

Dangers of Chinese Medicine Brought to Light by DNA Studies

Sequencing pinpoints origins and helps reveal unknown ingredients

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Traditional Chinese medicine (TCM) is enjoying increasing popularity all over the world. But two molecular genetics studies published this week show that the trendy treatments can be harmful, as well. The papers focus attention on the fact that not all of their ingredients are listed, or even legal, and that some can cause cancer.

"These two studies show very clearly how dangerous the products of TCM can be," says Fritz Sörgel, the head of the Institute for Biomedical and Pharmaceutical Research in Nuremberg, Germany, who was not involved in the work. "The public needs to be better informed about these dangers."

Hundreds of millions of dollars are spent on TCM products each year—a growing portion of it on the Internet—and some scientists are looking at these preparations hoping to discover new pharmacological substances. Many would like to emulate the success of Tu Youyou, the Chinese scientist who isolated *artemisinin*, now the world's most important malaria drug, from an ancient Chinese medicine. Tu won a Lasker award last year, and is rumored to be a Nobel candidate.

But critics have long warned that some mixtures can also contain naturally occurring toxins, contaminants like heavy metals, added substances such as steroids that make them appear more effective, and traces of animals that are endangered and trade-restricted.

Now, researchers at Murdoch University in Australia have investigated the problem using modern sequencing technology. The team, based at the university's Australian Wildlife Forensic Services and Ancient DNA Laboratory in Perth, analyzed 15 samples of traditional Chinese medicine seized by Australian border officials.

"We took these traditional preparations, smashed them to pieces, and extracted the DNA from the powder," explains molecular geneticist Michael Bunce. The scientists then fished out copies of two specific genes, *trnL*, a chloroplast gene common to all plants, and *16srRNA*, conserved among plants and animals, and multiplied and sequenced them. By comparing the sequences to those in genetic databases, they could pinpoint the animals and plants used to make the medicine. "Sometimes we really struggled to assign a particular DNA to a particular species," Bunce says. But as genetic databases expand, this should become easier.

Some products contained material from animals classified as vulnerable or critically endangered, such as the Asiatic black bear and the Saiga antelope—just as the producers claimed. But often, the medicine also harbored ingredients not mentioned on the packaging, the team reports online today in *PLoS Genetics*. "For example, a product labeled 100 percent Saiga antelope contained considerable quantities of goat and sheep DNA," Bunce writes.

"Using DNA to identify the animal species and thus prove illegal trading is very elegant," says Dietmar Lieckfeldt, who works in molecular forensics at the Leibniz Institute for Zoo and Wildlife Research in Berlin, Germany. Identifying animals by their DNA has been possible for a while, he says, but the next-generation sequencing technology makes it possible to nail different species in a mixture very quickly.

In the herbal preparations, Bunce and his colleagues found members of 68 different plant families, among them plants of the genera *Ephedra* and *Asarum*. Both can contain toxic chemicals such as aristolochic acid, a compound banned in many countries because it causes kidney disease and upper urinary tract cancer (UUC). While detecting DNA from a certain species does not mean that a toxin produced by that plant is present, chemical analysis of one of the four samples containing *Asarum* DNA did turn up aristolochic acid.

The threat posed by aristolochic acid is also highlighted in a paper published in the *Proceedings of the National Academy of Sciences* on Monday. The researchers, led by pharmacologist Arthur Grollman of Stony Brook University, focused on Taiwan, the country with the highest rate of UUC in the world. A previous analysis had shown that roughly one-third of the Taiwanese population consumed herbs likely to contain aristolochic acid.

The scientists sequenced the tumors of 151 patients with UUC. Among patients with characteristic mutations in the important tumor-suppressor gene *TP53*—which make people more vulnerable to cancer—84% also showed a known molecular signature of exposure to aristolochic acid, they found. The study provides compelling evidence that aristolochic acid is a primary cause of UUC in Taiwan.

Bunce and his colleagues also found DNA from plant families known to contain medicinally important species that could pose risks when used in combination with other drugs, as well as DNA from soybean and plants of the cashew family, which can contain allergens. "This just shows that the ingredients in these preparations aren't accurately declared," Bunce argues. Indeed, says Sörgel, the studies show that partaking in traditional Chinese herbal medicine is a gamble.