Spicy Approach to Cancer Treatment

By Sowmya Nath

With increasing curiosity into more holistic approaches to disease prevention and treatment, some researchers are rediscovering how an ancient spice may help treat and prevent many types of cancer.

Curcumin, or diferuloylmethane, is a yellow-orange powder that is the principal ingredient in turmeric (*Curcuma longa*), the Indian spice popularly known as curry. Cultivated in India, Southeast Asia, China, and other parts of Asia and tropical regions, turmeric has been used for centuries in Ayurveda, the Indian system of medicine. Known for its anti-inflammatory properties, curcumin is used to treat a variety of common ailments, including respiratory conditions, upset stomach, arthritis, acne, and skin and eye infections. In traditional Chinese medicine, it is used to treat diseases associated with abdominal pain.

Since 1815, when Harvard College laboratory scientists Vogel and Pelletier isolated curcumin, its medicinal properties have emerged. Its use in biliary diseases was reported in 1937, treating 67 patients; its antibacterial action, in 1949; and its ability to decrease blood sugar levels in human subjects, in 1972.

“Medicinal Gold”

But over the past decade, renewed interest in curcumin has focused on its antioxidant properties. Nearly 2,000 such publications have appeared in the National Library of Medicine’s PubMed database, many revealing curcumin’s antioxidant and anti-inflammatory powers.

Bharat Aggarwal, Ph.D., professor of cancer medicine and cancer research, and chief of the Cytokine Research Laboratory at the University of Texas M. D. Anderson Cancer Center in Houston, has been at the forefront of research on curcumin for two decades. Aggarwal calls it “medicinal gold,” citing the many studies in rodents and humans suggesting curcumin as a potential chemopreventive agent, as well as a suppressor of the tumorigenic activity of a wide variety of carcinogens in cancers of the gastrointestinal region, breast, prostate, and oral cavity, as well as leukemia.

Aggarwal discovered curcumin as an anti-inflammatory agent while researching tumor necrosis factor (TNF)—TNF-α blockers, and TNF-β blockers—the primary mediators of inflammation.

“Curcumin is the primary component of turmeric, and turmeric has been described in Ayurveda as an anti-inflammatory agent,” he said. “So I thought, ‘If it is truly an anti-inflammatory agent, it should block TNF.’”

His research showed that turmeric blocked both the production and the action of TNF.

Aggarwal said that because of its anti-inflammatory properties, curcumin could also combat other chronic illnesses, because inflammation is usually the culprit.

“Whether you talk about neurological disorders, whether you talk about cardiovascular, whether you talk about diabetes, whether you talk about obesity, whether you talk about pulmonary diseases such as asthma, and so forth, or immunological diseases, the common denominator in all these diseases is only one, and that is inflammation,” he explained.

Aggarwal said that most cancers are proinflammatory, and chemotherapy and radiation activate proinflammatory pathways. By blocking them, curcumin blocks cancer growth.

Inflammation can cause cancer by increasing levels of molecule microRNA-155, decreasing the activity level of proteins involved in DNA repair. The subsequent spontaneous gene mutations that occur at a higher rate could lead to cancer, according to a 2011 study published in *Proceedings of the National Academy of Sciences* by Esmerina Tili, Ph.D., and Carlo M. Croce, M.D., at the Ohio State University Comprehensive Cancer Center.

Aggarwal’s research has also established that curcumin has a diverse range of molecular targets, which supports the notion that curcumin influences many biochemical and molecular pathways. Among its molecular targets are transcription factors such as NF-κB.

“This is a master switch, and it controlled the expression of more than 300 different [inflammatory] genes,” Aggarwal said. “We have shown that most tumors have a constitutive NF-κB and the tumor is addicted to it, and if you were to inhibit the NF-κB, you can inhibit the growth of the tumor.”

Cyclooxygenase-2 (COX-2) protein is associated with a many cancers, including colon, lung, and breast. Several studies...
have shown that curcumin diminishes the expression of COX-2 in different tumor cell lines, most likely through minimizing the NF-kB required to activate COX-2.

Curcumin also reduces multiple tyrosine serine/threonine protein kinases that are activated by mutations that contribute to the malignant transformation and growth of human cancers. It also inhibits the expression of multiple genes and pathways involved in apoptosis, cell invasion, and adhesion. These functions of curcumin cause it to reverse cancer, Aggarwal said.

