

Ancient herbal medicine boosts influenza arsenal

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By Sara Shipley Hiles, Globe Correspondent | November 14, 2005

Slurp up a bowl of noodles at Pho Republique, a hip Asian fusion restaurant in Boston's South End, and you'll get a taste of the latest weapon in the world's war against bird flu.

Star anise, a fragrant, licorice-flavored spice used for centuries in Chinese cooking and medicine, plays a modern role in making one of the most sought-after drugs in the world. Eight-pointed seed pods picked from Chinese evergreen trees form the raw material for manufacturing Tamiflu, one of the few treatments for seasonal flu, and now a possible weapon against an avian flu pandemic.

Scientists who study botanicals -- plants used for medicinal purposes -- say it's not surprising that an herb used as a flavoring in Chinese Five Spice powder and the French liqueur Pernod could yield a powerful drug. Roughly 40 percent of medications come from botanicals, including aspirin and the breast cancer medication tamoxifen.

The process used to make star anise fruits into an antiviral drug is long and complicated, far removed from bowls of steaming noodles and the shelves of traditional Chinese pharmacies.

The star anise tree, a member of the magnolia family, grows in the misty mountains of four provinces in southwest China. Workers harvest its delicate star-shaped fruits by hand and then dry them in kilns.

The drug manufacturer Roche Holding AG of Switzerland processes the fruits to obtain shikimic acid, the raw material used to make Tamiflu. Spokesman Al Wasilewski would not describe the manufacturing process in detail, saying it was proprietary.

But Roche medical director Dominick Iacuzio said in testimony before Congress in May that making the drug takes eight to 12 months, using many intermediary steps, including a "potentially explosive" one that can be carried out only in specialized facilities.

Some reports claim that Roche already has bought up 90 percent of the star anise crop, creating a shortage that might limit future production of the drug. Wasilewski would not comment on those reports, but he said the company is not limited by availability of star anise.

Star anise got picked as the building block for Tamiflu because it happens to have a high concentration of shikimic acid, but the acid is found in nearly every plant, and Tamiflu was originally made from a different acid found in the bark of the cinchona tree grown in Zaire -- a source that was abandoned because of the political upheaval in that country.

Roche has since developed a method of obtaining shikimic acid from bioengineered *E. coli* bacteria using a fermentation process, Wasilewski said. This method currently accounts for a third of Roche's shikimic acid production, and the company is working to increase that amount, he said. It is also continuing to expand production, which, by the middle of next year, will have increased tenfold since 2003.

Roche has donated 3 million courses of the drug to the World Health Organization to be used in the event of an outbreak of human-to-human transmitted avian flu. The US Health and Human Services Department plans to stockpile about 4.3 million courses of Tamiflu, enough for about 1.5 percent of the American population.

Tamiflu works by preventing the flu virus from replicating. Even if Tamiflu does work against the bird flu virus, which is not entirely clear, it will shorten the period of infection, but probably not prevent someone from getting infected in the first place. With no vaccine to prevent bird flu yet developed, panicked consumers are rushing to buy any defense they can find.

Chinese and Western medicine practitioners alike said eating or drinking star anise -- which can cost nearly \$27 a pound for whole stars -- is not the answer.

Star anise "goes through several intermediate steps [to become Tamiflu], and some of them are very toxic," said Norman Farnsworth, director of a federally funded botanical research center at the University of Illinois at Chicago.

"I certainly wouldn't recommend to my patients to buy and eat star anise," said Weidong Lu, chairman of the Chinese herbal medicine department at the New England School of Acupuncture in Watertown.

Lu said using star anise for bird flu goes against the traditional theory of Chinese medicine, which calls for balancing a "hot" condition, like the fever that comes with flu, by using a "cold" treatment, such as eating mung bean sprouts. Star anise is considered a "hot" substance because it's spicy, so it wouldn't make sense to use it for the flu, he said.

Instead, star anise has been used traditionally to treat pain, hernia, and stomach discomfort, said John Chen, a registered pharmacist and traditional Chinese medicine practitioner in Los Angeles. "I use star anise mostly for gastrointestinal complaints, and it works well for that," he said.

The herb is also popular in making tea to treat cough or colic in babies, though the Food and Drug Administration issued an advisory two years ago against using star anise teas because some infants who drank the tea suffered seizures, vomiting and other neurological effects. The agency said the tea might have contained Japanese star anise, which contains a toxic chemical. Chinese star anise, an herb that looks the same but is botanically very different, is considered safe to eat.

Linda Barnes, a medical anthropologist and associate professor at Boston University School of Medicine, said star anise tea is still popular. She was coughing recently when she visited a local santero, a traditional Cuban medical practitioner. The man's wife jumped up and brewed her a tea made from ginger root, star anise, and honey. It worked, and Barnes thought it was good enough to try at home.

But by far the most common everyday use of star anise is as a cooking spice, in Chinese "red liquid" cooking, Thai iced tea, some Indian foods, and Western-style jams and pickled vegetables.

Armond Sreesuvan, a sous chef at Pho Republique, said the restaurant uses about 250 whole stars a week to make the pho, or noodle dishes, for which the restaurant is named. One star is boiled in the broth for each dish, then removed before serving. "You always need to put star anise in pho, always," he said.

Sreesuvan said he didn't know anything about bird flu, but star anise, he said, is "very special." ■