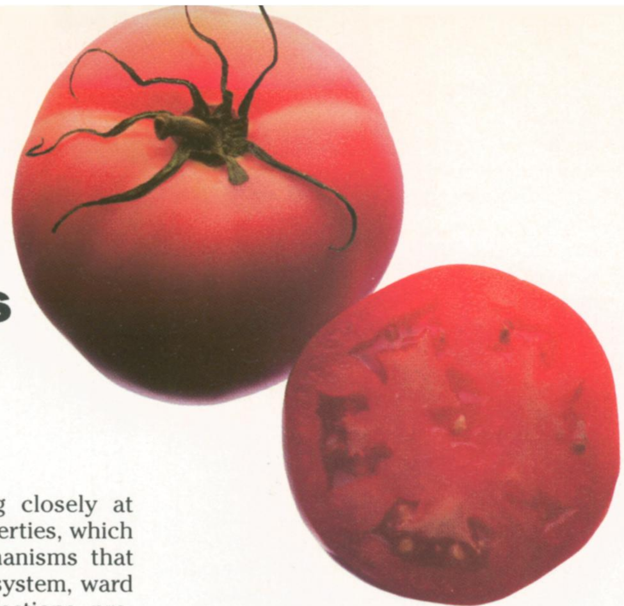
Vegemania

Scientists tout the health benefits of saponins

By RICHARD LIPKIN



Tomatoes, potatoes, and many other fruits and vegetables contain saponins.

It sounds like a plot—a vegetarian conspiracy against a carnivorous, burger-chomping public. As if fiber and antioxidants weren't enough, chemists studying the healthful properties of plants now say that vegetables contain yet another class of disease-fighting nutrients.

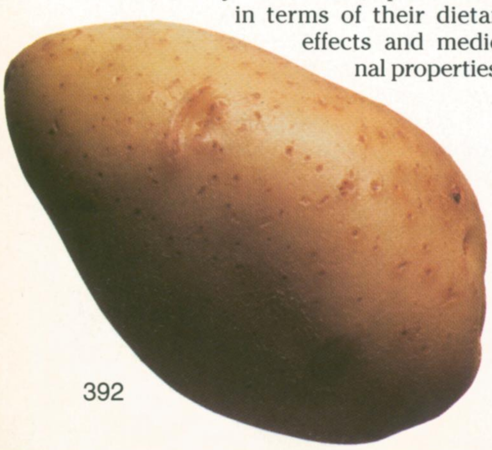
These ingredients, some sweet and some health-promoting, go by the name of saponins.

Found in a wide variety of vegetables and legumes—ranging from beans and spinach to tomatoes, potatoes, oats, and alfalfa—saponins are a class of nutrient molecules comprising sugars hooked up to alkaloid, steroid, or triterpene compounds. Saponins, appearing throughout the plant kingdom, display a creamy, even foamy, texture that distinguishes them from other plant materials.

Long-standing interest in saponins stems from their strong biological activity, says Manuel F. Balandrin, a chemist at NPS Pharmaceuticals in Salt Lake City. In plants, many of these compounds serve as "natural antibiotics," he says, helping fight infections and microbial invasions.

Moreover, saponins, if regularly included in the diet, may help the body protect itself from cancer, says A. Venket Rao, a chemist at the University of Toronto in Ontario. Saponins and saponinlike compounds have shown evidence that they can buttress the body's ability to thwart cancer and heart disease. The drug digitalis, for instance, obtained from the leaves of the foxglove and widely prescribed for heart disease, has a saponin-related molecular structure.

"There is now considerable interest in looking at saponins' biological properties in detail," says Balandrin, "particularly in terms of their dietary effects and medicinal properties."



Researchers are looking closely at saponins' biochemical properties, which they believe include mechanisms that can stimulate the immune system, ward off microbial and fungal infections, protect against viruses, and even act as a spermicide.

"We're past data gathering," says Balandrin. "We're now at the point of designing saponin molecules with specific biological and chemical properties."

Researchers in the pharmaceutical industry are investigating several saponin-based compounds. One agent, QS-21, being developed as an immunity booster by Cambridge Biotech in Worcester, Mass., has moved into clinical trials.

