	6.01 ± 0.34	78.1 ± 6.91
Stomachache Powder	5.21 ± 1.04	189± 9.50	1.87 ± 0.21	21.1 ± 1.50
Soo Hup Wan Tiny Pills	8.68 ± 0.71	1115 ± 52.1	8.89 ± 1.31	35.6 ± 4.89
Tou Seah San (Baby)	1.35 ± 1.07	108 ± 7.00	8.77 ± 0.77	16.7 ± 1.85
Hung Lien Shang Ching Pien	6.30 ± 1.60	245 ± 22.7	3.74 ± 0.93	22.3 ± 1.13
Min	BDL	0.70	BDL	0.03
Max	22.2	1873	54.5	78.1

Table 2: Concentrations (mean ± standard error, mg/kg dry weight) of Cu, Fe, Ni and Zn in the Chinese tradition herbal medicines bought from selected shops in Peninsular Malaysia.
BDL = Below Detection Limit

The present levels are relatively high when compared to Fe in most medicinal plants for the treatment of anemia. Nkansah, et al. (2016) [11] reported the mean Fe concentration of the 15 medicinal plant samples from

Kumasi (Ghana) was 4.66 mg/kg, ranging from 2.51 to 7.06 mg/kg. Dghaim, et al. (2015) [12] reported that the Fe concentrations in the in selected traditional herb sconsumedin the United Arab Emirates (UAE), purchased from the local market in Dubai were81.3 - 1101mg/kg. Konieczyński, et al. (2007) [13] reported that Fe levels in selected medical herbs known for the treatment of anemia in Poland, ranged from 6.67 to 223 mg/kg dw.

Zhu, et al. (2013) [14] reported the concentrations of Fe in the dried herbal flowers from China were in the range of 312-1.389 mg/kg dw. The present herbal tea (based on the leaves) from the present study was found to be 660 mg/kg dw for Fe. Nkuba and Mohammed (2017) [15] reported the concentrations of Fe in analyzed medicinal plants ranged from 89.02- 553.46 mg/kg, 246.44-572.81 mg/kg to 380.56 - 798.43 mg/kg for leaves and root of *Moringa oleifera* and in *Hibiscus sabsdariffa*, respectively.

Fe is an essential element for human growth and development and an essential component of haemoglobin. It facilitates the oxidation of carbohydrates, proteins and fats to control body weight, which is a very important factor is diabetes management. Iron is necessary for the formation of haemoglobin and also plays an important role in oxygen and electron transfer in the human body. Low iron content causes gastrointestinal infection, nose bleeding and myocardial infection [16].

Zn

Zn levels ranged from 0.03 to 78.1 mg/kg dw (Table 2) with the highest Zn level was found in Oh Ouh Pau Chee San Medicated Powder. However, maximum permissible/residue limits for Zn in herbal products have yet to be set at the global level [8], as reviewed by Sarma, et al. (2011) [9]. WHO does not recommend any MRL for Zn [10].

Nkansah, et al. (2016) [11] reported the mean Zn concentration of the 15 medicinal plant samples from Kumasi (Ghana) was 0.53 mg/kg. The highest concentration was recorded in G. kola (1.07mg/kg). The present Zn range is relatively comparable to other studies. For instance, a study on the levels of Zn in some medicinal plants from India gave concentrations in the range 21.3-48.5 mg/kg dw [17]. A study in Pakistan also gave Zn levels slightly above that of this study in the range of below detection – 502 mg/kg dw [18]. Dghaim, et al. (2015) [12] reported that the Zn concentrations in the in selected traditional herbs consumed in the United Arab Emirates (UAE), purchased from the local market in Dubai were12.7 -147mg/kg for Zn. Zhu, et al. (2013) [14] reported the concentrations Zn in the dried herbal flowers from China were in the range of 39.5-97.4 mg/kg dw. The present herbal tea (based on the leaves) from the present study was found to be 35.4 for Zn. Nkuba and Mohammed (2017) [15] reported the concentrations (mg/kg dw) of Zn in the analyzed plant samples ranged from 8.67 to 23.54, 15.51 to 27.13 and 7.09 - 15.1 in *M. oleifera* leaves, roots and *H. sabsdariffa*, respectively

Zn is an essential element, playing an important role as a cofactor for more than 100 metalloenzymes and its deficiency can have adverse effects on normal growth and development, reproduction, and immune function. Zn deficiency may also affect the bone metabolism and gonadal function [19].Nevertheless, at a level higher than the sufficient concentrations, a number of these essential metals is potentially toxic Obi et al., 2006 [20].

