C3 Curcumin Complex



THIS INFORMATION IS PROVIDED FOR THE USE OF PHYSICIANS AND OTHER LICENSED HEALTH CARE PRACTITIONERS ONLY. THIS INFORMATION IS INTENDED FOR PHYSICIANS AND OTHER LICENSED HEALTH CARE PROVIDERS TO USE AS A BASIS FOR DETERMINING WHETHER OR NOT TO RECOMMEND THESE PRODUCTS TO THEIR PATIENTS. THIS MEDICAL AND SCIENTIFIC INFORMATION IS NOT FOR USE BY CONSUMERS. THE DIETARY SUPPLEMENT PRODUCTS OFFERED BY DESIGNS FOR HEALTH ARE NOT INTENDED FOR USE BY CONSUMERS AS A MEANS TO CURE, TREAT, PREVENT, DIAGNOSE, OR MITIGATE ANY DISEASE OR OTHER MEDICAL CONDITION.

Curcumin -- the spice for life

C3 Curcumin Complex is a patented, unique composition of three bioactive, health-promoting curcuminoids: Curcumin, Bisdemethoxy curcumin, and Demethoxy curcumin. These are the strongest, most protective and best-researched constituents of the turmeric root.

The naturally occurring turmeric root powder contains only 5-7% curcumin, while the C3 Curcumin Complex extract is concentrated to contain 95% curcuminoids, among which Curcumin represents the majority, 70% of the total extract. This means supplementing C3 Curcumin Complex would be far more therapeutic than simply adding turmeric to our foods. The crystalline structure of curcumin renders it difficult to absorb in the GI tract, similar to CoQ10. Designs for Health added

Other Ingredients: Magnesium stearate (kosher), di calcium phosphate.

lecithin, a powerful emulsifier, to enhance absorption; and bioavailability. We recommend taking this with a meal that contains fat or with DFH Omega Marine Fish Oil or Genuine Arctic Cod Liver oil, which act synergistically on inflammation. Curcumin shows excellent safety. It has been demonstrated to be safe in six human trials and has demonstrated anti-inflammatory activity.⁸

Excessive inflammation is a common risk factor for disease occurrence and progression. Inflammation may lead to joint tissue destruction, cancer, cardiovascular events, insulin resistance/diabetes and brain/liver/kidney degenerative diseases. Curcumin was shown to reduce inflammation, whether acute or chronic, caused by physical injury, joint wear and tear (as in osteoarthritis), chronic infections or inadequate antioxidant protection.^{1-4, 8, 14, 15, 18, 56}

Curcumin was shown to be more effective than certain NSAIDs in reducing inflammation and pain associated with rheumatoid arthritis¹⁵ or post-operative trauma.⁵² It has a better cardiovascular safety profile than aspirin because it does not inhibit the arterial protective factor prostacyclin like aspirin does.¹⁸ We learned from Clinical Rounds guest speaker and researcher, Dr. Aggarwal, that curcumin acts on the mother compound NF Kappa beta. By suppressing this inflammatory marker, curcumin has a domino effect of reducing the entire cascade of inflammatory compounds that would be produced thereafter. Dr. Bharat Aggarwal discovered NF Kappa beta while working at Genentech in California.

"Different molecules involved in inflammation that are inhibited by curcumin include phospholipase, lipooxygenase, cyclooxygenase 2, leukotrienes, thromboxane, prostaglandins, nitric oxide, collagenase, elastase, hyaluronidase, monocyte chemoattractant protein-1 (MCP-1), interferon-inducible protein, tumor necrosis factor (TNF), and interleukin-12 (IL-12)."

Curcumin has an advantage over pharmacological anti-inflammatory agents because it is a powerful antioxidant so it can also reduce COX expression along with being a COX 1 and COX 2 inhibitor. Where NSAIDS are known to have potential GI side-effects such as GI bleeding, curcumin was shown in one study to heal GI injury caused by the NSAID indomethacin.⁴ Amazingly, curcumin and resveratrol have been proven to be even stronger antiinflammatories than ibuprofen and aspirin.

