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The Spices of Cancer Protection

For centuries, cultures have used spices to improve health and ward off disease. Research is now helping to unravel how these flavor enhancers may also protect against cancer.

From allspice to turmeric, the hundreds of available spices come packed with phytochemicals, many studied for their cancer-fighting properties. A growing body of research – primarily lab studies – is now zeroing in on the role specific spices may play in reducing cancer risk.

"There is more and more documentation that several compounds in spices have anti-cancer properties," says John Milner, PhD, Director of the Human Nutrition Research Center at the US Department of Agriculture and co-author of a recent review of spices for cancer prevention.

One reason for the increased interest stems from lab studies demonstrating plausible pathways in which spices may work to reduce cancer risk. "There are several potential mechanisms that go all the way from changing carcinogen metabolism to modifying the microbiome to cell signaling – all changes that would inhibit the growth of a tumor," says Milner.

The potential for spices to affect cancer risk is an appealing area of study for scientists because spices are non-caloric and eaten in combination with other foods. They are also easily incorporated into many dishes, adding flavor and variety.

There are dozens of spices that have pointed to cancer protection in lab studies, with much of the research in its early phases. Allspice has been shown to reduce inflammation and cell proliferation. Cinnamon has suppressed the growth of the bacterium *H. pylori*, a major risk factor in gastric cancer. The bioactive component in cumin, thymoquinone, seems to suppress tumor growth in colon, breast and pancreatic cells. Some of the more studied spices include turmeric and garlic. Research is emerging in other spices and cancer risk, such as black pepper.

Turmeric

Turmeric stands as one of the most extensively studied spices, with over 1,700 lab studies published over the last few decades. It has been used for centuries to treat numerous inflammation-related disorders, including skin conditions, pain and gastrointestinal problems. There are now clinical trials examining its role in reducing cancer risk.

Turmeric gets its yellow pigment from curcumin, a polyphenol that is the primary phytochemical scientists are investigating for its anticancer potential. In the lab, curcumin modulates cell signaling pathways, suppresses tumor cell proliferation and induces apoptosis of cancer cells. There is evidence that curcumin can suppress inflammation and inhibit tumor survival, initiation, promotion, invasion and metastasis.

The findings from lab studies have led to clinical trials in humans, which are generally small but have generated promising findings. In one trial, for example, five patients with Familial Adenomatous Polyposis (FAP) consumed supplement-level amounts of curcumin and quercetin daily. After six months these patients showed a reduction in the number and size of polyps compared to those on placebo. FAP is an inherited condition that causes hundreds of colon polyps to develop early in life, leading to an increased risk of colorectal cancer.

Safety testing for toxicity and tolerability shows that people can tolerate up to 12 grams per day of curcumin with no ill-effects, which equals approximately 88 tablespoons of turmeric. But the bioavailability of curcumin is poor, meaning only a small fraction consumed reaches the bloodstream and tissues. The low bioavailability is the primary reason why scientists like Dong M. Shin, PhD, Professor of Hematology, Oncology and Otolaryngology at Emory University is investigating curcumin analogs, compounds with an altered chemical structure. Shin, who wrote a review on curcumin and cancer prevention, says curcumin has the properties of an ideal chemopreventative agent.

By developing curcumin analogs with increased bioavailability, it's possible the compound will be able to "reach

Multiple cancer-related processes may account for spices' ability to inhibit experimentally induced cancers.

Adapted from: Kaefer CM, Milner JA. *Herbs and Spices in Cancer Prevention and Treatment*. CRC Press; 2011.

the tumor at a high concentration" and have more of an anti-cancer impact.

But low bioavailability does not necessarily mean low effect. Also, says Milner, "an analog is more of a drug effect than a dietary effect…. We don't know the biological consequence of having a modified compound. And I would rather use a natural compound in the spice itself rather than an unnatural compound."

Black Pepper

One possible way to increase the bioavailability of curcumin may take adding another spice to the diet: black pepper. Studies suggest piperine, a phytochemical in black pepper, can increase the bioavailability of certain anti-cancer compounds in foods, which may translate into greater anti-cancer protection. Piperine, when tested independently, exhibits anti-inflammatory, antioxidant and anticancer activities in cell studies.

