American Institute for Cancer Research

Taking A Closer Look At

PHYTOCHEMICALS

NEW CANCER RESEARCH

If you saw the following items listed as ingredients on a cereal box, you might be alarmed: isoflavones, terpenes, indoles, phenolic acids. But these tongue-twisters aren't artificial additives. They're naturally occurring chemicals found in fruits, vegetables, beans and whole grains—biologically active chemicals our bodies may use as part of their disease-fighting arsenal. These substances are called phytochemicals (phyto is Greek for plant). Some phytochemicals found in plants not commonly used for food, such as digitalis and quinine, have been used for medicinal purposes for centuries. The anticancer effects of many of them, however, are only beginning to be explored.

Phytochemicals in foods may offer frontline defenses against cancer.

The role of phytochemicals in metabolism has not been adequately defined. A single tomato or orange contains hundreds, and possibly thousands, of phytochemicals. Some are antioxidants, protecting against harmful cell damage from oxidation. Others perform different functions that can help to prevent cancer. Scientists are still deciphering the many ways phytochemicals in foods may offer frontline defenses against cancer.

Phytochemicals as Cancer Preventives

One reason scientists are so excited about phytochemicals is their apparent ability to stop the conversion of a cell from healthy to cancerous at so many different stages. Isothiocyanates, found in cruciferous vegetables (such as broccoli, cauliflower, cabbage and kale) switch on enzymes that actually detoxify carcinogens at an early stage; they also increase the antioxidant defenses of cells. Diallyl disulfides in garlic and onions can stop the growth of cancer cells at a later stage. Saponins, found in beans and other legumes, may prevent cancer cells from multiplying by influencing genetic material in the cells. Ellagic acid, a type of phenolic acid found in strawberries and raspberries, reduces the genetic damage caused by carcinogens in tobacco smoke and air pollutants.

One phytochemical that has received a lot of media attention is lycopene, a member of the vast carotenoid family, which contains more than 600 compounds (including the well-known beta-carotene, as well as lutein and zeaxanthin, which are found in leafy greens). Lycopene, the substance that makes tomatoes red, is being examined because of its possible effects in helping to prevent several types of cancer, including prostate cancer.

The phytochemical properties of soy foods are another hot media topic these days. For many years, research has suggested that soy may be an effective cancer fighter because of the presence of phytochemicals called isoflavones, which may inhibit cancer cell growth and division under some conditions. Cancer researchers began studying soy in an effort to explain why women in Asian countries had far fewer cases of breast cancer than American women; they suggested that soy isoflavones are partially responsible. However, some recent studies have signaled that isoflavones might also produce some negative effects. Dr. Mark Messina, a prominent soy foods expert at Loma Linda University in California, emphasizes that although soy is unique in that it contains isoflavones, most plant foods are rich in other phytochemicals that are potential cancer fighters. According to Dr. Messina, loading up on any one food is not advisable. Rather, he recommends eating a balanced diet that includes soy as well as plenty of vegetables, fruits whole grains and legumes. Eating soy foods should be the primary means of getting isoflavones, but research is still underway to evaluate the safety and efficacy of isoflavone supplements, he says.

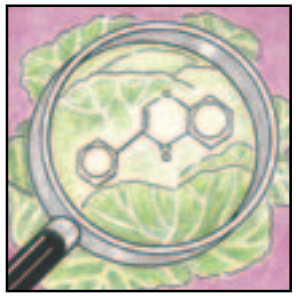
Supported by grants from the American Institute for Cancer Research (AICR), scientists have furthered research on phytochemicals. Recent studies have investigated how carnosol (found in rosemary) fights breast cancer tumors in laboratory rats, whether curcumin (found in turmeric, a spice) is effective against skin cancer, and the way a substance in green tea (known by the abbreviation EGCG) affects cells.

Resveratrol, a type of polyphenol found in the skin of grapes, red wine, peanuts and

mulberries, is being widely studied as a cancer-preventive agent. It has been found to inhibit human cancer cell growth in the breast, prostate and lung. Terpenes are another group of phytochemicals that show anticancer activity towards several cancers in rats (including mammary, colon, pancreatic and stomach). Terpenes are found in essential oils of many plants including citrus fruits. Dr. Steven Clark, at the University of Wisconsin Comprehensive Cancer Center, has shown that the terpenes perillyl alcohol and limonene stop growth of leukemia cells and cause them to die. With an AICR grant, he plans to study how these terpenes work to inhibit leukemia in mice. He will investigate whether they can reverse the resistance of leukemia to conventional chemotherapy agents and how they may be used in combination with other therapies.

