

## **FDA Alerts Americans of Possible Danger of Herbal Supplements that May Contain Aristolochic Acid**

On May 31, 2000, the Food and Drug Administration issued a bulletin alerting people of the possible danger of herbs that may contain Aristolochic Acid. They list in the bulletin all plants related to the herb species *Aristolochia* – some of which contain Aristolochic Acid and some that do not. This bulletin was issued as a result of findings from a Belgian study that were being published the following week in the *New England Journal of Medicine (NEJM)*.

### **Background.**

The study published in the *NEJM* on June 8, 2000 reported that the use of the Chinese herb, *Aristolochia fangchi*, is associated with end-stage kidney failure and urinary system cancer. This was discovered when 18 of 105 patients that entered a weight loss study in Belgium between 1990 to 1992 developed urinary cancer after ingesting a slimming preparation that contained fenfluramine, diethylprion, cascara powder, belladonna extract, acetazolamide, *Stephania tetrandra* and *Magnolia officinalis*. The kidney failure and urinary cancer were attributed to the inadvertent substitution of *Aristolochia fangchi* – a Chinese herb that is known to be toxic to the kidneys and cancer-causing – for *Stephania tetrandra*, the proper and safe herbal medicine (which does not contain Aristolochic Acid) that was intended for the weight loss prescription. This substitution was thought to have been made because it can be very difficult to visually differentiate between the two herbs and because their names in Chinese are similar. Aristolochic Acid was the component implicated as the carcinogenic substance and this herb, either alone or in conjunction with the other medicinals/botanicals in the formula, was suspected to have caused the kidney failure observed in study subjects.

### **Frequency of Use in the United States.**

Use of products with Aristolochic Acid is uncommon in the U.S., primarily limited to products purchased over the Internet and presumably by manufacturers with less rigid testing criteria and standards. No adverse events reports have been received by the FDA directly, but the medical literature does cite cases of nephrotoxicity and cancer development associated with products containing Aristolochic Acid.

### **Response by the Manufacturers of Chinese Herbal Formulas.**

The majority of Chinese Herbal/Medicinal distributors have strict tests to assure that their herbs do not contain Aristolochic Acid, and several have even tightened their quality assurance standards further in response to the FDA alert. Several companies have issued their own statements guaranteeing safety tests for suspected herbs and formulas that contain suspect herbs. The majority of manufacturers have voluntarily stopped all distribution of products containing suspect herbs even though scientific evidence is still considered inconclusive. It is best to consult a qualified, licensed Chinese Medical Herbalist for herbal

prescriptions and to assure safety precautions in obtaining herbal medicines. The FDA has issued a bulletin to health care professionals recommending they discard all products received prior to the alert that may contain suspect herbs.

### **Dose and Duration of Use Implicated in Adverse Events.**

While this and other recent reports in Europe have brought concern specifically regarding botanicals containing Aristolochic Acid, adverse events are quite uncommon when Chinese Herbs are used in traditional formulas and doses according to Traditional Chinese Medicine. The *NEJM* study prescription contained *Aristolochia fangchi* in a dose that was more than a thousand times greater than traditional doses and for a much longer duration than clinically appropriate. This was in addition to the fact that it was wrongly substituted for the intended *Stephania tetrandra*.

No recall or ban has been issued on products containing any of the suspected herbs, but the FDA has provided a list of herbs that are suspect and is considering imposing appropriate regulatory actions regarding these products. As of July 6, 2000, an import alert was issued by the FDA allowing for the detention of dietary supplements and other products that may contain Aristolochic Acid with the possibility of imposing charges. Improved quality assurance by manufacturers including full botanical naming, macroscopical and microscopical evaluations will help avoid any similar future occurrences with the inadvertent substitution of herbs containing Aristolochic Acid and their improper usage.

#### *References:*

Ellis, A. Aristolochic Acid and Chinese Herbs. *Golden Flower Chinese Herbs*, Summer 2000.

Gruenwald, J, Brendler, T, Jaenicke, C, eds. *PDR for Herbal Medicines*. New Jersey: Montvale, 1998.

Internet site: <http://www.vm.cfsan.fda.gov/~dms/ds-bot.html>. Accessed August 2000.

Nortier, JL, Martinez, MC, Schmeiser HH, Arlt, VM, et al. Urothelial carcinoma associated with the use of a Chinese herb (*Aristolochia fangchi*). *New England Journal of Medicine*. June 8, 2000; 342(23):1686-92.

Zhu, M, Phillipson, JD. Hong Kong Samples of the Traditional Chinese Medicine "Fang Ji" Contain Aristolochic Acid Toxins. *International Journal of Pharmacognosy*. 1996; 34(4):283-289.