Heavy Metals Contamination Status and Analyses of Traditional Chinese Medicine

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According to literatures published since 2003, statistical analysis of reported data on the heavy metals contamination in traditional Chinese medicine was carried out systematically in this article. The purpose of this investigation was to study the status of heavy metal content in traditional Chinese medicine systematically through objective assessment and then to provide reference for the future research and to promote the development of traditional Chinese medicine products with high quality at last. By analyzing heavy metal content of different types of traditional Chinese medicine, medicament portions, elements, preparations and sources, it was found that difference in respectively.

Key Words: Traditional Chinese medicine, Mineral drugs, Animal medicine, Chinese patent medicine, Heavy metal.

INTRODUCTION

Traditional Chinese medicine has been gaining interest and acceptance world wide¹. Reports of efficacy of traditional Chinese medicine are increasing in numbers. Traditional Chinese medicine includes both crude Chinese medicinal materials (plants, animal parts and minerals) and Chinese proprietary medicine (CPM). When used or prescribed according to Chinese medical philosophy and practice, through testing of time, those medications and crude materials recorded in the Chinese Pharmacopoeia have been approved for safe use². Despite the belief that traditional Chinese medicine, which is safe and without many adverse effects, is of natural origin, unlike western medicine³⁻⁶, there is a growing public concern on the potential accumulation of heavy metals in traditional Chinese medicine. These unfavourable incidents have possibly been due to the number and intensity of anthropogenic sources such as rubbish tips, smelter stack, waste incineration fertilizers, vehicle emission, mining activities, cultivation mode, agricultural waste and sewage sludge have increased the local environmental heavy metal concentrations in recent decades⁷⁻¹⁰. Heavy metal is highly hazardous to human body and can cause pathological change of organs and diseases related to cardiovascular, kidney, bone, *etc.* and can even cause cancer owing to excessive heavy metal accumulation in human body¹¹⁻¹⁵. Therefore heavy metal contamination of traditional Chinese medicine has become one of the most important factors that affect both the quality and the internationalization of traditional

Chinese medicine. A critical evaluation of their safety is extremely important¹⁶. This paper studies and analyzes the status of heavy metal contamination of traditional Chinese medicine in China from 2003, in order to offer reference for the future research on the controlling of the heavy metal content.

EXPERIMENTAL

Data source: In this paper, we discussed different types of questions addressed by the data commonly collected since 2003 and analyzed in heavy metal contamination of traditional Chinese medicine and the issues associated with analyzing these data. We also made suggestions for appropriate and useful methods of analyzing and presenting these data in a way that optimizes the information contained therein.

Standard limits of heavy metal: In this study, a limit of standard is according to "Green Trade Standards of Importing & Exporting Medicinal plants & Preparations" in China. $Pb \leq 5.0 \text{ mg kg}^{-1}$, $Cd \leq 0.3 \text{ mg kg}^{-1}$, $Hg \leq 0.2 \text{ mg kg}^{-1}$, $As \leq 2.0 \text{ mg kg}^{-1}$, $Cu \leq 20 \text{ mg kg}^{-1}$, total amount of heavy metals $\leq 20 \text{ mg kg}^{-1}$.

Statistical analysis: In this article summarized and analyzed the status of the heavy metal pollution of traditional Chinese medicine from the following aspects: among herbal drugs of different heavy metal elements, part and source of herb drugs; mineral drugs; animal medicine; Chinese Patent Medicine.

RESULTS AND DISCUSSION

Herbal drugs

Contamination of different heavy metal elements:

Different heavy metal elements such as lead, copper, arsenic, cadmium, mercury have different content level in traditional Chinese medicine. In the one hand, heavy metals are natural constituents of the earth, distribution of these metals is influenced by the nature of parent materials, climate and their relative mobility depending on soil parameters such as mineralogy, texture and classification of soil and pH¹⁷⁻¹⁹. In the other hand, vehicle exhaust, sinking particles in air, industrial wastes, fertilizers and pesticides that carried by air and water. Therefore we have a comprehensive data analysis on different heavy metal elements in plant-medicines and our main purpose is to find out their distribution in herbal drugs.

Table-1 shows that copper is of the highest exceeding rate, next is cadmium and the lowest is arsenic. The exceeding rate of heavy metals ranked in this order: Cu > Cd > Hg > Pb > As, which basically reflected the status of different heavy metal elements content in herbal drugs. According to the statistical analysis, copper and cadmium should be the focus of inspection items of quality control in herbal drugs.