Cu

The Cu concentrations ranged from BDL to 22.2mg/kg dw (Table 2), with the highest concentration in Biau Leng San (Table 2). It is the only TCHM that exceeded 20.0 mg/kg dw which has become maximum residue limit recommended by Chinese Pharmacopoeia (2015) [21]. The present Cu ranges are also well below national limit of 150 mg/kg dw for finished herbal products set by Singapore [10], but WHO does not recommend any MRL for Cu [10].

Ting et al. (2013) [22] reported a Cu range of 0.08-0.35 mg/kg (based on boiled and non-boiled decoctions) in four commonly consumed TCHMs in Malaysia namely "Eight Treasure Herbal Tea", "Herbal Tea", Xiyang shen (*Radix panacis quinquefolii*) and Dangshen (*Radix codonopsis*) ", which were bought randomly from two shops in Kuala Lumpur (but the sampling dates were not specified). Nkuba and Mohammed (2017) [15] reported the concentrations of Cu varied from 1.58 - 6.22 mg/kg, 1.20 - 3.79 mg/kg and 0-0.42 mg/kg in *M. oleifera* leaves, roots and *H. sabsdariffa*, respectively.

Zhu et al. (2013) [14] reported that the highest Cu content was15.3 mg/kg dw in herbal flowers *C. officinalis*, whereas the lowest Cu contentwas0.826 mg/kg in herbal flower Rosarugosa, most samples having concentrations between 5.0 and 15.0 mg/kg. The present Cu levels were in agreement with the literature data [16].

Ni

Ni levels ranged from BDL to 54.5 mg/kg dw (Table 2) with the highest Ni level was found in Guan Ying Chian. Zhu et al. (2013) reported that the minimum and maximum Ni levels observed were 0.189 mg/kg in *Lavandula angustifolia* and 18.9 mg/kg in *Chimonanthus praecox*. However, maximum permissible/residue limits for Ni in herbal products have yet to be set at the global level [8], as reviewed by Sarma et al. (2011) [9]. WHO does not recommend any MRL for Ni [10].

The Ni levels were in agreement with those reported in the literature [16]. Nkuba and Mohammed (2017) [15] reported the Ni levels (mg/kg dw) ranging from 0.09-4.89, 0.33-3.08 and 0.98-2.15 in *M. oleifera* leaves, roots and *H. sabsdariffa*, respectively. Dghaim et al. (2015) [12] reported that the Cu concentrations in the in selected traditional herbs consumed in the United Arab Emirates (UAE), purchased from the local market in Dubai were: 1.44 - 156 mg/kg dw.

The most common ailment arising from Ni is an allergic dermatitis known as Ni itch, which usually occurs when the skin is moisture state [23]. Ni has been also identified as carcinogen and adversely affects lungs and nasal cavities [23].

General Discussion

The present study revealed that levels of Fe and Zn were generally higher than Ni and Cu. This is in agreement of many reported for medicinal herbs. Zhu, et al. (2013) [14] reported that the order of the levels of metals in the herb flowers was found to be as Fe >Zn>Cu>Ni. There sults showed that these herbal flowers contained high concentrations of Fe and Zn. Based on 42 Chinese Herbal Medicinal plants, Wong, et al. (1993) [24] reported that the concentrations (mg/kg dw) of these plants were 1.50 - 26.0 for Cu, 28 - 1516 for Fe, <0.05 - 7.20 for Ni, and 3.80 - 595 for Zn. They that Fe and Zn were generally present in higher concentrations than the other heavy metals. These are essential metals for plants. The other essential metals for plants, Cu and Ni were present in lower concentrations.

