

## Dangerous supplements: Still at large

If you can buy it at a clean, well-lighted store, if it's "all natural," it's not going to do you serious harm, right? That's what many Americans assume about dietary supplements. But while most supplements are probably fairly benign, *Consumer Reports* has identified a dozen that according to government warnings, adverse-event reports, and top experts are too dangerous to be on the market. Yet they are. We easily purchased all 12 in February 2004 in a few days of shopping online and in retail stores.

These unsafe supplements include Aristolochia, an herb conclusively linked to kidney failure and cancer in China, Europe, Japan, and the U.S.; yohimbe, a sexual stimulant linked to heart and respiratory problems; bitter orange, whose ingredients have effects similar to those of the banned weight-loss stimulant ephedra; and chaparral, comfrey, germander, and kava, all known or likely causes of liver failure. (For a complete list of the "dirty dozen," see [12 supplements to avoid](#).)

U.S. consumers shelled out some \$76 million in 2002 for just three of these supplements: androstenedione, kava, and yohimbe, the only ones for which sales figures were available, according to the Nutrition Business Journal, which tracks the supplement industry.

The potentially dangerous effects of most of these products have been known for more than a decade, and at least five of them are banned in Asia, Europe, or Canada. Yet until very recently, the U.S. Food and Drug Administration had not managed to remove a single dietary supplement from the market for safety reasons.

After seven years of trying, the agency announced a ban on the weight-loss aid ephedra in December 2003. And in March 2004 it warned 23 companies to stop marketing the body-building supplement androstenedione (andro).

Despite these actions against high-profile supplements, whose dangers were so well known that even industry trade groups had stopped defending them, the agency continues to be hamstrung by the 1994 Dietary Supplement Health and Education Act (DSHEA, pronounced *de-shay*). While drug manufacturers are required to prove that their products are safe before being marketed, DSHEA makes the FDA prove that supplements on the market are *unsafe* and denies the agency all but the sketchiest information about the safety record of most of them.

"The standards for demonstrating a supplement is hazardous are so high that it can take the FDA years to build a case," said Bruce Silverglade, legal director of the Center for Science in the Public Interest, a Washington, D.C., consumer-advocacy group.

At the same time, the FDA's supplement division is understaffed and underfunded, with about 60 people and a budget of only \$10 million to police a \$19.4 billion-a-year industry. To regulate drugs, annual sales of which are 12 times the amount of supplement sales, the FDA has almost 43 times as much money and almost 48 times as many people.

"The law has never been fully funded," said William Hubbard, FDA associate commissioner for policy and planning. "There's never been the resources to do all the things the law would command us to do."

The agency has learned that it must tread carefully when regulating supplements. The first time it tried to regulate the dangerous stimulant ephedra, in 1997, overwhelming opposition from Congress and

### CR Quick Take

A CR investigation found that many dangerous supplements can easily be purchased in stores and online. Many of these supplements have been banned in other countries. Why can't the U.S. Food and Drug Administration ban these products now?

We found that regulatory barriers created by Congress, supplement-industry pressure, and a lack of resources at the FDA have resulted in major risks for consumers.

- These widely available dietary supplements (see [12 supplements to avoid](#)) may cause cancer, severe kidney or liver damage, heart problems, or even death. They should be avoided by consumers.
- These supplements are sold under a profusion of names, making it difficult for consumers to know what they're purchasing.
- Most also appear in combination products marketed for a broad array of uses, such as aphrodisiacs, athletic-performance boosters, and treatments for anxiety, arthritis, menstrual problems, ulcers, and weight loss.

industry forced it to back down.

As a result, the FDA is sometimes left practicing what Silverglade calls “regulation by press release”—issuing warnings about dangerous supplements and hoping that consumers and health practitioners read them.

There are signs of hope. The FDA has said that if the ban on ephedra holds up against likely legal challenges, it plans to go after other harmful supplements. Legislation has been introduced to strengthen the FDA’s authority under DSHEA and give the agency more money to enforce the act.

But the supplement marketplace still holds hidden hazards for consumers, especially among products that aren’t in the headlines. “Consumers are provided with more information about the composition and nutritional value of a loaf of bread than about the ingredients and potential hazards of botanical medicines,” said Arthur Grollman, M.D., professor of pharmacological sciences at the State University of New York, Stony Brook, and a critic of DSHEA.

## **A QUESTION OF SAFETY**

Supplement-industry advocates say the ephedra ban demonstrates that DSHEA gives the FDA enough power to protect consumers from unsafe products. “I don’t think there’s anything wrong except that FDA has only recently begun vigorous and active enforcement of the law,” said Annette Dickinson, Ph.D., president of the Council for Responsible Nutrition, a major trade association for the supplement industry.

But critics of DSHEA think the ban illustrates the extremes to which the FDA must go to outlaw a hazardous product.