Different medicament portions of herbal drugs: It is presumed that the heavy metals exceeding rate of herbal drugs come in root and rootstock are obviously higher than other parts according to Table-2. Exceeding rate of lead, copper, arsenic, cadmium, mercury in root and rootstock has no big difference. There are 2 and 3 kinds of heavy metal elements exceeding simultaneously which reach to 26 and 8, respectively. The reason may be that they grown in seriously polluted soil and absorbed actively and passively²⁰.

Following the roots are the group of entire plants and bark. In the comparison of different heavy metal elements in bark drugs, Cd and Hg are the most serious enriched elements with the exceeding rate of 70.8 and 31.3 %.

Five samples in bark exceed the standard on the contents of Cd and Hg simultaneously. One of the reasons that bark has a serious contamination of heavy metal is that most of the bark drugs gain from roots. Entire plants may be owing to inappropriate application of chemical fertilizer and pesticides and air pollution.

According to the statistical analysis on the original data of heavy metal content in different groups of herbal drugs, groups of flower, leaf, fungi, fruit and seeds were good with comparatively low concentrations of heavy metals and mostly not exceed the limit. The reason may be that most of these groups grow far away from the roots and have a short growth cycle.

Difference source: Owing to the impact of soil background values, discharge of various heavy metal sources and heavy metal accumulation has appeared in plant soil, thus different areas have different status of heavy metal contamination. As for different areas, there was a difference on the concentration and types of heavy metals. Therefore, it is necessary to do statistical analysis on the status of different heavy metal elements content in different sources of herbal drugs.

According to the data collected from 2003 on heavy metal content of herbal drugs in different provinces (Table-3), heavy metal contents in different areas not only presented different status in the overall situation but also reflected certain differences in different heavy metal elements. It can be seen relatively in large samples that the most serious contamination area is Guizhou, whose exceeding rates of Cu and Cr are respectively 40.7 and 32.4 %. Six samples from Guizhou exceed the limit simultaneously in two kinds of heavy metal elements, one sample in 3 kinds of heavy metal elements. The second most serious contamination area is Sichuan, whose exceeding rates of Cu, As and Hg are respectively 78.3, 26.3 and 16.7 %, 4 samples exceed the limit in 2 kinds of heavy metal elements. Different areas have different element distribution advantage, for example, Cu has the largest distribution

TABLE-1
STATUS OF FIVE HEAVY METAL ELEMENTS IN TRADITIONAL CHINESE MEDICINE

Metal	Total No.	Sample of the maximum content of heavy metal	Maximum (µg/g)	Plant part	Source of the sample	All of samples exceed rate (%)
Pd	308	Radix Codonopsis	83.12	Root	Sichuan	8.8
Cu	234	Aloe	74.30	Leaf	Hainan	19.2
Cd	317	Radix et Rhizoma Rhei Palmati	1.318	Root	Qinghai	15.5
As	317	Radix Aconiti Kusnezoffii Preparata	15.84	Root	Anhui	5.7
Hg	255	Radix Hedysari	9.11	Root	Gansu	10.6

TABLE-2
DIFFERENT TYPES OF HEAVY METAL CONTAMINATION STATUS OF HERBAL DRUGS

Plant part	Total No.	Pd		Cu		Cd		As		Hg		2 ^a	3 ^b
		No.	ER (%)	No.	ER (%)	No.	ER (%)	No.	ER (%)	No.	ER (%)		
Root and rootstock	202	202	10.4	135	22.2	202	17.3	175	9.7	156	12.2	26	8
Fruit and seeds	47	43	0.0	42	7.1	57	2.1	37	2.7	43	2.3	0	0
Flowers	3	3	0.0	3	0.0	3	0.0	2	0.0	0	0.0	0	0
Stem	4	4	25.0	3	33.3	4	25.0	3	0.0	3	0.0	0	0
Bark	24	20	0.0	23	4.3	24	70.8	20	0.0	16	31.3	6	0
Entire plants	20	20	15.0	12	50.0	20	40.0	19	0.0	19	5.3	3	1
Leaf	10	9	11.1	9	44.4	10	0.0	10	0.0	9	0.00	0	0
Fungi	9	9	0.0	9	0.0	9	22.2	9	0.0	9	11.1	0	0

^aThe number of samples have 2 kinds of heavy metal exceeding at same time; ^bThe number of samples have 3 kinds of heavy metal exceeding at same time; ER = Exceeding rate.

in Guizhou, Hainan, Guangxi and Shichuan; Pb in Hainan and Guangdong; Cd in Guizhou and Hainan; Hg in Shandong Gansu. However, we can see from these data that the amount and species of medicinal drugs determined in each province are different and the sample sizes of partial provinces are small, so our analysis can not be an evidence for evaluating the quality of one province's medicinal drugs, but a reference for the preliminary analysis and evaluation to the heavy metal contamination of drugs in each province.