"Overall these results indicate that aspirin and ibuprofen are least potent, while resveratrol, curcumin, celecoxib, and tamoxifen are the most potent anti-inflammatory and antiproliferative agents of those we studied."³

Benefits shown in research using curcumin extracts:

IMMUNE SYSTEM REGULATION

- Inflammation⁸ injury, post-operative⁵², joint wear and tear (osteoarthritis)⁵⁶
- Allergic reactions asthma⁵
- Autoimmune activity reduction^{15, 28} rheumatoid arthritis and multiple sclerosis in animals
- NK cell activity increase²
- Reduced cancer development and spread in certain animal models of carcinogenesis⁴⁰: breast¹⁹, prostate³⁵, colon²⁴, pancreatic [25], glioma²⁹, ovarian49

ANTIMICROBIAL

- Antiviral⁶ Epstein Barr² and HIV virus ^{22,23}
- Antibacterial, antiparasitic1

GI PROTECTION & HEALING

• stomach ulcer, Crohn's or proctitis⁵

CARDIOVASCULAR PROTECTION

- reduces cholesterol oxidation and levels, increases HDL²⁶
- reduces fibrinogen34
- reduces platelet aggregation 18, 37

BRAIN PROTECTION

- reduced brain damage following ischemia (reduced blood flow)⁴⁷
- reduced development and regression of Alzeimer's disease progression in animal models⁴⁶
- reduced gliomas (brain tumors)²⁹
- antidepressant effects¹⁶

LIVER PROTECTION from alcohol and aflatoxin (peanut fungus)^{54, 55}

TOXIC METAL CHELATOR53

• Effective chelator of copper and iron

ANTIOXIDANT27

BILE SUPPORT

• enhances bile flow and solubility³⁹

Lowers histamine and imroves allergies^{5,6}

"Curcumin and tetrahydrocurcumin (THC) caused a marked decrease in histamine release. These results suggest that the hydroxy groups of curcumin play a significant role in exerting both the anti-oxidative and anti-allergic activities, and that most of the compounds develop the anti-allergic activities through mechanisms related to anti-oxidative activities, but some through mechanisms unrelated to anti-oxidation activity." 5 "These results indicate that curcumin may have a potential effect on controlling allergic diseases through inhibiting the production of cytokines affecting eosinophil function and IgE synthesis." 6

Curcumin may be helpful for autoimmune conditions. Curcumin downregulates mediators characteristic of rheumatoid arthritis¹⁵, reduces disease activity in Crohn's⁹ and was shown to reduce disease activity in a model of multiple sclerosis in animals.²⁸ "These findings highlight the fact that curcumin inhibits experimental encephalomyelitis by blocking IL-12 signaling in T cells and suggest its use in the treatment of MS and other Th1 cell-mediated inflammatory diseases."²⁸

Also, by boosting NK cell activity increase,² curcumin may enhance the body's ability to fight infections.

There are many studies on curcumin and cancer. For patients undergoing chemotherapy, curcumin does not need to be avoided as it has been shown to enhance chemotherapy effectiveness.⁴⁸ Curcumin is the highlight of human clinical trials being performed at the M.D. Anderson Cancer Institute in Houston, Texas.

"In addition to antioxidation, curcumin could also induce apoptosis by targeting mitochondria, affecting p53-related signaling and blocking NF-kappaB activation. To further dissect its anticarcinogenic mechanisms, a number of curcumin targets were identified. These included the aryl hydrocarbon receptor, cytochrome P450, glutathione S-transferase, serine/threonine kinases, transcription factors, cyclooxygenase, ornithine decarboxylase, nitric oxide synthase, matrix metalloproteinases and tyrosine kinases. This review will summarize our current knowledge on how these important proteins are affected by curcumin, and hopefully, may provide a whole picture illustrating how the chemopreventive and antitumorigenic effect of curcumin is achieved." 40

