

Can a Common Spice B

Western science may be substantiating what Eastern medicine has long known: that curcumin, the main ingredient of the curry spice turmeric, is a powerful anticancer agent.

By Dianne C. Witter

Razelle Kurzrock, M.D., rigorously evaluates the laboratory data behind any new pharmaceutical agent she considers moving into clinical trials at M. D. Anderson Cancer Center. As a physician, she is cautious; as a scientist, she's a skeptic; she wants unbiased, evidence-based information. And that, to her own surprise, is how she became interested in studying curcumin—the primary ingredient of the curry spice turmeric—as a possible anticancer agent in humans.

"Dr. Bharat Aggarwal, chief of the cytokine research laboratory in the Department of Experimental Therapeutics, came to me and said, 'I want to show you some great results we've gotten in the lab with an exciting new agent,'" said Dr. Kurzrock. "But he wouldn't tell me what the agent was—he wanted me to see the data first."

Dr. Kurzrock, professor in and chair ad interim of M. D. Anderson's Department of Investigational Cancer Therapeutics (formerly the Phase I Clinical Trials program), was impressed with the data. "It was clear that this agent was just as potent at killing tumor cells in the lab as any experimental drug I'd seen from pharmaceutical companies," she said. When Dr. Aggarwal told her this active agent was curcumin, she was intrigued and began designing a clinical study to test curcumin's efficacy in humans.

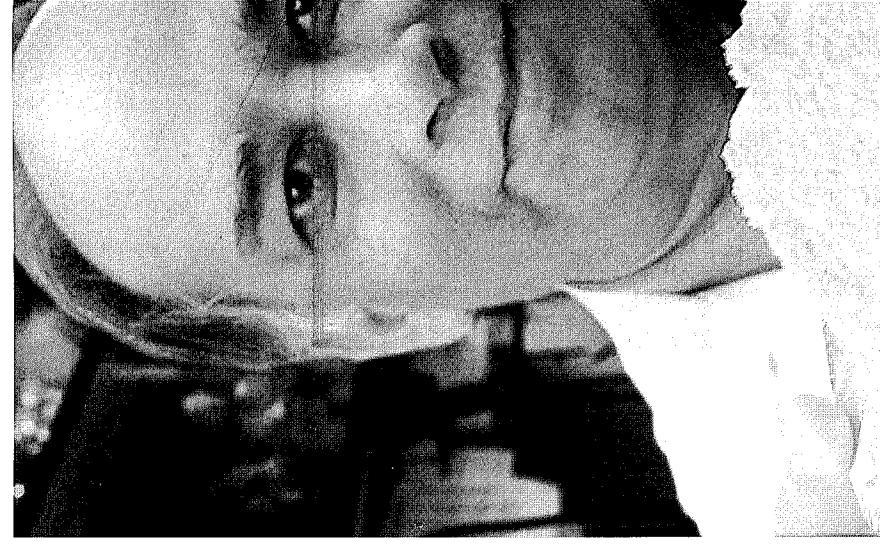
Shutting down the master switch

Curcumin's anti-inflammatory properties have been valued in Eastern medicine for centuries, but its specific mechanism of action has only recently been identified. In 1995, Dr. Aggarwal and colleagues demonstrated that curcumin shuts down nuclear factor kappa B (NF- κ B), which is involved in the regulation of inflammation and many other processes.

By blocking the activity of this "master switch," curcumin appears to interfere with the cancer process at an early point, impeding multiple routes of development: reducing the inflammatory response, inhibiting the proliferation of tumor cells, inducing their self-destruction, and discouraging the growth of blood vessels feeding tumors. These effects can shrink tumors and inhibit metastasis. Furthermore, shutting down NF- κ B can enable traditional chemotherapy drugs to destroy cancer cells more effectively.

Hundreds of laboratory studies by Drs. Aggarwal and Kurzrock and others have demonstrated that curcumin is biologically active against many types of cancer cells—melanoma, and breast, bladder, brain, pancreatic, and ovarian carcinomas, to name just a few. "In the lab, we haven't yet found a type of cancer it doesn't show activity against," Dr. Aggarwal said.

