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File: ■ Turmeric (*Curcuma longa*)
■ Curcumin
■ Colorectal Cancer

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RE: In Vitro and In Vivo Studies Indicate Curcumin Potential for Preventing and/or Treating Colorectal Cancer

Kunnumakkara AB, Guha S, Aggarwal BB. Curcumin and colorectal cancer: add spice to your life. *Curr Colorectal Cancer Rep*. 2009;5:5-14.

Curcumin, found from 3% to 5% in turmeric (*Curcuma longa*), is the major active component of this medicinal spice used in curry powder, an integral part of Indian cooking and lifestyle. Epidemiological studies have found that colorectal cancer is less prevalent in Eastern nations, including India (30 cases per million), where turmeric is regularly consumed, than in Western countries, including the U.S. (530 cases per million). The authors summarize data indicating that turmeric and curcumin may exercise protective effects specifically against colorectal cancer.

Besides curcumin, turmeric and commercial curcumin contains demethoxycurcumin and bisdemethoxycurcumin (around 17% and 3%, respectively, together with about 77% curcumin in commercial concentrates). While curcumin is considered the most active ingredient, it may be that complete turmeric is more potent than any single component. Compounds found in turmeric are chemically similar to those found in other medicinal plants, such as gingerol in ginger (*Zingiber officinale*), yakuchinone-A in Chinese galangal (*Alpinia chinensis*), and iso-eugenol in clove (*Syzygium aromaticum*).

Numerous molecular targets of curcumin in colon cancer are discussed, including inhibition of nuclear factor κB signaling, activation of peroxisome proliferator-activated receptor-γ in colon cancer cells, inhibition of the transcription factor early growth response-1, inhibition of β-catenin signaling, and inhibition of mitogen-activated protein kinases. Curcumin also inhibits cyclin-dependent kinases, blocks epidermal growth factor receptor signaling, reduces *N*-acetyltransferase carcinogen transformation, and inhibits inflammatory COX-2 and 5-LOX expression in mouse tumors. Studies have found that curcumin induces the tumor suppressor p53, inhibits B-cell lymphoma-2 and basal cell lymphoma-extra large in xenograft tumors in mice, inhibits the proinflammatory cytokine interleukin-8, and mediates ceramide generation and apoptosis in colon cancer cells. These molecular-level effects on cellular activity suppress proliferation, inhibit cell growth, reduce biotransformational enzymes, control DNA damage, inhibit cancer cell

cycle progression, reduce cancer cell survival, promote cancer cell apoptosis, and block cancer cell migration.

Numerous in vitro studies show that curcumin suppresses proliferation and increases apoptosis in several colorectal cancer lines. At least 8 rodent studies have found that ingested curcumin prevents colon cancer growth, and 2 studies showed it was an effective therapy in colon and colorectal cancers in mice.

Resistance to both standard chemotherapeutic drugs and radiotherapy is a serious problem in colorectal cancer treatment. Studies have found that curcumin sensitizes cancer cells to such treatments in mice.

Absorption and systemic bioavailability of curcumin are low, but for gastrointestinal diseases this is not a problem. Turmeric extract or curcumin must be consumed in rather large quantities to be useful. It is most effective in its cancer prevention and reduction activities in the gastrointestinal tract, and is believed to be metabolized in the intestines. Curcumin conjugation is much more extensive in intestinal fractions from humans than those from rats, but less extensive in human hepatic fractions than those from rats. The curcumin-reducing capacity of cytosol from human intestinal and liver tissue was greater than in corresponding rodent tissue by factors of 18 and 5, respectively. Results demonstrate that human intestinal tissue has more curcumin metabolites than rat intestinal tissue. Curcumin has been studied for toxicity in rodents; no toxicity was found, but dose-dependent increases in liver weight were observed in rats receiving curcumin versus controls. In humans, no toxicity has been found in doses up to 12 g daily.

A number of human clinical trials with curcumin have been conducted. Positive results have been achieved in some, indicating that curcumin may be useful in inhibiting expression of familial adenomatous polyposis and in treating ulcerative proctitis, Crohn's disease, and ulcerative colitis; and turmeric extract daily for 8 weeks helped in reducing symptoms of irritable bowel syndrome.

In 15 patients with advanced colorectal cancer refractory to standard chemotherapy, ingestion of turmeric extract for 4 months showed radiological stable disease for 2 to 4 months in 5 patients. No dose-limiting toxicity was observed. Other studies have also reported limited results, perhaps a function of study design and limited objectives. In the authors' own study of pancreatic cancer, 25 patients received 8 g curcumin for two months; of 21 available for response, two had clinical biological activity, one was stabilized for over 18 months, and one had a brief but marked (73%) tumor regression. The authors state that due to its potent anti-inflammatory activity, "curcumin has potential for preventing and treating CRC" (colorectal cancer), though more studies are needed to assess this potential.

—Mariann Garner-Wizard

The American Botanical Council has chosen not to reprint the original article.