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Research from the University of Michigan has found that the combination of curcumin and piperine improves curcumin bioavailability and inhibits breast stem cell self-renewal. The cancer stem cell theory proposes that a smaller population of cancer cells act as stem cells to reproduce and sustain the cancer. Cancer stem cells may also be responsible for metastases.

In addition, studies have found that piperine in combination with the green tea polyphenol epigallocatechin-3-gallate (EGCG) increased the bioavailability of EGCG. "What we found was that when we gave mice EGCG together with piperine, we could increase the amount of the compound [EGCG] that got into the blood and into some of the tissues compared to just giving them EGCG alone," said Joshua Lambert, PhD, Associate Professor of Food Science at Penn State University and the lead researcher on the animal study.

"We have a study going on right now that AICR funded where we are studying human subjects looking at the same bioavailability markers and we are seeing improved bioavailability in people," Lambert adds. The piperine dose used was 230 mg, which is about one-eighth of a teaspoon of black pepper.

Garlic

Although technically a vegetable, garlic is considered a spice because it is typically used for flavoring. Garlic is abundant in phytochemicals: it contains flavonoids, but is especially under study for its sulphur-containing compounds. When raw garlic is crushed or chopped, an enzyme breaks down the compound alliin to allicin, which is then converted to a variety of allyl sulfide compounds that have biologic activity in the body.

AICR's report and its continuous updates concluded that garlic protects against stomach and colorectal cancer. In one study, for example, women in the Iowa Women's Study consuming the highest amounts of garlic had a 50 percent lower risk of colon cancer than those with the lowest garlic consumption.

Spice	Phytochemical(s)	Potential health benefits
Allspice	Eugenol	Antimicrobial, antioxidant, anti-inflammatory
Black pepper	Piperine	Antioxidant, antimicrobial, promotes digestion
Cumin	Thymoquinone	Antioxidant, anti-inflammatory
Cinnamon	Cinnamaldehyde	Antimicrobial, anti-inflammatory, may help reduce blood sugar
Saffron	Alpha-crocin	Antioxidant, antidepressant
Turmeric	Curcumin	Antioxidant, anti-inflammatory
Red Chili	Capsaicin	Anti-inflammatory, pain reliever
Garlic	Allicin, Alliin, Allyl	Antioxidant, may help reduce cholesterol, antimicrobial
Ginger	Gingerol, Shogaols	Antioxidant, anti-inflammatory, alleviates pain

To date, three randomized clinical trials have looked at the effect of garlic on stomach and colorectal cancer risk; two out of the three studies showed garlic reducing the risk. In a study looking at precancerous stomach lesions, garlic supplementation with garlic extract and garlic oil daily did not reduce the risk of stomach cancer.

However, in another randomized control trial of 5,000 Chinese men and women, researchers found that those taking a combination of a garlic extract and selenium had one third reduced risk of all tumors and half the risk for stomach cancer compared to placebo. More clinical trials need to confirm these findings, scientists agree.

The potential protective effects of garlic may come from its antimicrobial properties, ability to block the formation of and activation of cancer-causing compounds, improve DNA repair, reduce cell proliferation and promote cell death.

How and How Much

"Not all spices are created equal," Milner says. Similar to fruits and vegetables, spices all have different antioxidant potentials, and it's possible that some spices may have a greater impact on one type of cancer than another or be beneficial across all cancers. However, this is still an area that has been inadequately examined.

Scientists also need to better understand how much of each spice is needed for cancer protection. Laboratory studies showing health benefits from spices and other flavor enhancers generally involve larger amounts than people use in cooking, usually supplement doses.

But, note experts, if these compounds show the synergy with one another as suggested in some studies, the high amounts necessary for effect in the lab may not be needed when a variety of spices are consumed regularly as part of a healthful predominantly plant-based diet that provides thousands of phytochemicals each day.