While it's a long road from lab to clinic, Dr. Aggarwal sees promise in curcumin both as a possible preventive agent and as a cancer treatment. As a medicinal agent, its potential extends far beyond cancer. Laboratory studies have demonstrated curcumin's promise in a number of different diseases that are also affected by inflammation, including arthritis, inflammatory bowel disease, Alzheimer's disease, diabetes, cardiovascular disease, autoimmune diseases, and others. In light of these findings, the number of clinical studies of curcumin has grown substantially in the past few years and continues to rise.



Dr. Aggarwal is conducting laboratory studies on curcumin, which is the main ingredient of the curry spice turmeric.

Studying activity in cancer patients

The clinical research on curcumin in cancer is new but promising. Early studies at M. D. Anderson and elsewhere have shown curcumin to be well tolerated and non-toxic at high oral doses.

Dr. Kurzrock and colleagues recently conducted a trial of curcumin in 49 patients with advanced pancreatic cancer, which is notoriously resistant to treatment. Two of those patients had clinically meaningful responses and remained stable for 8 months and more than 22 months, respectively. Another had a brief but dramatic response (73% reduction in tumor size).

"In advanced pancreatic cancer, the response rate to the Food and Drug

e Used to Treat Cancer?

Western medicine has maintained for centuries—
since turmeric, has some potent medicinal qualities.



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Dr. Kurzrock is designing clinical trials of curcumin, based on promising lab results.

Administration-approved treatments is only about 5%, so we were very encouraged that we saw any activity at all in this group," said Dr. Kurzrock. "That tells us curcumin does have biologic activity in pancreatic cancer—there was a true antitumor effect. It's too soon to know if it will affect survival rates, but more study is definitely warranted." The fact that some patients benefited is encouraging, since there were questions about whether therapeutic concentrations could be achieved with oral administration.

To address the issue of absorption, Dr. Kurzrock is leading the development of an intravenous, liposome-encapsulated delivery system for curcumin that she says has so far been "very potent" in

the lab: Liposomal curcumin would be given intravenously, thereby circumventing the problem of poor absorption.

"The fact that the curcumin did show some activity in the study even though it was poorly absorbed suggests that if we can develop a more effective method to get it to the tumors, it may well have promise as an anticancer treatment," said Dr. Kurzrock. She hopes to have the liposome-encapsulated delivery system ready to test in a phase I clinical trial for patients with a variety of cancers in 2008. Whether the intravenous formulation would have more side effects in patients because of the higher blood levels of the agent is not yet known, but preliminary testing

in mice has shown no toxicity, even at maximum doses.

Currently under way at M. D. Anderson is a clinical trial of curcumin in multiple myeloma, and researchers are seeking funding for a trial in breast cancer. Trials of curcumin in colorectal cancer and in myelodysplastic syndrome are in progress at other institutions. Curcumin is also in clinical trials as a treatment for non-cancer diseases such as Alzheimer's disease, arthritis, and psoriasis.

Food for thought

Dr. Aggarwal, for one, is not surprised at the evidence that curcumin may have efficacy in treating cancer. He feels curcumin has the potential to one day be an inexpensive and non-toxic alternative to harsher oncology drugs; a chemopreventive agent; and an adjunct to chemotherapy. But he notes that progress

in developing curcumin for medical use is likely to be much slower than for pharmaceutical agents because curcumin can't be patented on a broad scale and therefore is unlikely to attract the interest and the funding of pharmaceutical companies.

For his part, Dr. Aggarwal takes a curcumin tablet every day, and he offers this food for thought: "The combined rate of the four most common cancers in the United States—lung, prostate, breast, and colon—is at least 10 times lower in India, where curry is a staple in the diet." ●

For more information, call Dr. Aggarwal at 713-794-1817 or Dr. Kurzrock at 713-794-1226.