Curry Compound Fights Cancer in the Clinic

By Andrea Carter

Kavita Chopra recalls the way that her grandmother would dissolve a teaspoon of the Indian curry spice turmeric in water each morning to promote good health. Today, Chopra takes an 8-g pill of curcumin—the molecule that gives turmeric its bright yellow color—to fight the follicular lymphoma she was diagnosed with 2 years ago.

Curcumin, a compound in the spice turmeric, has shown its cancer-fighting potential in the lab and, more recently, in the clinic.

Chopra learned about curcumin from a newspaper article that described research by Bharat Aggarwal, Ph.D., which showed that curcumin slows cancer growth in the lab and in mice. After speaking with Aggarwal, a professor of cancer medicine at the University of Texas M. D. Anderson Cancer Center in Houston, she started taking curcumin even though her oncologist doesn't believe it will do any good.

Chopra is not alone in her faith in curcumin. People have used turmeric, derived from the plant *Curcuma longa*, in traditional Indian Ayurvedic medicine for thousands of years to treat inflammation associated with such ailments as fever, stomachaches, and skin abrasions. People have safely ingested turmeric, a key ingredient in Indian curries, for centuries. Researchers began looking into the spice's anticancer properties after epidemiological studies reported a 10%–50% lower incidence of certain cancers in India. An array of lab and animal studies have shown that curcumin kills cancer cells and slows tumor growth.

These early studies have prompted researchers to take curcumin from the lab to the clinic. It is too early to tell whether curcumin can make the jump from being a nutraceutical to an accepted treatment for cancer, yet some early results from clinical trials to treat cancer appear intriguing.

"My sense, from the large amount of preclinical and anecdotal evidence, is that things will work out well for curcumin," said biologist Tim Corson, Ph.D., at Yale University in New Haven, Conn.

Medicines from nature are nothing new. Aspirin comes from willow tree bark and the chemotherapy drug paclitaxel comes from the Pacific yew tree. Still, Western medicine, skeptical of "snake oil" solutions, has been slow to adopt many Eastern remedies. Also, because many of these medicines are not big money makers, most pharmaceutical companies overlook them.

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Nevertheless, curcumin has a long history in research. Chemists first described curcumin's structure in 1910. But only in the last 30 years have lab and animal studies provided data on curcumin's use in a range of diseases including cancer, cardiovascular disease, and Alzheimer disease. In the 1980s, Aggarwal began studying the transcription factor NF-κB, which activates both inflammation and cell proliferation pathways in the cell. Curcumin acts on hundreds of cell targets, such as genes, transcription factors, growth factors, inflammatory cytokines, and kinases. But it is curcumin's ability to block NF-κB levels and certain cyclooxygenases involved in inflammation that researchers think may provide anticancer properties.

Hundreds of rodent studies have suggested curcumin's cancer-fighting potential. In the lab, curcumin blocks cells from multiplying and kills a range of cancer cells, including colon, breast, prostate, and melanoma cells. It slows tumor and blood vessel growth in mice injected with human pancreatic cancer cells. In another study, mice with a gene mutation that makes them prone to developing intestinal tumors ate curcumin for 10 days. Tumor growth was reduced by about 60% in these mice compared with mice not taking curcumin.

This preclinical research has taken curcumin from the lab to the clinic. In 2007, there were 22 phase I or II cancer-related clinical trials with curcumin, most of which are still ongoing. An unpublished phase II study at M. D. Anderson Cancer Center monitored 25 pancreatic cancer patients taking curcumin without any other treatment. The study found a 73% tumor reduction in one patient (it did grow back 1 month later), and the disease stabilized in four patients, one of whom lived 2.5 years longer than predicted.

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just a few patients show a benefit at the beginning," said Razelle Kurzrock, M.D., who led the study.

An unrandomized trial at Johns Hopkins University in Baltimore found that curcumin taken with quercetin, a compound found in apples, slowed the growth of precancerous polyps in the colon by about 60% in five patients with an inherited colorectal cancer syndrome known as familial adenomatous polyposis.

These studies may lay the groundwork for more randomized trials investigating curcumin in cancer prevention and treatment, as well as preventing cell resistance to chemotherapy and radiation. But some clinicians believe that the research is too preliminary to get excited about. "I'm afraid that a lot of the enthusiasm is a bit premature," said David Alpers, M.D., of the Washington University School of Medicine in St. Louis.

Curcumin's molecular design may make it difficult to develop into an effective anticancer drug. For example, it may be impossible for people to take enough curcumin to produce an effect. Scientists must use large amounts (sometimes 1,000 mg or more) in vitro. The hydrophobic molecule does not dissolve in water, so it's not readily absorbed in the intestines. Also, because curcumin strikes the cell at many sites, it's difficult to determine which target is causing the desired effect in a certain disease. Industry has avoided natural compounds with multiple targets because what can be beneficial at one site can cause side effects at another, Corson said. To date, curcumin's published success has been primarily with lab studies. Taking it to the next step can be a challenge, especially to treat chronic diseases where drugs must be taken over several years.

Researchers, however, continue to look for ways around curcumin's limitations. Studies showed that the molecule piperine from black pepper increases absorption in rats by 154% and in humans by much more. When people took curcumin on its own, blood levels of the molecule were negligible, yet when taken with 20 mg of piperine per kilogram of body weight, bioavailability increased by 2,000%.

Anirban Maitra, M.D., an associate professor of pathology and oncology at Johns Hopkins University, has applied nanotechnology to the problem. He enclosed curcumin in a nanoparticle envelope made of polymers, making it soluble in water. Maitra is hesitant to share his data at this point but says that a biotechnology company has licensed the particle to develop for clinical trials.

In the past 10 years, looking to alternative medicine for answers has become more accepted. Some researchers argue that if a compound has been used for thousands of years, there may be more to it than just the placebo effect. Cancer is not caused by one cellular defect; several mechanisms can go wrong. "Dirty" drugs that target multiple cellular sites may be effective. Ultimately, "we want something that shrinks a tumor," Maitra said, "What does it matter if it hits three, four, or five targets?"

However, Aggarwal, one of curcumin's biggest proponents, doesn't believe that the unpatentable curcumin will ever become a drug in the conventional sense. His hope is that it may be an alternative option, with the science to back it up, for people struggling with cancer.

"Patients may anecdotally accept it—but a drug, no," Aggarwal said.

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