

Edgard O. Espinoza,¹ Dr.PH.; Mary-Jacque Mann,¹ M.F.S.; Bob Bleasdel,² Ph.D.; Steve DeKorte,² B.S.; and Marcus Cox,² B.S.

Toxic Metals in Selected Traditional Chinese Medicinals

REFERENCE: Espinoza, E. O., Mann, M.-J., Bleasdel, B., DeKorte, S., and Cox, M., "Toxic Metals in Selected Traditional Chinese Medicinals," *Journal of Forensic Sciences*, JFSCA, Vol. 41, No. 3, May 1996, pp. 453-456.

ABSTRACT: An examination of traditional Chinese medicine preparations that purport to contain endangered-species products revealed the presence of inorganic forms of mercury and arsenic. We analyzed 12 types of commercially produced herbal ball preparations ($n = 85$) using X-ray fluorescence spectroscopy and atomic absorption spectroscopy. Mercury levels ranged from 7.8 to 621.3 milligrams and arsenic levels ranged from 0.1 to 36.6 milligrams per ball. The recommended adult dose for these preparations is two balls daily. At this dose the maximum elemental intake per day is up to 73.2 milligrams of arsenic and 1.2 grams of mercury. While arsenic poisoning is usually associated with foul play, and mercury poisoning is usually associated with environmental contamination, forensic scientists should be aware that these elements may be consumed in connection with cultural and lifestyle preferences.

KEYWORDS: forensic science, arsenic poisoning, mercury poisoning, traditional Chinese medicine, alternative medicine

Traditional Chinese medicine preparations contain animal, plant, and mineral components that are used alone or in complex combinations to treat illnesses. The Chinese Medicinal Formulas & Strategies (1) lists in excess of 700 pills, powders, and decoctions for the treatment of the same spectrum of symptoms as those dealt with by western clinicians and pharmacists. Traditional Chinese herbal medicines are sold as premixed patented preparations, or they are freshly made by individual practitioners or herbalists. Herbal remedies are generally considered to be mild and safe (2), however, poisonings, deceptive labeling, and adulteration with Western-style pharmaceuticals have been reported (2-11). Analyses conducted by the National Fish & Wildlife Forensic Laboratory of herbal ball medicinals that claim to contain endangered-species products such as rhinoceros horn, tiger bone, and musk deer glandular secretions revealed the presence of toxic metals.

Herbal balls are aromatic, malleable, earth toned, roughly spherical, hand-rolled mixtures with diameters that range from approximately 1.5 to 2.5 cm and weights that range from approximately 2.5 to 9.0 g. Some balls display a thin gold outer coating. With one exception, all the balls examined in connection with this study were individually sealed within hollow wax or wax-coated plastic

¹Forensic Science Branch Chief and Criminalistics Section Chief respectively, National Fish and Wildlife Forensic Laboratory, Ashland, Oregon.

²Professor, and Senior Students, respectively, Chemistry Department, Southern Oregon State Collage, Ashland, Oregon.

Received for publication 5 June 1995; revised manuscript received 11 Sept. 1995; accepted for publication 16 Oct. 1995.



FIG. 1—Samples of traditional Chinese medicines.

spheres.³ The spheres are individually packaged in clear plastic sleeves or in brightly colored cardboard boxes. Balls can be purchased in cartons of six to ten or as singles. Literature accompanying most of the herbal ball preparations instructs the patient to dissolve and consume the balls in warm wine or water. Adults take two or more balls per day. Children take portions of balls. The instructions with five of the twelve herbal ball preparations advised women against taking the balls during pregnancy. All of the examined herbal balls were factory produced patented medicinals manufactured in China. The major uses for the herbal balls examined with connection with this study are listed in Table 1.

We identified the presence of arsenic and mercury in these herbal balls by X-ray fluorescence and/or atomic absorption spectroscopy.