Curcumin and vitamin D3 can act in synergy

"agents discussed include those that have differentiation-inducing activity of their own that is increased by combination with vitamin D(3) or analogs, such as retinoids or plant-derived compounds and antioxidants, such as curcumin." ³⁰

Many spices protect us from bacteria and parasites in our food while boosting our bodies' antioxidant abilities. Research shows curcumin to have anti-microbial activities. Curcumin was shown to reduce transcription of Epstein Barr²¹ and HIV virus.^{22,23} Curcumin seems to inhibit growth of Staphylococcus aureus, Staphylococcus albus, and Bacillus typhosus [1] It is also effective against nematocidial parasite and certain protozoa.¹

GI Protection

Curcumin may benefit ulcer, proctitis (inflammation of the rectum common in ulcerative colitis and Crohn's disease) and reduce leaky gut syndrome.

"We conclude that antiulcer activity of curcumin is primarily attributed to matrix metalloproteinases -9 inhibition, one of the major path-ways of ulcer healing." 4 "A pure curcumin preparation was administered in an open label study to five patients with ulcerative proctitis and five with Crohn's disease. All proctitis patients improved, with reductions in concomitant medications in four, and four of five Crohn's disease patients had lowered CDAI scores and sedimentation rates." 9

Cardiovascular Protection

Curcumin may lower total cholesterol, fibrinogen and platelet aggregation, while increasing HDL and decreasing lipid peroxidation.^{26, 34, 18, 37}

"ten healthy human volunteers, receiving 500 mg of curcumin per day for 7 days. A significant decrease in the level of serum lipid peroxides (33%), increase in HDL Cholesterol (29%), and a decrease in total serum cholesterol (11.63%) were noted." Our reviewed data show that, in human healthy subjects, the daily intake of 200 mg of the above extract results in a decrease in total blood lipid peroxides as well as in HDL and LDL-lipid peroxidation. This anti-atherogenic effect was accompanied by a curcuma antioxidant-induced normalization of the plasma levels of fibrinogen and of the apo B/apo A ratio, that may also decrease the cardiovascular risk." 34

Brain Protection

Curcumin pretreatment reduced brain damage following ischemia/stroke⁴⁷ and from heavy alcohol intake.⁵⁰ Curcumin reduced development and severity of Alzeimer's disease in animal models by reducing plaque aggregation and plaque induced oxidative stress and was even capable of dissociating existing plaque.¹⁷ It's chelating ability for iron and copper ions is also believed to play a beneficial role in reducing progression of the disease.⁵³

"Initially, we reported the impact of non-steroidal anti-inflammatory drugs (NSAIDs), notably ibuprofen, which reduced amyloid accumulation, but suppressed few inflammatory markers and without reducing oxidative damage. Safety concerns with chronic NSAIDs led to a screen of alternative NSAIDs and identification of the phenolic anti-inflammatory/anti-oxidant compound curcumin, the yellow pigment in turmeric that we found targeted multiple AD pathogenic cascades. The dietary omega-3 fatty acid, docosahexaenoic acid (DHA), also limited amyloid, oxidative damage and synaptic and cognitive deficits in a transgenic mouse model. Both DHA and curcumin have favorable safety profiles, epidemiology and efficacy, and may exert general anti-aging benefits (anti-cancer and cardioprotective.)" 46

Liver Protection

Curcumin pretreatment was shown to reduce the liver damage induced by alcohol⁵⁴ and aflatoxin⁵⁵ (the fungal toxin often found along with peanuts/peanut butter).

Dosage: There is no upper level of toxicity established for turmeric or curcumin. A range of 200-1200mg/day was used for various applications with significant benefits. The effective dose may depend on the severity of inflammation. One factor that affects inflammation and proliferation is the AA/EPA ratio in cell membranes. The higher the AA/EPA ratio the higher the demand for the inhibition of COX and LOX enzymes, so a higher dose of curcumin may be necessary.

