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FILE: · **Aristolochia (*Aristolochia fangchi)***
· **Herb safety**
· **Herb adulteration**
· **Traditional Chinese Medicine (TCM)**

DATE: December 6, 2000 HC 060806

RE: Urinary Cancer Associated with Chinese Herb Aristolochia

Nortier, J.L. et al. Urothelial carcinoma associated with the use of a Chinese herb (*Aristolochia fangchi*). *The New England Journal of Medicine,* No. 23, 2000, pp. 1686–1692.

Kessler, D.A. Cancer and Herbs. Editorial. *The New England Journal of Medicine,* No. 23, 2000, pp. 1742–1743.

Kidney failure has been reported in some women who have taken a Chinese herbal weight-reducing formula and the condition has been named Chinese-herb nephropathy. The herbal formula purportedly contained *Stephania tetrandra* and *Magnolia officinalis*, however, analysis determined that *Stephania tetrandra* had been inadvertently substituted with *Aristolochia fangchi*. This was based on the presence of aristolochic acids, a component of *A. fangchi* but not the other ingredients. Because aristolochic acids are known to be potently carcinogenic and several patients with Chinese-herb nephropathy subsequently developed urinary tract cancer, the authors undertook a study of all patients in their practice with Chinese-herb nephropathy to determine the prevalence of cancer and to see if a correlation existed between cumulative dose and cancer incidence.

One hundred and five patients in the authors' practice in a Belgian weight-loss clinic had Chinese-herb nephropathy. All but one were women, and all had taken the adulterated herbal formula distributed over the years 1990-1992 for an average of 13.3 months. Some patients were also taking appetite suppressants (serotonin agonists) and acetazolamide. End-stage kidney failure occurred in 43 of these patients 3 to 85 months after ending treatment. All patients were informed of their risk of cancer and were given the option to undergo prophylactic removal of the kidneys and ureters. Of these, 39 opted for surgery. The removed organs were examined for signs of cancer. Cancer was found in 18 out of 39 cases, and mild to moderate dysplasia (a pre-cancerous condition) was found in 19 of the 21 remaining cases. DNA adducts typical of those found upon exposure to aristolochic acid were found in the kidneys of all patients, but not in kidneys of control patients who had had kidney removal for other diseases. No adducts were found of a kind expected upon exposure to another renal toxin, ochratoxin A. Of the patients ingesting greater than 200 g *A. fangchi* cumulatively, 66% had cancer, whereas only 33% of those ingesting less than 200 g cumulatively did.

The Chinese herb industry has noted that there are other possible explanations for the observed kidney pathology, including the other treatments that were administered along with the herbal formula. However, the data presented in this paper strongly support the assertion that aristolochic acids from *A. fangchi* are the causa-

tive agent in both Chinese-herb nephropathy and subsequent urinary tract cancer. The evidence includes: the known carcinogenic property of aristolochic acid in humans and animals, the presence of aristolochic acid in the herbal formula, the presence of DNA adducts specific to aristolochic acid in patient kidneys, the correlation of *A. fangchi* cumulative dose with cancer incidence, the lack of symptomology associated with other renal toxins (ochratoxinA), and the absence of alternative causative factors in the histories of some patients developing cancer (use of tobacco, analgesics or serotonin). The authors urge physicians to question their patients about use of herbs when renal disease is presented.

In an accompanying editorial, D. Kessler, M.D., former commissioner of the U.S. Food and Drug Administration (FDA) and current Dean of the Yale School of Medicine, points out that the study had no comparison group and that the analysis of the removed kidneys was not done in a blinded fashion. Despite this, he considers existing evidence compelling enough to urge banning the sale of *A. fangchi* in the U.S., as it is in Canada, Australia, the United Kingdom and Germany. The herb is available today for purchase in the U.S. although it is not widely found. (The American Herbal Products Association previously notified it's members to check for possible substitutions of some Chinese herbs with *Aristolochia* in 1997.) Kessler, who was FDA Commissioner when Congress passed the Dietary Supplement Health and Education Act of 1994 and unsuccessfully opposed it's passage, argues that the Aristolochia case is evidence of the need to have Congress alter DSHEA "to ensure the safety and efficacy of dietary supplements before more people are harmed." However, according to provisions by DSHEA, the FDA is required to promulgate stricter good manufacturing practices (GMPs) for the manufacture of dietary supplements, which the agency has yet to do. If there were a system of enhanced GMPs in place to deal with these products, it is most likely that problems of adulteration and substitution of safe herbs like *Magnolia* and *Stephania* with toxic herbs like *Aristolochia* would be greatly reduced or prevented altogether. Thus, the enactment of GMPs as already stipulated by DSHEA should come before Congress begins to tinker with this law, as suggested by Dr. Kessler. Also, it should be noted that all cases of *Aristolochia fangchi* toxicity published to date have occurred in other countries – not in the U.S. For more on this subject, please see Chen J, Nephropathy Associated With the Use of Aristolochia, *HerbalGram* Vol. 48, 2000.

—Risa N. Schulman, Ph.D.
—Mark Blumenthal

Enclosure: Notier, J.L. et al. Urothelial carcinoma associated with the use of a Chinese herb (*Aristolochia fangchi*). *The New England Journal of Medicine,* No. 23, 2000, pp. 1686–1692. Kessler, D.A. Cancer and Herbs. Editorial. *The New England Journal of Medicine,* No. 23, 2000, pp. 1742–1743.

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