Curcumin blocks fibrosis in anti-Thy1 glomerulonephritis through increasing hemoxygenase-1 (HO-1) gene expression, suggesting that it has antifibrotic effects in glomerular disease. Curcumin can induce HO-1 expression in the same way through generating reactive oxygen species, activating p38, and inhibiting phosphatase.

**Symptom Relief**

According to Aggarwal, curcumin also relieves common cancer-related symptoms such as cachexia, a loss of skeletal muscles. Cachexia in cancer patients often manifests as anemia, muscle wasting, reduced appetite, and altered immune function, which result in fatigue, diminished quality of life, and reduced survival.

In a study appearing in *Cancer Prevention* in 2011, led by Zhen-Yu He, Ph.D., at the Nanjing Medical University in China, colorectal cancer patients received curcumin for anywhere between 10 and 30 days every day in 360-mg capsules. The body weight of these patients statistically significantly increased after taking curcumin.

According to Aggarwal, an ongoing clinical trial in the U.S. is also studying how curcumin may affect symptoms of cachexia. He says curcumin treatment may also help prevent secondary cancers, which 25% of cancer survivors experience, and is helpful in controlling conditions that cancer often brings on.

“We are using curcumin to control depression, lack of appetite, lack of sleep, neuropathic pain, and fatigue. These are all symptoms very common to cancer patients, and chemotherapy and radiation further make it worse. And we postulated that all these symptoms are mediated through inflammation: chronic, unregulated inflammation.”

For all curcumin’s anti-inflammatory and antioxidant prowess, the main reason Aggarwal is a fierce proponent of using it to battle cancer is its nontoxicity, even when consumed in doses as high as 2,500 mg per day. The U.S. Food and Drug Administration has approved curcumin as a GRAS (generally recognized as safe) compound.

“Chronic diseases caused by chronic inflammation require chronic treatment,” he said. “However, there is no drug that can be used chronically without side effects. That is one reason natural products that have been used for centuries came into the picture for chronic treatment.”

**Limited Clinical Trials**

Not everyone in the field shares Aggarwal’s enthusiasm. Barrie Cassileth, Ph.D., chief of the Integrative Medicine Service at the Memorial Sloan–Kettering Cancer Center in New York and member of the advisory panel of cancer.net, said that although curcumin is one of the most promising natural products in regard to cancer research, its effects have been proven largely in a laboratory setting, with limited clinical trials, which would not impress physicians enough to consider it a viable remedy for cancer.

“The biggest problem that we have to worry about for herbal remedies is that herb–drug interactions are common and serious,” she said. “Herbs can produce side effects particularly in the way that they’re sold. They’re not always purified. They’re frequently contaminated. There are very few herbal remedies on the market that are produced at pharmaceutical grade.”

Cassileth explained that curcumin could interact with other medications a cancer patient may be taking, or with chemotherapy itself, and cause serious side effects.

“First of all, most people who have cancer are older, and most of them have more than one medical problem, and usually they’re on medication,” she said. “They probably are on medication for—in addition to chemotherapy—diabetes, perhaps, or for heart disease, or who knows what.”

Even in younger patients who may not be taking medications for other health problems, Cassileth said curcumin could interfere with chemotherapy and hence advises against it.

But Aggarwal said he administers curcumin for most of his patients without serious side effects.

“However, some people react to it... they get diarrhea because they are not used to taking it,” Aggarwal explained.

He said he refrains from giving curcumin in only a couple of instances: when the patient is taking blood thinners—because curcumin has been documented as a blood thinner as well and could amplify the effects of the medication—and when the patient is likely to undergo surgery.

Cassileth stressed that cancer patients not suspend their treatments in favor of unproven natural therapies or treatments.

Cassileth added that before curcumin is prescribed as a drug for cancer treatment, researchers must prove the value of curcumin in clinical settings.

“We need more clinical research to make sure that curcumin (1) is beneficial, (2) does not interfere with other therapies that the patient might be on, and (3) has no untoward side effects we don’t know about,” she said. “All these things are very important. That’s the way science proceeds. You don’t get one little study that shows something, and that’s not going to be a gamechanger. It’s not going to change how we treat patients.”

© Oxford University Press 2011. DOI: 10.1093/jnci/djr526