Materials and Methods

Herbal balls examined in connection with this study were from commercial shipments intercepted at U.S. ports of entry by the U.S. Fish & Wildlife Service. X-ray fluorescence (XRF) spectroscopy and/or atomic absorption (AA) spectroscopy were used to

³The exception was *Dendrobium Moniliforme* Night Sight Pills in which each plastic sphere contained 50, approximately 0.5 cm 150 mg mini-balls.

TABLE 1—Name and major uses of herbal ball samples.

Samples	Pidgin name	Name in English	Major uses:
1	An Gong Niu Huang Wan	Calm the Palace Pill with Cattle Gallstone	High fever, irritability and restlessness, delirious speech.
2	Da Huo Luo Wan	Bolus for Easing Tendons and Collaterals	Expelling wind and dampness, easing the tendons and collaterals.
3	Unknown	Dendrobium Moniliforme Night Sight Pills	Dim eyesight, blurred vision, cataracts.
4	Niu Huang Chiang Ya Wan	Pills of Calculus Bovis for Lowering Blood Pressure	Vertigo, Dizziness, tinnitus, headache.
5-8	Niu Huang Ching Hsin Wan	Bezoar Antifebrile Pills	Febrile illness, dysphasia, delirium, vertigo, fever.
9	Niu Huang Qing Xin Wan	?	?
10	Ta Huo Lo Tan	Veins and Arteries Relieving Pills	Rheumatism, stiff neck, backache, dysphasia.
11	Tsai Tsao Wan	Revival Pills	Rheumatism, facial paralysis, dysphasia, apoplexy.
12	Yan Shen Jai Jao Wan (Chu Kiang Brand)	Revival Pills	Hemiplegia caused by apoplexy and sputum, palsy.

analyze 85 herbal balls representing 12 distinct manufactured preparation types (Table 2). Each distinct manufactured preparation type was identified by the product name and the name and location of the manufacturer as printed on the box or carton. In most cases these names were factory printed in pidgin English (phonetic spellings for Chinese words or characters). Each preparation type was assigned a sample number from one to twelve. Each sample number contains from one to 28 individually analyzed herbal balls.

Qualitative elemental analysis was non-destructively performed using an Asoma (Baird) EX-6000 X-ray fluorescence spectrometer equipped with a rhodium tube and operated with 40 kV at 100 uA. Dead time was maintained between 30 and 50%. No sample preparation was required for XRF analysis beyond halving individual balls for placement in the instrument.

For quantitative analysis by AA, herbal balls were digested in 80 mL of 1:1 concentrated HCl and concentrated HNO₃ for 3 h at 100°C. Each digest solution was filtered and the volume was adjusted to 100 mL with water and diluted (10 fold) with HCl/HNO₃/H₂O (40:40:20). The solutions were analyzed for arsenic by flame atomic absorption spectroscopy using the Instrumentation

Laboratory 151, 455 AA/AE with an arsenic hollow cathode lamp (Cathodeon Ltd., type 3QNY/As. 13 mA max. current, neon filler gas). The 193.7 nm line was used for analysis with a slit width of .32 nm. Mercury analysis was conducted on the same instrument, with an Hg hollow cathode lamp (Instrumentation Lab. Inc. #62847A, 15 mA max. current, type A filer gas). The 253.7 nm line was used as the analytical wavelength with a slit width of .32 nm. Quantitative arsenic standards (2, 10, 20, 50, 120 µg/g; $y = 0.9992x + 0.766$; $R^2 = 0.995$) were prepared from a 1000 ppm arsenic standard (by High-Purity®). Quantitative mercury standards (50, 100, 200, 400, 600, 800 and 1000 µg/g; $y = 0.0008x^2 + 0.0745x + 52.934$; $R^2 = 0.9972$), were prepared from a 1000 ppm mercury standard (by High-Purity®). Standards contained HCl/HNO₃/H₂O (40:40:20).

Results

Table 2 lists the results of the XRF and AA analysis.

XRF analysis of samples 1, 5, 6, 7, 9 and 11 revealed the presence of arsenic and mercury. Samples 4 and 10 contained

TABLE 2—Analysis of herbal ball samples using X-ray fluorescence and atomic absorption spectroscopies.