"The question is always how and how much is needed to do that. We need more research on individual spices and their biological consequences," says Milner. "This is a really exciting area that we need to know more about."◆

New American Plate Challenge: New Online Weight Loss Program

With the research now clear that excess body fat increases risk of seven cancers and other chronic diseases, AICR has launched an online weight-loss program based on the popular and evidence-based New American Plate (NAP) model for cancer prevention: a plate filled with two-thirds or more whole grains, vegetables and other plant-based foods and one-third or less meats or other animal foods. AICR's New American Plate Challenge is an interactive 12-week program that focuses on moving toward a plant-based plate and adding activity into each day.

The Challenge provides a visual approach to weight loss and maintenance that can supplement an existing weight loss plan or act independently, making it a versatile resource for health professionals, says AICR's Nutrition Communications Manager Alice Bender, MS, RD.

"The New American Plate Challenge is based on total health, not just total weight loss," said Bender. "We were always hearing how much health professionals and others loved the New American Plate approach because it's easy and visual. This introduces that concept to anyone who wants to lose weight healthfully but is not necessarily thinking about cancer prevention."

The first nationwide roll-out was completed in August; the program will launch again this fall.

Building the Challenge

The NAP Challenge was developed following a small feasibility study conducted over a four-month period. Participants provided information about their diet, alcohol consumption and activity level at the beginning, middle and end of the Challenge. Participants were supplied with a pedometer and a goal: 10,000 steps.

By the end of the 12 weeks everyone lost some weight and/or reduced their waist circumference. On average, participants improved their overall diet, consuming more plant foods, fewer calories and total fat. Physical activity also increased an average of two and a half miles more per day, 4,800 extra steps.

It's exciting to see people really take to this visual approach, says Dori Mitchell, MS, RD, the NAP Challenge Manager. "People are trying new foods and really looking at their plate … taking photos of their plate and sharing it with others, which made it fun and real."

> "It's exciting to see people really take to this visual approach … people are trying new foods and really looking at their plate."
>
> - Dori Mitchell

The pedometer was also incredibly motivating: "Participants realize they can fit physical activity into different pockets of the day: it doesn't have to be running, it could be walking around while waiting for their kids to finish soccer practice."

Snap and Share

Each week members receive a new challenge for healthier eating or getting active, becoming part of an online community in which they can share their successes, struggles and support one another.

Members receive information on why each challenge is important and related recipes and/or strategies for success. Each person makes small-step improvements based on his/her current eating and lifestyle habits; members can repeat the program to continue their healthy changes.

The program encourages snapping and sharing: members taking pictures of their plates to show how they are moving toward the two-thirds – one-third model, either keeping the pictures for themselves or posting so others can see their progress. With this approach, "its so easy – you don't have to measure, or weigh, worry about nutrients or count calories to know you are eating healthfully," said Bender.

Challenge members have their own page to track progress, post photos and share experiences. Participants can join the online sharing forum at any time, either following along with the online community or independently.

"It is so frustrating as a dietitian to see people go on a popular diet that is tough to stay on; they might lose some weight, then gain it back," said Bender. "This program is a way to change your overall dietary pattern and way of living – it's a new American plate way."

There are three options when joining the NAP Challenge community.

1. Free NAP Version
- Weekly emails with challenge information and reminders
- Access to online recipes, activity tips and weight loss strategies
- Participation in the sharing forum

2. Full Program with Starter Kit
- Weekly emails, online information and participation in sharing forum
- Sample menu plans
- Serving size guide and NAP brochures
- Exercise stretch band
- Pedometer

3. Premium Program (limited enrollment)
- Includes all from the Full Program
- "Lifeline" coaching session with a registered dietitian

Summer Books Recommendations

It's the last few weeks of summer, and there's still time to catch up on some great health-related reads. We asked a range of health professionals what books they're now enjoying and received an inspiring list of titles.

