

# Bitter Orange Under Scrutiny as New Ephedra

By **MARY DUENWALD**

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A year and a half ago, when the Food and Drug Administration banned the sale of [diet supplements](#) containing ephedra, many doctors worried that people who had been taking them would switch to other appetite suppressants of questionable safety.



Bitter orange peel was one often mentioned, because it is the main ingredient in many products marketed as "ephedra free."

Bitter orange peel, weight-loss specialists warn, may be as dangerous as ephedra, which had been the subject of thousands of reports of adverse reactions, including heart attack, stroke and sudden death. Its main component, synephrine, is chemically similar to ephedrine, the active ingredient in ephedra.

A new study from the University of California, San Francisco has found evidence that in similar doses bitter orange alone is not as potent as ephedra. In the 10 experimental subjects who tried it, bitter orange increased the heart rates, but not as much and not for as long as ephedra, said Dr. Christine Haller, an assistant professor of medicine who led the study.

The same study also suggests that when bitter orange peel is combined with caffeine, as it is in many supplements advertised as ephedra free, it can raise the heart rate and the [blood pressure](#). That may be a cause for alarm, Dr. Haller said, because the 10 subjects who tried the supplements were healthy people from 19 to 42.

"We don't know what happens to older people who take bitter orange and caffeine who are obese or have any other health problems," Dr. Haller said.

Dr. Jonathan Waitman, a specialist in internal medicine and clinical [nutrition](#) at the Comprehensive Weight Control Program at New York-Presbyterian/Weill Cornell hospital, said the study pointed out the risks inherent in taking untested over-the-counter weight-loss pills.

"My take-home point would be that you don't know what you're getting when you take one of these supplements," Dr. Waitman said. "There's no way for the consumer to use caution other than not to buy these at all."

The F.D.A. does not require manufacturers of dietary supplements to prove that the products are safe and effective before they are sold.

Michael McGuffin, president of the American Herbal Products Association, a trade association, in Silver Spring, Md., said the study showed that the ingredient to be concerned about is caffeine, not bitter orange.

His association advocates special labeling for dietary supplements that contain caffeine, telling consumers how much the product contains by comparing it to cups of coffee. A supplement with 200 milligrams of caffeine, for example, should say that it is the equivalent of two cups of coffee, Mr. McGuffin said.

"We are concerned about the potential for abuse with caffeine, which is a strong and well-known stimulant," he said.

The sales of bitter orange products have increased since the ephedra ban started in April 2004. In the year that ended Aug. 6, sales in grocery stores and drugstores, excluding Wal-Mart, were up 23 percent from the previous year, to more than \$665,000, according to Spins Inc., a company in San Francisco that tracks the sales of natural products. The supplements are still not as popular as ephedra was, however. In 2003, sales were nearly \$890,000, Spins reported.

In scientific trials, the study participants sampled two kinds of ephedra-free supplements - Advantra Z, which contains bitter

orange alone, and Xenadrine EFX, which at the time of the study contained bitter orange along with [vitamins](#) and minerals and about as much caffeine as is contained in two large cups of coffee. (Cytodyne, the company that makes Xenadrine EFX, no longer uses bitter orange as an ingredient in the supplement.)

Although the Advantra Z had 15.6 milligrams of synephrine and the Xenadrine EFX 2.75, only the Xenadrine EFX raised blood pressure. The increase could not be attributed to the caffeine alone, Dr. Haller said, because although caffeine can boost systolic blood pressure (when the heart beats), it does not affect diastolic blood pressure (when the heart is at rest). Xenadrine EFX increased the two.

"In a study with only 10 people, to have a significant increase in blood pressure of that type was amazing," Dr. Haller said. "We didn't expect it.

"What needs to be determined is the interaction between caffeine and bitter orange, and how is that going to translate into potential problems."

Bitter orange is also known by its scientific name, *Citrus aurantium*. In traditional Chinese medicine, it is called Zhi shi and is used as a remedy for gastrointestinal ailments like bloating, abdominal pain and constipation. In Britain, bitter orange is an ingredient in orange marmalade, Dr. Blumenthal said.

Bitter orange does not appear to work as well as ephedra to help people lose weight.

A few studies have suggested that bitter orange can boost a person's resting metabolic rate, and others have indicated that combination supplements that contain bitter orange with caffeine and other ingredients may help subjects lose weight. But bitter orange itself does not appear to work as well as ephedra for weight loss.

"There are no clinical studies that show it's an effective weight loss agent," said Adam Myers, a professor of physiology and biophysics at Georgetown University Medical Center in Washington, who recently reviewed the research on the supplement.

Nor has bitter orange been observed to be as dangerous as ephedra. Dr. Haller found a few published reports of heart problems and stroke that were possibly, but not conclusively, connected to the supplement.

The subjects in the University of California study were asked to describe how they felt after taking the supplements. Those who took the pills with both bitter orange and caffeine reported "a little bit of increase in alertness," Dr. Haller said. But when given bitter orange alone, she said, they said they felt nothing.

That was a noticeable difference from what subjects in earlier studies of ephedra had reported.

"With ephedra," she said, "we'd see them fidgeting in the bed."