Sample	Medicinal	Manufacturer	Arsenic (XRF)	Mercury (XRF)	Arsenic range per herbal ball (mg) (AA)	Mercury range per herbal ball (mg) (AA)
1	An Gong Niu Huang Wan (n = 4)	Tung Jen Tang Pharmaceutical Factory, Nanjing, China	Yes	Yes	3.21-36.6	80.7-621.3
2	Da Huo Luo Wan (n = 9)	Guangzhou Chen Li Ji Pharmaceutical Factory, Guangzhou, P.R. China	No	Yes	ND-0.1	12.9-23.3
3	Dendrobium Moniliforme Night Sight Pills (n = 5)	Tientsin Drug Manufactory, Tientsin, China	No	No	ND-0.6	18.9-28.1
4	Niu Huang Chiang Ya Wan (n = 9)	Tianjin Drug Manufactory, Tianjin, China	Yes	No	6.9-9.5	ND-45.4
5	Niu Huang Ching Hsin Wan (n = 28)	Peking Tung Jen Tang, Peking, China	Yes	Yes	1.3-2.7	22.3-181.8
6	Niu Huang Ching Hsin Wan (n = 8)	Tientsin Manufactory, Tientsin, China	Yes	Yes	3.4-9.9	24.5-70.5
7	Niu Huang Ching Hsin Wan (n = 4)	Beijing Tongren Tang, Beijing, China	Yes	Yes	—	—
8	Niu Huang Ching Hsin Wan (n = 1)	Beijing Tung Ren Tang, Beijing, China	No	No	—	—
9	Niu Huang Qing Xin Wan (n = 1)	JH	Yes	Yes	—	—
10	Ta Huo Lo Tan (n = 6)	Beijing Tung Jen Tang, Beijing, China	Yes	No	14.9-22.1	41.6-99.0
11	Tsai Tsao Wan (n = 7)	Peking Tung Jen Tang, Peking, China	Yes	Yes	ND-0.6	7.8-15.9
12	Yan Shen Jai Jao Wan (n = 3)	United Pharmaceutical Manufactory, Fushan, China	No	Yes	—	—

arsenic only. Mercury alone was found in samples 2 and 12. No toxic metals were found in samples 3 or 8.

Additional herbal balls from samples 1, 2, 3, 4, 5, 6, 10 and 11 were also analyzed by AA. Mercury and arsenic were detected in all of the preparation types. Mercury levels ranged from 7.8 to 621.3 mg per ball and arsenic levels ranged from 0.1 to 36.6 mg per ball.

Discussion

Significant variability of toxic metals within a manufacturer's preparation was observed. Samples 1 and 5 exemplify this content variability. AA analysis of three herbal balls from the same carton in sample 1 (An Gong Niu Huang Wan) revealed mercury levels that ranged from approximately 80 to over 600 mg. A similarly broad mercury range was observed in sample 5 (Niu Huang Ching Hsin Wan) where a range of approximately 22.0 to over 180.0 milligrams was detected both within and between three different lot numbers.

Product variability may be explained by the batching process, large scale manufacturing, and minimal to no government regulation of the herbal industry in some of the producing countries. There are hundreds of medicinal factories in China (12), however, little has been published on the medicinal manufacturing process. Anecdotal reports indicate that the process is human labor intensive and with minimal mechanization by Western standards. The process has been characterized as involving large scale aqueous or alcoholic extractions in 200–300 gallon vats. Scores of ingredients are manually introduced and mixed. This method lends itself to the type of batch heterogeneity that we have observed and is consistent with the data of Fraser et al. in the analysis of other medicinal products (9). Hong Kong and The People's Republic of China are two of the largest exporters of medicinal products to Western nations. In Hong Kong, local Chinese medicines and traditional Chinese herbal practitioners are exempted from regulations due to legal protection of ethnic Chinese customs and a general lack of governmental knowledge about herbs (5,6). The Chinese government regulates, subsidizes, and promotes herbal products produced in China. Chinese labeling practices are reportedly more commercial than scientific, and substitution of listed ingredients without consumer notification is permitted (12–14).