Phytochemicals in Cancer Treatment

Some scientists are now studying the use of phytochemicals in cancer treatments, where they are used in such large amounts that they are classified as drugs. This initially involves identifying the active cancer fighting substances in whole fruits or vegetables and then purifying the effective compound. Dr. Peter Ferguson at the London Regional Cancer Center is trying to determine the phytochemicals in cranberry products that may inhibit the growth of breast cancer cells and slow metastasis. Just like other chemicals, however, phytochemicals may be toxic in large amounts and must be properly formulated and tested before using.



Choose Whole Foods

Although there's still much that is unknown about phytochemicals, what scientists do know from many human population studies worldwide is that people who eat large quantities of fruits and vegetables have reduced cancer risks.

What about supplements? Phytochemicals are already appearing in pills, potions, powders and drinks, but experts believe that it is more effective to get cancer-protective substances by eating whole foods—vegetables, fruits, whole grains and beans. "A good example of how we learned this was with beta-carotene," says Stephen Barnes, Ph.D., a pharmacology professor at the University of Alabama at Birmingham.

"All the evidence showed that foods rich in beta-carotene were beneficial, but when we tested the chemical by itself [in supplement form] it was not effective in preventing cancer." Two beta-carotene studies showed that smokers taking the supplement developed more cases of lung cancer. It could be the same story with other phytochemicals. "It may be that these compounds are highly interactive and do not work well when they're isolated," says Barnes. Most of these compounds, however, have yet to be tested as part of a mixture.

Because phytochemicals are so diverse, as are their biochemical and molecular targets and interactions, cancer-related phytochemical research is an immense challenge to researchers. Some scientists are studying how phytochemicals modify specific genes to fight cancer, and are discovering the metabolic pathways that are involved. One goal is to manipulate these pathways to increase specific phytochemical levels in foods. However, important questions remain – such as what amounts of phytochemicals are most effective and safe, as well as how phytochemicals interact with each other.

People who eat large quantities of fruits and vegetables have reduced cancer risks.

In other words, would megadoses of certain phytochemicals really head off cancer? Could they have harmful side effects? Does the preventive punch of phytochemicals depend upon dozens or hundreds of them working together, as they exist naturally in foods?

Dr. Mark Messina does not endorse the trend towards fortified cereals, snack foods or "phytamin" pills. "I think we should focus our time on getting people to consume the type of diet we know will reduce cancer risk. The notion of 'designer foods' is one of trying to supplement your way to good health. It doesn't make up for a poor diet," he says.

The Take-Home Message

Although soy foods, cruciferous vegetables and citrus fruits are developing reputations as phytochemical powerhouses, these are only the most studied foods to date. Scientists are learning more about phytochemicals that exist in all plant-based foods every day. Eating a wide variety of vegetables, fruits, whole grains and beans is more important than concentrating on particular foods, in order to get the full gamut of phytochemicals found in nature.

Here are some easy ways of increasing your intake of phytochemicals:

• **Eat a variety of vegetables.** Broccoli is very nutritious, but you don't have to eat it every day. Also try carrots, cauliflower, leafy greens, winter and summer squashes, green and red peppers, onions, snow peas, red cabbage … the list is endless. Eat a wide variety every day and aim for at least three servings of vegetables a day.

• **Eat more fruits.** A glass of juice at breakfast is nice, but how about some peaches, blueberries or bananas atop your cold or hot whole-grain cereal? A fruit salad with lunch or a juicy orange as a midday snack? A bowl of perfectly ripe strawberries after dinner? Branch out and have cherries, figs, melon, kiwi, plums, mango, pineapple or grapes. Aim for at least two servings of fruits per day.

• **Eat more whole grains.** Don't limit your choices to bread, rice and pasta. Try quinoa, bulgur, barley and kasha for variety. Once available only in health food stores, most of these foods have become supermarket staples.