Mineral drugs and animal medicine: Mineral drugs have long been used in traditional Chinese medicine for more than 2000 years, such as Cinnabar^{21,22}, Gypsum Fibrosum, Arsenicum Sublimatum. Most of them contain heavy metal elements, for example Cinnabar is a naturally occurring mineral composed of more than 95 % HgS, which has long been used in combination with other traditional Chinese medicine as a sedative and hypnotic²³. Minerals that are of value as drugs are formed under a wide variety of geological conditions in many types of igneous, metamorphic and sedimentary environments. They are created also in hydrothermal replacement deposits and in veins^{24,25}. Therefore different types of mineral drugs have different content of heavy metal. In our study we find a lot of mineral drugs were misused, such as arsenic trioxide and arsenic stone, gypsum, red gypsum and a mix of agricultural gypsum for gypsum, alumen and dried alum, lead cream and gouache, natural instead of artificial cinnabar, these confusion occur from time to time. A lot of substances misused may be potentially hazardous as most of these misused substances contain higher levels of heavy metal, as we know; venenation caused

by misuse is not rare in medicating. As mentioned above mineral drugs should be identified whether it is true (good) or false (bad) seriously.

Animal medicine only occupies a small part of traditional Chinese medicine, but frequently used in clinical application. The problem of heavy metal contamination of animal medicine becomes much more serious, due to the pollution of environment and heavy metal contamination of food, too. A research article reported margarita is the animal sample that has the highest concentration of mercury due to pollution in sea²⁶.

Chinese patent medicine (CPM): The great number of CPM containing excessive metal besides of contamination is due to the use of heavy metal as one of compound in CPM products. Mercury content is due to the use of cinnabar (Chinese name "Zhu Sha") commonly^{21,27}. Lead has also been detected at high levels due to the use of litharge (Chinese name "Mi Tuo Seng") and minium (Chinese name "Qian Dan"). One arsenic compound commonly used in CPM is realgar (Chinese name "Xiong Huang"), which is used for treatment of insect and snake bites, malaria, cough, piles and as an antidote (PRC, 1995)²⁸. Copper compound, a green coloured mineral existing as Chalcantithum (Chinese name "Dan Fan"), has been used in CPM for treatment of insomnia²⁹. According to the statistical analysis on heavy metal content of 8 preparations, 79 kinds of CPM (99 samples in total) (Table-4). Chinese patent medicine has the lowest heavy metals contamination level in traditional Chinese medicine. The reason is that processing, extraction, production and processing process remove most of the heavy metal. According to these data we have not found

TABLE-3
STATUS OF DIFFERENT SOURCE

No.	Source	Total No.	Pd		Cu		Cd		As		Hg		2 ^a	3 ^b
			Total No.	ER (%)	Total No.	ER (%)	Total No.	ER (%)	Total No.	ER (%)	Total No.	ER (%)		
1	Anhui	8	8	12.5	2	0.0	8	12.5	6	33.3	7	0.0	2	0
2	Fujian	3	3	0.0	3	0.0	3	33.3	3	0.0	3	0.0	0	0
3	Gansu	68	68	0.0	68	0.0	68	5.8	68	1.6	53	7.5	0	0
4	Guangdong	25	25	16.0	25	0.0	25	4.0	14	0.0	14	7.1	1	0
5	Guangxi	9	4	25.0	9	22.2	9	11.1	5	0.0	5	0.0	1	0
6	Guizhou	34	34	5.8	27	40.7	34	32.4	34	5.9	34	2.9	6	1
7	Hainan	19	19	13.8	19	42.1	19	10.5	19	5.3	19	0	4	1
8	Hebei	4	4	25.0	3	0.0	4	75.0	4	25.0	4	25.0	1	1
9	Henna	4	4	50.0	1	100.0	4	25.0	4	25.0	4	0.0	0	0
10	Heilongjiang	5	5	0.0	2	0.0	5	40.0	5	0	5	0.0	0	0
11	Hebei	2	2	50	1	0.0	2	50.0	2	50.0	2	0.0	0	0
12	Hunan	3	1	0.0	3	0.0	3	33.3	2	0.0	2	0.0	0	0
13	Jilin	10	10	10.0	1	100.0	10	20.0	10	0.0	10	10	2	0
14	Jiangsu	8	8	0.0	1	0.0	8	0.0	8	0.0	8	0.0	0	0
15	Jiangxi	3	3	0.0	2	50	3	0.0	0	0.0	3	0.0	0	0
16	Liaoning	2	2	0.0	0	0.0	2	0.0	2	0.0	2	50	0	0
17	Neimenggu	3	3	66.7	1	0.0	3	33.3	3	0.0	3	66.7	2	0
18	Qinghai	6	6	0.0	3	100.0	6	50.0	6	16.7	3	0.0	1	1
19	Shandong	22	22	4.5	22	0.0	22	0.0	21	4.8	21	14.3	1	1
20	Shanxi	3	3	66.7	1	0.0	3	0.0	3	33.3	3	33.3	1	1
21	Shaanxi	2	2	0.0	2	0.0	2	100	2	0.0	2	0.0	0	0
22	Shanghai	1	1	0.0	1	0.0	1	100	1	0.0	1	0.0	0	0
23	Sichuan	24	24	8.3	23	78.3	24	0.0	19	26.3	6	16.7	4	0
24	xinjiang	1	1	0.0	1	0.0	1	100.0	1	0.0	1	100	1	0
25	Yunnan	2	2	100.0	0	0.0	2	50.0	2	50.0	2	0.0	2	0
26	Zhejiang	12	1	8.3	10	0.0	1	8.3	9	0.0	10	50.0	1	0