Although we could not identify the molecular forms of arsenic and mercury in the herbal balls, we believe they are the sulfide salts of arsenic and mercury because of 1) physical/chemical observations, 2) the prevalence of sulfide forms of arsenic and mercury in nature, and 3) the official listing of arsenic sulfide (realgar and pyritum) and mercury sulfide (cinnabaris [*sic*], cinnebar) in the Chinese pharmacopeia (15).

An extensive review of the literature did not reveal listings for the LD₅₀ values for mercury sulfide or arsenic sulfide (16–23). Toxicity data is inferred from arsenic sulfide (As₂S₃, and/or As₄S₄) and mercury sulfide (HgS) poisonings from herbal preparations consumed in Singapore and London.

Arsenic Sulfide

Chronic and acute arsenic poisoning of 74 traditional Chinese medicine consumers in Singapore was reported in 1975. Tay et al. reported chronic arsenic sulfide poisoning from an average intake of approximately 10.3 mg per day. A total of 64% of the patients had consumed a locally produced anti-asthmatic herbal medicinal containing 12,000 µg/g (12 mg/g) of arsenic sulfide (24).

Mercury Sulfide

Cinnabar was present in Indian ethnic herbal remedies taken by two patients treated for heavy metal intoxication at London hospitals. Kew et al. reported chronic mercury sulfide poisoning in these patients from consuming approximately 262 mg per day. It is interesting to note that the medicinal consumed by one of the patients also contained inorganic arsenic (25).

The minimum recommended adult dose for the preparations in this study was two balls daily. At this dose the maximum elemental intake per day are up to 73.2 mg of arsenic and up to 1.2 g of mercury. These levels exceed the injurious quantities for arsenic sulfide reported by Tay et al. (24) and mercury sulfide reported by Kew et al. (25).

The use of traditional Chinese medicine is closely associated with Asian countries, however, these products are also widely available to Western consumers. Herbal exports, including fresh herbs and patented medicinals, bring an estimated annual income of US \$1 billion in foreign currency to China. Herbs and medicinals sold in the U.S. are imported from China, Hong Kong, Japan, North and South Korea, Malaysia, Taiwan, and Thailand (14). Chinese type herbal products are beginning to appear in U.S. health food stores and may also be obtained through local traditional Chinese medicine practitioners, mail orders, and Asian pharmacies (12).

Eisenberg et al. (26) reported that approximately one-third of the respondents in a nationwide U.S. survey had used unconventional therapies, including herbal medicines. While arsenic poisoning is usually associated with foul play, and mercury poisoning is usually associated with environmental contamination, forensic scientists should be aware that these elements may be consumed in connection with cultural and lifestyle preferences.

Acknowledgments

We thank Joey Ngan, Director of Security and Safety, Southern Oregon State College for translating Chinese characters; Bruce Taylor, M.D., Research Associate, NFW Forensic Laboratory and Mark Kirms, Ph.D., Senior Forensic Chemist, NFW Forensic Laboratory for critical reviews; Larry Elliott, Analytical Chemist, FDA Seattle District for quantitative analytical work in our preliminary paper on Asian medicinals; David B. Chandler, Ph.D., Director, Hazardous Materials Program, Oregon Health Sciences University, and Mary Maruca, USFWS, for providing invaluable toxicology reference materials.