When the agency initially tried to rein in ephedra use in 1997, after receiving hundreds of reports of adverse events, it sought not an outright ban but dosage restrictions and sterner warning labels. The industry mounted a furious counter-attack, including the creation of a public-relations group called the Ephedra Education Council and a scientific review from a private consulting firm, commissioned by Dickinson’s trade group, that concluded ephedra was safe. After the U.S. General Accounting Office said the FDA “did not establish a causal link” between taking ephedra and deaths or injuries, the agency was forced to drop its proposal.

## SUFFERED SEIZURE

Gretchen Fitzgerald, age 21, Fort Collins, Colo.



**PROBLEM** She took Xenadrine EFX "thermogenic" diet pills to boost her energy while studying for final exams, believing they were safe because they were labeled ephedra-free. After three weeks of taking the product she had a seizure. The neurologist consulted told her the bitter orange in the Xenadrine was the probable cause. Xenadrine's manufacturer did not return our phone calls. Since going off the Xenadrine, Fitzgerald has had no further problems.



The industry continued to vigorously market and defend ephedra. Metabolife International, a leading ephedra manufacturer, did not let the FDA know that it had received 14,684 complaints of adverse events associated with its ephedra product, Metabolife 356, in the previous five years, including 18 heart attacks, 26 strokes, 43 seizures, and 5 deaths. It took the pressure of congressional and Justice Department investigations to get the company to turn over the complaints in 2002. Then Steve Bechler, a pitcher for the Baltimore Orioles, died unexpectedly in 2003 while taking another ephedra supplement, Xenadrine RFA-1. With sales suffering from the bad publicity, manufacturers began to replace ephedra with other stimulants such as bitter orange, which mimics ephedra in chemical composition and function.

"All of a sudden Congress dropped objections to an ephedra ban and started demanding the FDA act," said Silverglade.

To amass the necessary scientific evidence that it hoped would satisfy the demanding standard set by DSHEA, the FDA took aggressive action: It commissioned an outside review from the RAND Corporation, analyzed adverse-event reports, and pored over every available shred of scientific evidence.

"We've gone the whole nine yards to collect and evaluate all the possible evidence," Mark McClellan, commissioner of the FDA, said in announcing the ban. "We will be doing our best to defend this in court, and if that's not sufficient, it may be time to re-examine the act."

## DRUGS VS. SUPPLEMENTS

In an October 2002 nationwide Harris Poll of 1,010 adults, 59 percent of respondents said they believed that supplements must be approved by a government agency before they can be sold to the public. Sixty-eight percent said the government requires warning labels on supplements' potential side effects or dangers. Fifty-five percent said supplement manufacturers can't make safety claims without solid scientific support.

They were wrong. None of those protections exist for supplements--only for prescription and over-the-counter medicines. Here are the major differences in the safety regulations:

**Testing for hazards.** Before approval, drugs must be proved effective, with an acceptable safety profile, by means of lab research and rigorous human clinical trials involving a minimum of several thousand people, many millions of dollars, and several years.

In contrast, supplement manufacturers can introduce new products without any testing for safety and efficacy. The maker's only obligation is to send the FDA a copy of the language on the label (see [Supplement labels](#)).

"Products regulated by DSHEA were presumed to be safe because of their long history of use, often in other countries," said Jane E. Henney, M.D., commissioner of the FDA from 1998 to 2001. "As their use dramatically increased in this country after the passage of DSHEA, the presumption of safety may have been misplaced, particularly for products other than traditional vitamins and minerals. Some, like ephedra, act like drugs and thus have similar risks."

The only exceptions to this “presumption of safety” are supplement ingredients that weren’t being sold in the U.S. when DSHEA took effect. Makers of such “new dietary ingredients” must show the FDA evidence of the products’ safety before marketing them. The FDA invoked that rarely used provision in its action against androstenedione. After years of allowing andro to be marketed without restriction, the agency declared that it was “not aware” that the supplement was used before DSHEA, so it couldn’t be sold without evidence of safety.

**Disclosing the risks.** Drug labels and package inserts must mention all possible adverse effects and interactions. But supplement makers don’t have to put safety warnings on the labels, even for products with known serious hazards.

We bought a product called Relaxit whose label had no warning about the kava it contained, even though the American Herbal Products Association, an industry trade group, recommends a detailed, though voluntary warning label about potential liver toxicity on all kava products.

**Ensuring product quality.** Drugs must conform to “good manufacturing practices” that guarantee that their contents are pure and in the quantities stated on the label. While DSHEA gave the FDA authority to impose similar standards on supplements, it took until 2003 for the agency to propose regulations--as yet not final--to implement that part of the law.

Contaminants, too, regularly turn up in supplements. In 1998 Richard Ko, Ph.D., of the California Department of Health Services reported that 32 percent of the Asian patent medicines he tested contained pharmaceuticals or heavy metals that weren’t on the label. In 2002, the FDA oversaw a voluntary manufacturer recall of a “prostate health” supplement called PC SPES that, according to tests by the California department, contained a powerful prescription blood thinner, warfarin.

**Reporting the problems.** By law, drug companies are required to tell the FDA about any reports of product-related adverse events that they receive from any source. Almost every year, drugs are removed from the market based on safety risks that first surfaced in those reports.