"This compound appears greatly to enhance the effectiveness of certain vaccines, including ones for herpes simplex, HIV, and influenza, when administered together with them," says Balandrin. "The compound functions as a helper agent, increasing the potency of the vaccine's action."

Derived from the bark of the South American tree *Quillaja saponaria,* this drug promotes the formation of disease-specific antibodies, helping the body to fight pathogens.

Looking at the antitumor activities of specific saponins, Yutaka Sashida, a chemist at the Tokyo University of Pharmacy and Life Science in Japan, reports that agents extracted from plants in the Liliaceae family, which includes garden lilies, test well in fighting cancer. Specifically, glycosides from the bulbs of *Ornithogalum saundersiae*, a perennial plant native to southern Africa, exhibit "potent cytotoxic activities against various human malignant tumor cells," particularly lung and blood cancers.

In fact, Sashida finds that these glycosides are 10 to 100 times more potent than some clinically approved anticancer agents, including adriamycin and taxol. When treated with glycoside derivatives, mice with leukemia survived nearly two-thirds longer than those left untreated.

In another set of cancer studies, Takao Konoshima, a chemist at Kyoto Pharmaceutical University in Japan, and his colleagues successfully treated skin tumors growing on mice. They employed saponins extracted from the knots of *Wistaria brachybotrys*—agents long used in Japanese folk medicine to fight cancer.

Moreover, a saponin from the fruits of the *Gleditsia japonica* showed strong antitumor effects in mice, as did another saponin culled from the roots of *Panax ginseng.* Konoshima says that the inhibitory effects of these agents on skin tumors induced by ultraviolet radiation are "very significant."

Because the human digestive system has evolved to handle plants, it's almost impossible to overdose on saponins by eating vegetables, Balandrin says. "They're broken down in the digestive tract, releasing cholesterol-like compounds and sugars. We're already used to having saponins in our diets, so our bodies are tuned to these substances. There's little risk of toxicity from saponins eaten as part of a plant."

The high concentrations of saponins in drugs, however, may provoke side effects. "Their potential for toxicity at high doses needs careful study," he says. "We're still not sure what level of saponin consumption is ideal."

In producing saponin-derived drugs, the key issue is to regulate the molecules' actions on specific cell membranes, Balandrin says. "You want a drug to affect target cells, such as cancer cells, and leave other cells alone. The design process requires careful tuning."

For the treatment of certain conditions, such as tumors of the gastrointestinal tract or skin, saponin-derived compounds could act directly on cancer cells. In these instances, the body does not have to absorb the molecules and circulate them in the bloodstream. Other conditions, however, require that the drugs be digested and absorbed—or injected—into the blood.

Meanwhile, scientists are evaluating other saponins' potential for lowering cholesterol in the blood, thereby reducing the risk of heart disease. "Some saponins, taken orally, combine with cholesterol in the gastrointestinal tract, making cholesterol unavailable for absorption," says Balandrin. Thus, a saponin derivative may yield a natural agent for treating or preventing heart disease.

Moreover, saponins' natural tendency to ward off microbes makes them good candidates for treating fungal and yeast infections, says Uri Zehavi, a chemist at the Hebrew University of Jerusalem. He and his colleagues tested the compound G2, derived from the saponins of alfalfa roots, in mice and guinea pigs. They found that it killed 10 of the most medically troublesome yeasts, as well as 6 fungi that cause infections.

Saponins can be toxic not only to microbes but also to some mollusks. Kurt Hostettmann, a chemist at the University of Lausanne in Switzerland, and his colleagues are seeking ways to use saponins to fight the snailborne parasitic disease schistosomiasis. Endemic in 76 countries and affecting 200 million people, the tropical disease can cause blindness and death. Hostettmann's team has found that extracts of the saponin-rich fruit of the African trees *Swartzia madagascariensis* and *Tetrapleura tetraptera* kill schistosomiasis-transmitting snails.

"The capacity of saponin-containing plant material to kill the intermediate host [snails] has wide-ranging implications in developing countries," he says.

Investigating the impact of dietary saponins on the management of chronic diseases, Rao says that current data on diet prompt two recommendations: "Consume less fat, and eat more plant-derived foods, including fruits, vegetables, cereals, and legumes. Without doubt, the first step in treating illness is prevention, which begins with proper food intake."