^aThe number of samples have 2 kinds of heavy metal exceeding at same time; ^b The number of samples have 3 kinds of heavy metal exceeding at same time; ER = Exceeding rate.

TABLE-4
STATUS OF DIFFERENT PREPARATIONS IN CHINESE PATENT MEDICINE (CPM)

Preparation	Total No.	Total No. ^a	Pd		Cd		As		Hg		2 ^b	3 ^c
			Total No. ^a	ER (%)	Total No. ^a	ER (%)	Total No. ^a	ER (%)	Total No. ^a	ER (%)		
Tablets	13	20	20	0.0	20	0.0	20	15	20	75	3	0
Capsules	10	12	12	0.0	12	0.0	12	0.0	12	0.0	0	0
Injections	5	7	7	0.0	7	0.0	7	0.0	7	0.0	0	0
Pills	36	36	36	2.7	36	0.0	36	5.6	36	33.3	2	0
Emulsions	1	3	3	0.0	3	0.0	3	0.0	3	100.0	0	0
Granule	5	7	7	0.0	7	0.0	7	0.0	7	0.0	0	0
Oral Liquid	6	11	11	0.0	11	0.0	11	0.0	11	54.5	0	0
Wines processing	3	3	3	0.0	3	0.0	3	0.0	3	0.0	0	0

Part of them contain heavy metal in combination with CPM; ^aContain different batch numbers; ^b The number of samples have 2 kinds of heavy metal exceeding at same time; ^c The number of samples have 3 kinds of heavy metal exceeding at same time; ER = Exceeding rate.

heavy metal elements exceeding in wines processing, oral liquid, granule, injections and capsules. Other preparations are much more serious especially in pills for they contain the crude drugs. In the 99 samples, Cd doesn't exceed the limit in any preparations; Pd and As exceed the limit only in some pills and tablets; while Hg-contamination is very common in all preparations and the exceeding rates reach as high as 100, 75, 54.5 and 33.3 % in emulsions, tablets, oral liquid and pills, respectively. Part of mineral drugs contains heavy metal in combination with CPM, such as Niu Huang Jie Du Pian, which should not recognize as contamination.

According to the statistical analysis that different types of traditional Chinese medicine, medicament portions, elements, preparations and sources helped to explain the distribution of heavy metal elements in traditional Chinese medicine in china. The results of these study illustrated that most of traditional Chinese medicine have different degrees of heavy metal elements contamination. However, The Pharmacopoeia of the PRC 2005 only provides the following six herbal drugs the top limits on Pd, Cu, Cr, As and Hg, they are Radix Astragali Mongolici, Radix Astragali Mongolici, Radix Salviae Miltiorrhizae, Radix Paeoniae Alba, Radix Panacis Quinquifolii and Flos Lonicerae. In the future work, it is necessary for governmental departments in China, such as State Administration of Traditional Chinese Medicine and State Food and Drug Administration to determine much more traditional Chinese medicine of heavy metal elements. What is more, they should strengthen the regulation on the quality assurance about all of planters, breeder, environment of growth or raise and products-related treatment of traditional Chinese medicine.