Wonder by R.J. Palacio
This is an excellent book about a child with facial deformity attending school for the first time after being home schooled for years. The story is told from multiple points of view and explores the perspective of the child, the family members and other members of the community.
– Timothy Gershon, MD, PhD
University of North Carolina (UNC) at Chapel Hill

The China Study by T. Colin Campbell
I get asked about this book by so many people when I'm talking about my research during community events. While I've read many of the research articles that form the basis for the book, I wanted to see how Dr. Campbell explains the findings to non-scientists.
– Kate Wolin, PhD, Loyola University Chicago

The Immortal Life of Henrietta Lacks by Rebecca Skloot
This is a wonderful reminder of ethical issues in the conduct of research and the delicate balance between advancing science and protecting human rights. It is based on a true story and I think anybody doing research in minority populations should read it.
– Elisa Bandera, MD, PhD
The Cancer Institute of New Jersey

Blue Zones by Dan Buettner
This shows how people live in areas of the world where longevity – a healthy, vibrant longevity – is most common. It is a reminder of how we can each find ways that work for us to develop plant-focused eating habits, keep active, and value our social supports.
– Karen Collins, MS, RDN, CDN, AICR Nutrition Advisor

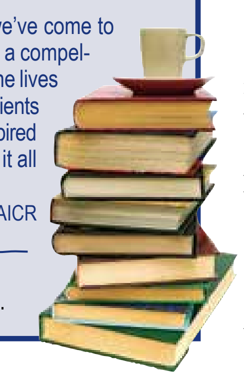
Hero Food by Seamus Mullen
Mullen is a top New York chef who discovered that changing his diet helped alleviate symptoms of his rheumatoid arthritis, which were becoming increasingly debilitating. His story and recipes are a testament to the power of food and nutrition, and that healthful eating can still be unspeakably delicious.
– Patrick Bradshaw, PhD, UNC at Chapel Hill

What Color Is Your Diet? by David Heber
This book is focused on getting people to put more color in their diet and in doing so, both increasing the amount of phytonutrients as well as reducing calories and increasing overall health. Dr. Heber established the Division of Clinical Nutrition at UCLA in 1983.... I am interested in his take on what to eat and why.
– Susan Bratton, Meals to Heal CEO

The Happiness Project by Gretchen Rubin
This book is an enlightening and fun narrative about the author's resolutions to reach a happier state of mind and make every day meaningful. It's honest, insightful, inspirational and well researched, with interesting facts about the science of happiness; a perfect book club summer read!
– Anjali Patel, MPH, RD, Healthy Dining

Naked Statistics: Stripping the Dread from the Data by Charles Wheelan
Wheelan delivers on his promise – he loves numbers and his enthusiasm shows on every page. If you'd like to have a better understanding of probability or how to interpret data from a research study, take a look at this witty and entertaining book.
– Susan Higginbotham, PhD, RD, AICR

The Emperor of All Maladies: A Biography of Cancer by Siddhartha Mukherjee
Mukherjee makes this story – how we've come to understand, study and view cancer – a compelling read. I love the way he explores the lives and passions of scientists, doctors, patients and activists who have shaped and inspired the research and treatment and puts it all in historical context.
– Alice Bender, MS, RDN, AICR



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Scientist in the Spotlight

Henk De Feyter, PhD

An AICR-funded researcher, Henk De Feyter, PhD, Associate Research Scientist at Yale University School of Medicine, focuses his research on cancer metabolism. Using a novel imaging technique called magnetic resonance (MR) spectroscopy, De Feyter's studies are shedding light on how metabolic changes and diet may link to helping treat brain tumors.

Q: Can you explain MR spectroscopy?

A: Magnetic resonance spectroscopy (MRS) uses the same machine as magnetic resonance imaging, MRI. From a subject's perspective the experience of going for an MRI scan versus an MRS scan is indistinguishable. Instead of reconstructing the signal of water molecules to get pictures out of it, MRS makes a spectrum from the signal of molecules other than water. A spectrum is a sort of graph with a bunch of peaks. Those peaks represent various molecules and they scale with the concentration of their molecules: if more of a molecule is present, than the peak is larger.

Q: How are you using this in your research?

A: MR spectrometry has several applications related to metabolism. We have developed MR methods to study the normal metabolism in the brain, skeletal muscle and liver. We are now moving toward studying brain tumors. In cancer, there are often altered metabolic pathways and/or metabolites and we can detect this with MR spectrometry.

One can now also use MR spectrometry to look for specific genetic changes in brain tumors that are related to cancer.

Q: You're using this technique for your AICR-funded study looking at brain cancer and the ketogenic diet (a high-fat, low-carbohydrate diet), correct?