In contrast, supplement makers don’t have to report adverse events. Indeed, in the five years after DSHEA took effect, 1994 to 1999, fewer than 10 of the more than 2,500 reports that the FDA received came from manufacturers, according to a 2001 estimate from the inspector general of the U.S. Department of Health and Human Services. (Other sources of reports included consumers, health practitioners, and poison-control centers.) Overall, the FDA estimates that it learns of less than 1 percent of adverse events involving dietary supplements.

## THE ‘NATURAL’ MYSTIQUE

Many makers market their supplements as “natural,” exploiting assumptions that such products can’t harm you. That’s a dangerous assumption, said Lois Swirsky Gold, Ph.D., director of the Carcinogenic Potency Project at the University of California, Berkeley, and an expert on chemical carcinogens. “Natural is hemlock, natural is arsenic, natural is poisonous mushrooms,” she said.

A cautionary example is aristolochic acid, which occurs naturally in species of Aristolochia vines that grow wild in many parts of the world. In addition to being a powerful kidney toxin, it is on the World Health Organization’s list of human carcinogens. “It’s one of the most potent chemicals of 1,400 in my Carcinogenic

## KIDNEYS FAILED

Beverly Hames, age 59, Beaverton, Ore.



**PROBLEM** Hames went to an acupuncturist in 1992 seeking a “safe, natural” treatment for an aching back. She got a selection of Chinese herbal products, at least five of which were later found to contain aristolochic acid. By mid-1994, she had symptoms of kidney failure, and in 1996 she underwent a kidney transplant. She must take anti-rejection drugs (below) for life. The herbs’ distributor said his Chinese suppliers had substituted Aristolochia for another herb without his knowledge.



Potency Database,” Gold said. “People have taken high doses similar to the doses that animals are given in tests, and they both get tumors very quickly.”

## KIDNEYS FAILED

Donna Andrade-Wheaton, age 40, Cranston, R.I.



### PROBLEM

Andrade-Wheaton's acupuncturist prescribed more than a half dozen Chinese herbal supplements to treat health conditions, including endometriosis. At least one of the products listed Aristolochia as an ingredient, even after the FDA issued a nationwide Aristolochia safety warning in 2001. She underwent a kidney transplant in September 2002 and must take anti-rejection drugs (below) for life.

The dangers of aristolochic acid have been known since at least 1993, when medical-journal articles began appearing about 105 patrons of a Belgian weight-loss clinic who had suffered kidney failure after consuming Chinese herbs adulterated with Aristolochia. At least 18 of the women also subsequently developed cancer near the kidney.

These findings prompted the FDA to issue a nationwide warning against Aristolochia in 2001 and to impose a ban on further imports of the herb. But in early 2004, more than two years after the import ban went into effect, *Consumer Reports* was able to purchase products online that were labeled as containing Aristolochia. In 2003, Gold identified more than 100 products for sale online with botanical ingredients listed by the FDA as known or suspected to contain aristolochic acid.

Donna Andrade-Wheaton, a former aerobics instructor in Rhode Island, learned those facts too late to save her kidneys. After taking Chinese herbs containing Aristolochia for more than two years, she suffered severe kidney damage; her kidney tissues were found to contain aristolochic acid. In late 2002, at age 39, she underwent a kidney transplant.

Andrade-Wheaton is suing both the acupuncturist who gave her the herbs and several companies that manufactured them. The acupuncturist declined to discuss the case on the record, and the manufacturer did not return our phone calls.

There's another widespread and false assumption about natural supplements: that they're always pure, unprocessed products of the earth. Because DSHEA permits the marketing of concentrates and extracts, supplement makers can and do manipulate ingredients to increase the concentrations of pharmacologically active compounds.

That's especially true of the many weight-loss supplements designed for "thermogenic" stimulant effects--boosting calorie expenditure by revving the metabolic rate.

On one Internet shopping tour, for instance, we bought a product called Thermorex--"the Hottest new Thermogenic on the market!" Its label says it contains, among its 22 ingredients, 30 milligrams of theophylline derived from a black tea extract and the stimulant bitter orange. Sold as Theo-Dur and other brands, theophylline is a prescription drug and an effective asthma treatment, but most doctors seldom prescribe it because it can cause seizures and irregular heartbeats at relatively low doses.

Larry Berube, president of Anafit, Thermorex's manufacturer, based in Orlando, Fla., described how the product's combination of ingredients was developed: "Once we find out that the FDA says it's OK, we put them together in the lab, run our tests, and do our trials, and if it comes up good, we capsule it, put it online and in the stores and sell it," he said. Those tests involved asking fitness professionals to use the supplement, and measuring their heart rate and blood pressure, Berube said. The company doesn't use a control group, he said. Then "we go to the fitness discussion boards and let trainers and people know we have a new product and do they want to try it," he said. "And then they try it, and they report back." Berube said he has not heard of any bad reactions to Thermorex.