At last, what should be emphasized is that some mineral drugs which contain heavy metals as active ingredient should not be treated as contamination. In the future, we should do more research on its pharmacology, efficacy, pharmacokinetics and so on about heavy metal. Research is urgently needed on these areas to provide much more theoretical basis for clinical application, receive the international recognition about the scientificity of mineral drugs with heavy metal and open the international market.

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REFERENCES

- WHO, Herbal Medicines, World Health Organization, Geneva Vol. 16 (2002).
- The Pharmacopoeia Commission of PRC, Pharmacopoeia of the People's Republic of China (2000).
- W.M. Gessler, *Soc. Sci. Med.*, **34**, 735 (1992).
- R.A. Friedman, Natural doesn't mean safe, *The New York Times*, 19 April, A29 (1996).
- L. Yinghong, K.J. Ming, C.L. Sai and G.N. Khang, *Asian J. Chem.*, **19**, 867 (2007).
- A.G. Ramli, Regulatory Control on Toxic Heavy Metals and Therapeutic Drugs, In: Paper Presented at the 3rd International Congress of the Asia Pacific Association of Medical Toxicology, Bayview Beach Resort, Penang, Malaysia, 12-15 November (Abstract 95) (2001).
- R. Bargagli, Trace Elements in Terrestrial Plants: An Ecophysiological Approach to Biomonitoring and Biorecovery, Berlin: Springer, 1-324 (1998).
- M. Koch and W. Rotard, *Water Sci. Technol.*, **43**, 67 (2001).
- B. Isikli, T.A. Demir and T. Akar, *Chemosphere*, **63**, 1546 (2006).
- B.H. Shomar, *Chemosphere*, **65**, 898 (2006).
- K. Steenland and P. Boffetta, *Am. J. Ind. Med.*, **38**, 295 (2000).
- A.S. Andrew, A.J. Warren, A. Barchowsky, K.A. Temple, L. Klei, N.V. Soucy, K.A. O'Hara and J.W. Hamilton, *Environ. Health Perspect.*, **111**, 825 (2003).
- L. Jarup, *Br. Med. Bull.*, **68**, 167 (2003).
- A. Oskarsson, A. Widell, I.M. Olsson and K.P. Grawe, *BioMetals*, **17**, 531 (2004).
- F. Maffucci, F. Caurant, P. Bustamante and F. Bentivegna, *Chemosphere*, **58**, 535 (2005).
- K. Chan, *Chemosphere*, **52**, 1361 (2003).
- M.H. Wong, *Chemosphere*, **50**, 775 (2003).
- Omar, A. Al-Khashman, *Jordan Atmos. Environ.*, **38**, 6803 (2004).
- W. Luo, Y.L. Lu, G. Wang, Y.J. Shi, T.Y. Wang and J.P. Giesy, *Chemosphere*, **72**, 797 (2008).
- L. Kabelitz, *Eur. J. Herb. Med.*, **4**, 25 (1998).
- E. Kang-Yum and S.H. Oransky, *Vet. Hum. Toxicol.*, **34**, 235 (1992).
- A.D. Hardy, H.H. Sutherland, R. Vaishnav and M.A. Worthing, *J. Ethnopharmacol.*, **49**, 17 (1995).
- C.F. Huang, S.H. Liu and S.Y. Lin-Shiau, *Toxicol. Appl. Pharmacol.*, **224**, 192 (2007).
- C.W. Chesterman and K.E. Lowe, The Audubon Society Field Guide to North American Rocks and Minerals, New York: Alfred A. Knopf (1978).
- W.A. Deer, R.A. Howie and J. Zussman, The Rock-Forming Minerals, London: Longman. Group Ltd., pp. 31-45 (1992).
- C. Chuang, K.S. Chen, Y.L. Huan, P.N. Lee and T.H. Lin, *Biol. Trace Elem. Res.*, **76**, 235 (2000).
- Y.P. Zhu, Chinese Material Medica: Chemistry, Pharmacology and Applications, Amsterdam: Harwood Academic Publ. 445-448 (1998).
- The Pharmacopoeia Commission of the People's Republic of China (PRC), 1995, Pharmacopoeia of the People's Republic of China, 1995 ed. Guangdong, China: Guangdong Technology Press and Chemical Industry Press (1995).
- S.L. Yee, S.S. Chu, Y.M. Xu and P.L. Choo, *Med. Singapore Health Policy*, **71**, 133 (2005).