References

- (1) Bensky D, Barolet R. Chinese medicinal formulas and strategies. Eastland Press, Inc. Seattle, Washington, 1990.
- (2) But PPH. Herbal poisoning caused by adulterants or erroneous substitutes. *J Tropical Med Hygiene* 1994;97:371–74.
- (3) But PPH, Tai YT, Young K. Three fatal cases of herbal aconite poisoning. *Veterinary Hum Toxicol* 1994;36(3):212–15.
- (4) Dickens P, Tai YT, Tomlinson B, Ng HK, Yan KW. Fatal accidental aconite poisoning following ingestion of Chinese herbal medicine: a report of two cases. *Forensic Sci Int* 1994;67:55–58.
- (5) Ng THK, Chan YL, Chang CM, Ho HC, Leung SY, But PPH. Encephalopathy and neuropathy following ingestion of a Chinese herbal broth containing podophyllin. *J Neurolog Sci* 1991;101:107–13.
- (6) Tai YT, But PPH, Young K, Lau CP. Cardiotoxicity after accidental herb-induced aconite poisoning. *Lancet* 1993;340:1254–56.
- (7) Wu YB. Aconite poisoning: review of experience in China over the past 30 years. *Fiangsu Zhong Yi (Fiangsu J Chin Med)* 1988;12:39–42.

- (8) Roberts RQ. Is there Valium in your tea? *Toxi-News* 1991;3(3):8.
- (9) Fraser DB, Tomlinson J, Satzger DR. Analysis of black pearl and other herbal preparations. Abstract. *Proc Am Acad Forensic Sci* 1995;208.
- (10) Anonymous. Chinese herbal medicine toxicity. *Herbalgram* 1995; 33:16.
- (11) Abt AB, Oh JY, Huntington RA, Burkhart KK. Chinese herbal medicine induces acute renal failure. *Arch Int Med* 1995;23, 155(2):211-2.
- (12) Anonymous. AHPA issues Chinese patent medicine policy. *Herbalgram* 1995;33:22.
- (13) Chang, Hsien-cheh. Overview of rhinoceros horn and tiger bone problem in Taiwan. *China Medical College*, October 1994:10.
- (14) Gaski AL, Johnson KA. Prescription for extinction: Endangered species and patented oriental medicines in trade. *Traffic USA* 1994;13:4-5.
- (15) Bensky D, Gamble A. *Chinese herbal medicine materia medica*. Revised edition, Eastland Press Inc., Seattle, Washington, 1993:287, 400, 449.
- (16) Luckey TD, Venugopal B. *Metal toxicity in mammals, Vol. 1*. Plenum Press, New York, 1977.
- (17) Venugopal B, Luckey TD. *Metal toxicity in mammals, Vol. 2*. Plenum Press, New York, 1978.
- (18) Doull J, Klaassen CD, Amdur MO. *Casarett and Doull's toxicology*. Second edition. Macmillan, New York, NY, 1980.
- (19) Burman E. *Toxic metals and their analysis*. Heyden & Son Ltd. 1980.
- (20) Gosselin RE, Smith RP, Hodge HC. *Clinical toxicology of commercial products*. Fifth Edition. Williams & Wilkins, Baltimore, MD, 1984.
- (21) Goodman and Gilman's *The pharmacological basis of therapeutics*. Eighth edition. Pergamon Press, New York, NY, 1990.
- (22) Dreisbach RH, Robertson WO. *Handbook of poisoning: prevention, diagnosis & treatment*. Twelfth edition. Appleton & Lange, Los Altos, CA, 1987.
- (23) TOXNET Database. National Institute of Health, Bethesda, MD, April 1995 Search.
- (24) Tay CH, Seah CS. Arsenic poisoning from anti-asthmatic herbal preparations. *Med J Australia* 1975;2:424-28.
- (25) Kew J, Morris C, Aihie A, Fysh R, Jones S, Brooks D. Arsenic and mercury intoxication due to Indian ethnic remedies. *Br Med J* 1993;306:506-07.
- (26) Eisenberg DM, Kessler RC, Foster C, Norlock FE, Calkins DR, Delbanco TL. Unconventional medicine in the United States. *New Engl J Med* 1993;328(4):246-52.

Address requests for reprints or additional information to
Edgard O. Espinoza
National Fish and Wildlife Forensic Laboratory
1490 E. Main Street
Ashland, OR 97520