Rao wants to know which of the multifarious chemicals in plants, known as phytochemicals, pack the greatest punch in supporting good health. Looking primarily at saponins and phytosterols (the plant equivalents of animal cholesterol), Rao finds that many saponins have anticarcinogenic properties.

"We're more interested in the impact of saponins in the diet than in their use as pharmaceuticals," he says. "We want to focus our energies on disease prevention."

"At the cellular level, we find that saponins inhibit the growth and viability of cancer cells," he says. In animal studies, mice placed on saponin-enriched diets, then exposed to colon cancer carcinogens, show fewer incidences of cancerous and precancerous tumors than the controls do.

"We think that some of these agents may select cancer cells," he says. "Cancer cells have a different membrane structure, with more cholesterol-like compounds," he says. "Since saponins bind cholesterol, they have a natural affinity for cancer cell membranes."

Analyzing the relationship between saponins' varied structures and tumor-suppressing tendencies, Rao stresses the subtlety of the molecular differences. The particular plant compounds constitute a class of molecules, he says, not just one, and "each one has different properties."

To firm up the epidemiological studies, the researchers have started controlled human trials to examine the absorption and metabolism of dietary saponins, particularly their impact on cholesterol in the blood and the liver's production of bile acid.

Evaluating data from populations that eat healthful portions of plant-based foods, Rao finds that the "groups consuming foods richest in saponins have lower incidences of breast, prostate, and colon cancer."

"We're particularly interested in seeing the effects of dietary saponin and phytosterol supplements on the progression of these diseases," Rao says.

Rao's research aims not only at public health but also at the food industry, he says. His team is providing guidelines for food processors, enabling them to maintain the beneficial attributes of foods during preparation and packaging.

He envisions a day when saponin supplements become as commonplace as vitamins and table salt, with companies fortifying their products—whether bread or breakfast cereal—with saponins.

"Phytochemicals could play a major role in helping human beings prevent or control chronic illnesses," he says.

In addition to the health benefits they endow on soybeans, chickpeas, bean sprouts, and asparagus, saponins have other appealing properties. A. Douglas Kinghorn, a chemist at the University of Illinois at Chicago, points out one of those rare ironies of nature: Saponins are not only healthful, they're tasty.

"Some saponins are 50 times sweeter than sucrose," he says. Among the hundreds of known saponins, about 75 can be classified as high-potency sweeteners.

Kinghorn's group has recently isolated a particularly sweet set of compounds called abrusosides. Extracted from the rosary pea—a weedy vine, *Abrus precatorius,* native to Florida—these saponins are 30 to 100 times sweeter than sucrose. Because the plant grows abundantly in many tropical countries, especially Indonesia, he believes the prospects of developing these natural sweeteners for general use look promising, particularly since the extract has "a very pleasant taste."

Moreover, abrusosides dissolve easily in water and survive cooking.

Other saponins under scrutiny include pterocaryosides, extracted from the Chinese sweet leaf tree, *Pterocarya paliurus.* Used as a sweetener in remote regions of China's Hubei province, these saponins are 50 to 100 times sweeter than sucrose. Their only drawback, says Kinghorn, comes from a "distinctive aftertaste," which could preclude widespread popularity.

From the roots of the Brazilian legume *Periandra dulcis,* the researchers have extracted the compound periandrin V, the fifth and most potent sweetener culled from this plant species. With roughly 200 times the potency of sucrose, it's one of the sweetest saponins yet discovered, he says.

Other sweet saponins come from more familiar plants, Kinghorn adds. The North American fern *Polypadium glycyrrhiza* contains the saponins called polypodosides, which rank well against those of exotic plant species.

Kinghorn/Univ. of Illinois at Chicago

Leaves of the Abrus precatorius *vine are readied for saponin extraction.*

Although sucrose still holds sway over the world's sweet tooth, concern about the sugar's high calories and promotion of tooth decay have increased the demand for alternative sweeteners, he says—particularly given the public perception that "natural compounds are more healthful than synthetic ones."

"Remember, if the saponins are 100 times sweeter than sucrose, then you only need one one-hundredth as much to make food just as sweet," Kinghorn says. "This means that people would consume much smaller amounts of saponins, lessening the risks of adverse effects."

Delicious, yet healthful—ah, how sweet it is. □