



ANNUAL REPORT ON
**COMPLEMENTARY
AND ALTERNATIVE
MEDICINE**



Black Raspberries Studied To Prevent Oral Cancer



Division of
Cancer Prevention

The Ohio State University (OSU) Comprehensive Cancer Center and College of Public Health have a long and successful tradition of studying food for its health and anticancer properties. One of the well-studied components found in ripe black raspberries is anthocyanins, which give the berries their deep purple color. A number of studies in different animals (such as rats and hamsters) have shown that a liquid mixture of these fruits taken orally interferes with the growth of tumors in the oral cavity, esophagus, and colon.

“We think the primary reason that the berry mixture inhibits cancer is because it makes physical and biological contact with the precancerous tissue all along the digestive route of the animals,” noted Christopher Weghorst, Ph.D., a professor of Environmental Health Sciences and Otolaryngology at OSU. He said that many of the compounds found in black raspberries are not well absorbed through the digestive system into the bloodstream. “This certainly includes some of the components we think might be responsible for the protective effect we are finding,” he added. “We and others have also designed some novel delivery methods aimed at extending the period of time the berry components remain in contact with the target tissue.”

Many CAM researchers face a dilemma when trying to determine which ingredient in a food plant is responsible for the health effects they find in their studies, said Dr. Weghorst. While it is often possible to isolate just a single compound from the plant, test it for activity against a particular health problem, and then produce (and market) it as a supplement, “this may not be the best approach,” he commented. “In fact, there is a lot of evidence to the contrary.”

The study that NCI is funding* in Dr. Weghorst’s lab is not intended to isolate and test the anthocyanins in black raspberries that many believe are the “active ingredient.” Instead, he is testing the relative importance of anthocyanins by using green berries before they fully ripen into black raspberries. Anthocyanins are not developed in green berries because the fruit has not yet ripened. In hamsters, when the green

berries were compared to the ripe raspberries, their inhibiting impact on oral cancer in the test animals was about the same, he reported.

One possible mode of action for the berries’ beneficial impact on cancer cells may involve gankyrin, a cancer-causing gene (or oncogene) “that produces a cell growth stimulus and is over-expressed in head and neck cancers,” said Dr. Weghorst. “Both the green and the ripe black raspberries reduced the expression of this oncogene to a more normal level. Thus, the anthocyanins cannot logically be the sole cause.” On the other hand, the researchers found that the P16 tumor suppressor gene, which is often inactivated in oral cancers, was found in abundance in animals given the ripe black raspberries but not in those given the green berries. Thus, there are numerous helpful ingredients in the berries which can change gene expression patterns in a manner that might favor cancer prevention, Dr. Weghorst explained.

“All of this demonstrates there are multiple pathways involved in this type of cancer development and cancer prevention,” Dr. Weghorst said. “We now know that that there are also bioactive components of the green forms of these plants that are effective against oral cancer.” This helps confirm the food-based approach to cancer prevention, even using food at various stages of ripeness, he believes, and emphasizes the capability of the complex mixtures of chemicals found in “whole” foods to inhibit multiple processes of cancer development.

These types of animal studies have set the stage for larger studies in humans, Dr. Weghorst stated. One such study already underway is evaluating the molecular effects of ripe black raspberries on “at risk” normal oral cells in post-surgical oral cancer patients. “Oral cancer has a strong connection with alcohol consumption and smoking,” he noted, “and reducing these behaviors would have a really dramatic impact.” But proving the preventive value of berries could enhance the options available to people, despite the consequences of their past behaviors or their personal risk of cancer recurrence, he commented.

*Grant number:
5R03CA137798-02





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Soy Bread Studied in Men with Prostate Cancer

Compared with men in the United States, men living in many Asian nations have a lower risk of prostate cancer. “If you look at what factors may contribute to the differences in risk, one of the many variables that jumps out is the much greater consumption of soy in Asia,” said Steven Clinton, M.D., Ph.D., a professor of Medical Oncology at Ohio State University (OSU), who studies the role of dietary factors in prostate and other cancers.

Research in Dr. Clinton’s laboratory and elsewhere – including studies in mouse models of prostate cancer – have shown that certain phytochemicals (chemicals that are found in plants) in soy have potential anti-prostate-cancer properties. However, the ability of soy to help prevent or treat prostate cancer in men remains unproven.

One of the challenges researchers face in studying this question is coming up with a convenient – and tasty – way to incorporate adequate, well-defined amounts of soy phytochemicals into the typical Western diet. With support from NCI*, Yael Vodovotz, Ph.D., an associate professor in OSU’s Department of Food Science and Technology, is collaborating with Dr. Clinton to compare two types of soy bread that the researchers developed for that purpose. The soy bread “provides in two slices a dose of soy phytochemicals that would be similar to that consumed daily by many Asian populations,” said Dr. Clinton.

The researchers are focusing on soy bread as a so-called functional food (foods that have potential health benefits, beyond just basic nutrition), rather than giving people individual soy phytochemicals, and in particular, soy compounds known as isoflavones. “The idea is that not only the isoflavones, but also the other components of soy may be very critical” for the biological effects in humans, Dr. Vodovotz said. She said that using soy bread as a “phytochemical delivery system” allows researchers to create a consistent product, yet provide a complex variety of soy components.

The OSU researchers are conducting a small clinical study to compare two types of soy bread as a source of phytochemicals in the diet. Both varieties contain isoflavones, but one of the

breads includes an enzyme that yields twice as much of an altered form of isoflavone, known as the aglycone form, Dr. Vodovotz explained. The aglycone form is believed to be more biologically active and more readily absorbed from the digestion into the bloodstream than unaltered forms of isoflavones.

The 40 men in the study all had active prostate cancer and rising prostate specific antigen (PSA) – a biological marker of prostate cancer – levels but were not undergoing active therapy during the 20-week study period. For the first 8 weeks, half of the men ate three slices per day of the regular soy bread, while the other half ate three slices daily of the aglycone-enriched bread. After a 2-week, soy-free period, each study participant ate the other form of soy bread for another 8 weeks.

The researchers found that about 90% of the men could eat the soy breads on a daily basis without any difficulties, while about 5% experienced very minor gastrointestinal distress. No other serious problems were observed, Dr. Clinton said. “Overall, the majority of men found the food easily incorporated into the diet, and some men are even purchasing soy bread that is now on the market, while others are making their own soy bread at home,” he noted. “At least a third of the men suggested that we need to improve the product to make it competitive with breads available on the market.”

The researchers are analyzing blood samples from the men and running a range of tests to find out whether the aglycone form of isoflavones is in fact better absorbed and has a greater effect on various biomarkers that have been linked with anti-cancer activity.

Once the final results are in, the researchers hope to use an optimized form of soy bread in clinical trials that will rigorously test the ability of soy phytochemicals to improve the treatment of prostate cancer or to prevent the disease in men who are considered at high risk. Dr. Vodovotz commented, “We hope to eventually have the bread in a commercially available form, because if you’re going to recommend something for prostate cancer, it better be available in the marketplace.”

*Grant number:
R21CA125909-02



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NIH Publication No. 11-7768
Printed February 2012