• **Eat more beans.** Think kidney beans, chickpeas, white beans, navy beans, pintos and dried legumes like lentils and split peas. Many are available canned, so you don't have to cook them from scratch—just rinse under water to get rid of extra sodium.

• **Don't forget herbs and spices.** Even though you don't eat much of them, they contain phytochemicals, too. Garlic, oregano, basil, parsley, orange peel, ginger and other fresh and dried herbs and spices add zip to lowfat foods.

• **Decrease portion sizes of meat, fish and poultry.** You'll naturally eat more vegetables, beans and grains if you do. Remove half the meat filling from an overstuffed deli sandwich and pile on the veggies. Add more beans and less beef to your chili. Make a stir-fry with more vegetables and brown rice and less chicken.

• **Explore new foods and new recipes.** Tofu may be a phytochemical-filled option, but knowing how to prepare it may be a challenge. The same may be true for unfamiliar offerings in the produce department, like jicama, fennel, tomatillos, daikon, papaya or passion fruit. Some supermarkets offer recipe cards or fliers to encourage customers to try more exotic fare. Pick up a lowfat or vegetarian cookbook for tips. Call AICR for free recipe brochures, or get healthy recipes online at www.aicr.org.

Phytochemicals: The Next Frontier

Phytochemical Family	Major Food Sources
Diallyl Disulfides	Onions, garlic, leeks, chives
Carotenoids (beta-carotene, lycopene, lutein, zeaxanthin)	Carrots, cooked tomatoes, leafy greens, sweet potatoes, apricots
Flavonoids	Tea, coffee, citrus fruits
Indoles	Cruciferous vegetables (broccoli, cabbage, kale, cauliflower, Brussels sprouts)
Isoflavones	Soybeans (tofu, soy milk)
Isothiocyanates	Cruciferous vegetables
Phenolic Acids (ellagic acid, ferulic acid)	Berries, citrus fruits, apples, whole grains, nuts
Polyphenols	Green tea, grapes, wine
Saponins	Beans and other legumes
Terpenes (perillyl alcohol, limonene, carnosol)	Cherries, citrus fruit peel, rosemary

AICR Research Grants on Phytochemicals

The American Institute for Cancer Research (AICR) has taken a leadership role in supporting research in the area of phytochemicals, nutrition and cancer. Following is a partial list of grants awarded by AICR in this area.

Effect of Soy Isoflavone Consumption on Plasma Hormones Related to Prostate Cancer Risk in Healthy Young Men
Alison Duncan, Ph.D.
University of Guelph
Guelph, Ontario, Canada

Inactivation of CYP1A1 by Flavones – Lung Cancer Prevention
Thomas Walle, Ph.D.
Medical University of South Carolina
Charleston, South Carolina

Determination of Cranberry Constituents with Antiproliferative Activity Against Human Tumor Cell Lines
Peter Ferguson, Ph.D.
London Regional Cancer Center
London, Ontario, Canada

Preclinical Evaluation of the Anti-leukemia Effects of Plant-derived Monoterpenes
Steven Clark, Ph.D.
University of Wisconsin
Madison, Wisconsin

Mechanisms of Flavonoids as Chemoprotective Agents
Thomas Gasiewitz, Ph.D.
University of Rochester
Rochester, New York

Antitumor Effects of Dietary Isothiocyanates on Prostate Cancer
Tse Hua Tan, Ph.D.
Baylor College of Medicine
Houston, Texas

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References

Eat to Heal, Kristine M. Napier, Warner Books, Inc.,1998.

Food, Nutrition and the Prevention of Cancer: a global perspective, World Cancer Research Fund/American Institute for Cancer Research, 1997. Chapter 5.8 "Other Bioactive Compounds."

Functional Foods & Nutraceuticals in Cancer Prevention, Ronald R. Watson, ed., Iowa Press, 2003.

Natural Compounds in Cancer Therapy, John Boik, Oregon Medical Press, 2001.

Interviews with: Stephen Barnes, Ph.D., University of Alabama at Birmingham; and Mark Messina, Ph.D., Port Townsend, WA.

For More Information

The American Institute for Cancer Research supports research and provides public education in the area of diet, nutrition and cancer. For free publications, to reach the Institute's Nutrition Hotline or to make a memorial donation, call toll-free or write:

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