

Why the Buzz about Turmeric?

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It sounds like the ideal cancer chemopreventive – natural, safe, well-tolerated, and effective. Curcumin, from the familiar spice turmeric, has served as a traditional treatment for thousands of years for skin wounds, inflammation, and tumors.ⁱ Now it has gained the attention of contemporary investigators as in, “Curcumin appears to possess all the desirable features of a desk-designed, multipurpose drug”ⁱⁱ and, “No natural agent has yet been described which modulates so many signal transduction pathways as curcumin does.”ⁱⁱⁱ M.D. Anderson Cancer Center researchers offered, “From numerous studies..., it is quite apparent that curcumin has tremendous potential for prevention and therapy of various cancers.”^{iv}

How It Works

Cancer cells employ multiple pathways to evade host defenses, so a drug or plant compound that attacks cancer in heterogeneous ways offers unique advantages, especially when it completes this mission relatively risk-free. In its interaction with several cellular proteins, curcumin antioxidates, induces phase II detoxification enzymes, suppresses tumor cell proliferation in several cancer cell lines, and down-regulates transcription factors (NF- κ B, AP-1, Egr-1). It down-regulates enzymes such as cyclo-oxygenase-2 (COX-2), lipo-oxygenase (LOX), nitric oxide synthase (NOS), matrix metalloproteinase 9, urokinase-type plasminogen activator, and more. Curcumin also down-regulates other factors and receptors such as tumor necrosis factor, chemokines, cell surface adhesion molecules, and growth factor receptors (e.g., EGFR, HER2). Curcumin acts antiangiogenically and enhances the cytotoxicity of certain chemotherapy drugs.

Curcumin causes cell death in several human cancer cell lines, including breast, lung, prostate, colon, melanoma, kidney, hepatocellular, ovarian, leukemia. The effect curcumin has on cell death involves both the usual apoptotic mechanisms such as oligonucleosomal DNA degradation and alternative means. That is, when resistance develops to apoptosis-inducing factors, curcumin can overcome this impediment through alternative cell-signaling pathways such as mitotic catastrophe.^v Mitotic catastrophe involves a morphologically distinct and aberrant mitotic process that distinguishes it from apoptosis, characterized by the formation of giant, multinucleated cells carrying uncondensed chromosomes. Curcumin may also counteract the induction of pro-survival factors in cells generated by radiation therapy and chemotherapy.

Beyond Cancer

Curcumin's versatility allows it to help with conditions other than cancer. Two studies from India indicate that topical turmeric helps control dermatomycoses and bacterial dermatitis.^{vi} Curcuminoids act synergistically against *Toxocara canis*.^{vii} A randomized, double-blind, placebo-controlled parallel group trial of turmeric in dogs with osteoarthritis showed a statistically significant treatment effect for curcumin (known in this study as P54FP) according to investigator assessment.^{viii} Curcumin inhibits proliferation of human retinal endothelial cells exposed to high glucose levels likely by affecting vascular endothelial growth factor (VEGF), and thus may forestall diabetic retinopathy.^{ix} The antioxidants found in curcumin increase the life span of experimental animals, offset senescent immune decline, and protect the function of mitochondria.^x Curcumin inhibits glutamate-mediated excitotoxicity and prevents the pathogenic aggregation of proteins that typically occur in neurodegenerative conditions such as Parkinson's and Huntington's diseases, amyotrophic lateral sclerosis, and Friedrich's ataxia. It limits lipid peroxidation and the accumulation of substances such as lipofuscin and beta-amyloid, associated with cognitive impairments. In fact, researchers are now studying this agent in Phase II clinical trials on patients with mild to moderate Alzheimer's disease.

Safe at any dose?

Human clinical trials demonstrate no dose-limiting toxicity when given up to 10 g of curcumin in one day.^{xi} The amount of curcumin contained in turmeric averages only about 3% by weight^{xii}; concentrated curcumin supplements therefore supposedly provide higher levels of the active constituent, provided that the label and actual contents agree.

The hurdles of gaining and maintaining adequate blood levels of curcumin pertain to its low bioavailability outside of the gastrointestinal tract, although absorption varies between species.^{xiii} One way to overcome delivery challenges could include coupling it with compounds that focus curcumin's activity toward specific target cells.

Herb-drug interactions

In that it affects so many pathways, curcumin could hypothetically negate some of the effects of chemotherapy. Certain reports suggest that curcumin can inhibit chemotherapy-induced apoptosis in breast cancer cells specifically in combination with camptothecin, mechlorethamine, or doxorubicin.

Other dietary chemopreventives

Several foodstuffs offer chemoprevention. The main polyphenol in green tea, epigallocatechin-3-gallate (EGCG), induces apoptosis and promotes cell growth arrest.^{xiv} Apigenin, found at high levels in peppermint, parsley, and thyme, possesses antioxidant, anti-tumor, and anti-inflammatory activities. However, “not all antioxidants are created equal” and antioxidant mixtures can potentially either undo or augment one another, due to their sometimes antagonist or synergistic mechanisms of action.^{xv} Food-sourced cancer-fighters thus provide an ongoing bounty of fruitful investigational arenas.

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ⁱⁱⁱ Aggarwal BB, Kumar A, and Bharti AC. Review. Anticancer potential of curcumin: preclinical and clinical studies. *Anticancer Research*. 2003;23:363-398.

^{iv} Aggarwal BB, Kumar A, and Bharti AC. Review. Anticancer potential of curcumin: preclinical and clinical studies. *Anticancer Research*. 2003;23:363-398.

^v Salvioli S, Sikora E, Cooper EL, et al. Curcumin in cell death processes: a challenge for CAM of age-related pathologies. *eCAM*. 2007;4(2):181-190.

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^{ix} Rema M and Pradeepa R. Diabetic retinopathy: an Indian perspective. *Indian J Med Res*. 2007;125:297-310.

^x Miquel J, Bernd A, Sempere JM, et al. The curcuma antioxidants: pharmacological effects and prospects for future clinical use. A review. *Archives of Gerontology and Geriatrics*. 2002;34:37-46.

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^{xiii} Tayyem RF, Heath DD, Al-Delaimy WK, et al. Curcumin content of turmeric and curry powders. *Nutrition and Cancer*. 2006;55(2):126-131.

^{xiv} Balasubramanian S and Eckert RL. Keratinocyte proliferation, differentiation, and apoptosis – Differential mechanisms of regulation by curcumin, EGCG and apigenin. *Toxicology and Applied Pharmacology*. 2007, in press.

^{xv} Eckert RL, Crish JF, Efimova T, et al. Review. Opposing action of curcumin and green tea polyphenol in human keratinocytes. *Mol Nutr Food Res*. 2006;50:123-129.