The higher metal levels found in some TCHM products were probably from contamination during the drying and preservation steps [24]. Unless consumed in large quantity continuously, at the levels present in the herbal plants, they are unlikely to cause any adverse health effects.

In the present study, there is one TCHM product that used rhizome cymbopogon as parts of ingredients namely Soo Hup Wan Tiny Pills. The mean metal levels (mg/kg dw) of this product were 8.68 for Cu, 1115 for Fe, 8.89 for Ni and 35.6 for Zn. Nkansah et al. (2016) [11] reported *Cymbopogon citratus* (Lemom grass) from Ghana as 2.51 mg/kg dw for Fe and 0.86 mg/kg dw for Zn. This comparison shows that the Fe and Zn were not highly accumulated in Cymbopogon. Therefore, the high levels of Fe and Zn found in Soo Hup Wan Tiny Pills could be possibly not attributable to the ingredient of Cymbopogon.

In the present study, there is one TCHM product that used *Artemisia* as parts of ingredients namely Biau Leng San. The mean metal levels (mg/kg dw) of this product were 22.2 for Cu, 1026 for Fe, 12.9 for Ni and 61.2 for Zn. Wong et al. (1993) [24] reported that the whole metal levels (mg/kg dw) in the plant of *Artemisia* sp. were 10.0 for Cu, 618 for Fe, 2.30 for Ni and 30.0 for Zn. The metal levels (mg/kg dry weight) in the leaves of *Artemisia nilagirica* from India were reported as 23.2 for Cu, 820.4 for Fe, 0.30 for Ni and 33.7 for Zn [25]. This comparison shows that the levels of Cu, Fe and Zn found in could be highly accumulated in Artemisia. Therefore, the high levels of Cu, Fe and Zn found in Biau Leng San could possibly be attributable to the ingredient of *Artemisia*.

In the present study, there are three types of TCHM products that used Mentha herbs as parts of ingredients namely Oh Ouh Pau Chee San Medicated Powder, Stomachache Powder and Herbal Tea Leaves. Their metal ranges were 5.21-12.2 for Cu, 189-660 for Fe, 1.87-23.6 for Ni and 21.1-78.1 for Zn. The metal levels (mg/kg dry weight) in the leaves of *Mentha piperitae* from India were reported as 0.10 for Cu, 3.71 for Fe, 1.01 for Ni and 0.10 for Zn [26].This comparison shows that the Cu, Fe, Ni and Zn were not highly accumulated in Mentha. Therefore, the high levels of the four metals found in the three types of TCHM products could be possibly not attributable to the ingredient of mentha herbs

From a review by Sarma, et al. (2011) [8] on accumulation of heavy metals in selected medicinal plants, they concluded that 1) medicinal plants are prone to contamination from heavy metals, b) authorities should establish a more standardized and universally accepted value for safe levels of heavy metal contents in medicinal plants, and c) steps should be taken to prevent collection and marketing of such medicinal plants that are prone to heavy metal accumulations. Perhaps, steps no. 2 and 3

should be given emphasized and they can be recommended based on the present study.

Conclusion

Based on samples collected from selected shops in Peninsular Malaysia, the levels of Cu, Fe, Ni and Zn in the TCHM samples were comparable to reported studies of TCHM products in the literature. The levels of essential Fe and Zn were found to be higher than the levels of the essential Ni and Cu. The present levels of the 20 TCHM products from Malaysia can serve as important baseline information for future reference in the establishment of MRLs of the four less common heavy metals in Malaysia as well as in this region. Therefore, it is difficult to conclude whether the TCHM products are safe from contamination of Cu, Fe, Ni and Zn since the MRLs for Cu, Fe, Ni and Zn have not been recommended by WHO (2007) [9] . However, we recommend regular monitoring and control of these popular TCHM products in order to safeguard the consumers' heath on the short- and long-term consumption basis.

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