A: Yes. I'm looking at dietary manipulation and brain metabolism. The idea has been around that we may be able to use diet to treat brain tumors. We are particularly interested in how a ketogenic diet may impact brain tumor development by exploiting the tumor's inability to metabolize ketone bodies. We're using MR spectroscopy to detect metabolism of ketone bodies in brain tumors.

> "If we can manage to transfer what we have learned about the healthy brain to brain tumors, it would be an amazing step."

Q: Can you explain what a ketone body is?

A: Ketone bodies are an energy source derived from fat. Our body produces ketone bodies in times of fasting. While the brain is usually a huge consumer of glucose – sugar – during times of fasting the brain can perfectly metabolize ketone bodies as well. The rationale for using the ketogenic diet is that brain tumors, in contrast to the healthy brain, would not be able to metabolize ketone bodies. One could "starve" the brain tumor while preserving the healthy brain's energy metabolism through ketone bodies.

Q: How did you become interested in metabolism and cancer?

A: I'm from Belgium and began my career as a physical therapist. The program was fun, but I realized it was not what I wanted to do. I decided to go to the Netherlands to study health and movement sciences. There, I focused on exercise physiology. Once at Yale, I focused on brain metabolism and now also brain tumor metabolism. And from the moment I learned how to use MR spectroscopy, that technique has been a constant factor in my research.

Cancer metabolism appears to have many subtle and less subtle changes in metabolism compared to healthy cells. To try to study the metabolic changes in tumors using [imaging] methods seemed an obvious step to me.

Q: What are some future applications for MR spectrometry?

A: If we can manage to transfer what we have learned about the healthy brain to brain tumors, it would be an amazing step. I hope we can apply MR spectroscopy to study brain tumor metabolism in humans.… Especially for cancer research and diagnostics, this new application has a lot of potential.

Q: What do you hope your study on ketogenic diet/brain tumors accomplishes?

A: My first aim is to understand more about the ketone body metabolism in tumors because that has been a fundamental aspect in making the case to use the ketogenic diet to treat brain tumors. As we have been using MR spectroscopy to study the human brain, we hope to get enough support to transfer our techniques and study brain tumors in patients.◆

Science Shorts

Believing but Not Meeting Recommendations

More than half of women who think they are eating healthy and being physically active enough to prevent cancer are not meeting the cancer-preventive recommendations, suggests a June study published in the *Journal of Women's Health*.

In a telephone survey of 800 women, more than half reported not meeting the minimum recommendations for physical activity and/or for daily consumption of fruits and vegetables. Among the women who believed they were eating a cancer-preventive diet, less than 10 percent of these respondents reported eating at least five servings of daily fruits and vegetables, which is the minimum recommended by AICR and the American Cancer Society.

Among the women who believed they were doing enough activity to prevent cancer, less than 40 percent reported being moderately active for 30 minutes five days per week. AICR recommends 30 minutes or more of daily moderate activity to reduce cancer risk.

Following AICR Recommendations to Prevent Aggressive Prostate Cancer

A new study published in *Nutrition and Cancer* suggests that men have a lower risk of developing an aggressive form of prostate cancer by following at least four of AICR recommendations for cancer prevention, including eating healthy and exercising, with each recommendation lowering the risk.

Researchers gathered the diet and activity habits of approximately 2,200 men ages 40 to 70, who were recently diagnosed with an aggressive form of prostate cancer. Using a point scale, they gauged how closely the men adhered to the 8 (of 10) relevant AICR recommendations.

Adherence to fewer than four of the recommendations predicted a 38 percent increased risk of aggressive tumors compared with adherence to four or more. Each point in a patient's total adherence score linked to a 13 percent reduction in risk of the cancer.

Sipping Less Calories but Still a Soda per Day

Americans of all ages are sipping fewer calories from sugary sodas, energy drinks and other sweet beverages compared to over a decade ago, but still drinking the equivalent of about a can of soda per day on average, about 150 calories, according to a May study published in *The American Journal of Clinical Nutrition*.

Researchers used data from approximately 51,000 NHANES participants. Between 1999 and 2010, the 2 to 19 year olds were drinking on average 155 calories per day, which is 68 fewer calories than in the 1999-2000 survey. Adults were consuming an average of 151 calories each day, a drop of 45 calories.

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