<u>Interactions</u>: Patients on blood thinning therapy¹⁰, with gall stones (stimulates bile flow), ulcers, GI inflammatory conditions (although beneficial in most cases) should be monitored closely. Not recommended during pregnancy. Inhibits various P450 enzymes.⁴³ Inhibits growth of lactobacillus¹ so supplementation with probiotics is recommended.

References

- 1. Araujo CC, Leon LL.Biological activities of Curcuma longa L. Mem Inst Oswaldo Cruz. 2001 Jul;96(5):723-8.
- 2. Yadav VS, Mishra KP, Immunomodulatory effects of curcumin. Immunopharmacol Immunotoxicol. 2005;27(3):485-97.
- 3. Takada Y, Bhardwaj A. Nonsteroidal anti-inflammatory agents differ in their ability to suppress NF-kappaB activation, inhibition of expression of cyclooxygenase-2 and cyclin D1, and abrogation of tumor cell proliferation. Oncogene. 2004 Dec 9;23(57):9247-58.
- 4. Swarnakar S, Ganguly K.Curcumin regulates expression and activity of matrix metalloproteinases 9 and 2 during prevention and healing of indomethacin-induced gastric ulcer. J Biol Chem. 2005 Mar 11;280(10):9409-15. Epub 2004 Dec 22
- Suzuki M, Nakamura T. Elucidation of anti-allergic activities of curcumin-related compounds with a special reference to their anti-oxidative activities. Biol Pharm Bull. 2005 Aug;28(8):1438-43
- 6. Kobayashi T, Hashimoto S Curcumin inhibition of Dermatophagoides farinea-induced interleukin-5 (IL-5) and granulocyte macrophage-colony stimulating factor (GM-CSF) production by lymphocytes from bronchial asthmatics. Biochem Pharmacol. 1997 Oct 1;54(7):819-24.
- 7. Yamamoto H, Hanada K. Inhibitory effect on curcumin on mammalian phospholipase D activity. FEBS Lett. 1997 Nov 10;417(2):196-8.
- 8. Chainani-Wu N.. Safety and anti-inflammatory activity of curcumin: a component of tumeric (Curcuma longa). J Altern Complement Med. 2003 Feb;9(1):161-8.
- 9. Holt PR, Katz S Curcumin therapy in inflammatory bowel disease: a pilot study. Dig Dis Sci. 2005 Nov;50(11):2191-3.
- 10. Heck AM, et al. Potential interactions between alternative therapies and warfarin. Am J Health Syst Pharm. Jul2000;57(13):1221-7.
- 11. Reddy AC, et al. Effect of Dietary Turmeric (Curcuma longa) on Iron-induced Lipid Peroxidation in the Rat Liver. Food Chem Toxicol. Mar1994;32(3):279-83.
- 12. Subramanian M, et al. Diminution of Singlet Oxygen-induced DNA Damage by Curcumin and Related Antioxidants. Mutat Res. Dec1994;311(2):249-55.
- 13. Ruby AJ, et al. Anti-tumour and Antioxidant Activity of Natural Curcuminoids. Cancer Lett. Jul1995;94(1):79-83.
- 14. Ammon HP, et al. Mechanism of Anti-inflammatory Actions of Curcumin and Boswellic Acids. J Ethnopharmacol. 1993;38:113.
- 15. Deodhar SD, et al. Preliminary Studies on Anti-Rheumatic Activity of Curcumin. Ind J Med Res. 1980;71:632.
- 16. Xu Y, Ku BS, The effects of curcumin on depressive-like behaviors in mice. Eur J Pharmacol. 2005 Jul 25;518(1):40-6.
- 17. Yang F, Lim GP. Curcumin inhibits formation of amyloid beta oligomers and fibrils, binds plaques, and reduces amyloid in vivo. J Biol Chem. 2005 Feb 18;280(7):5892-901. Epub 2004 Dec 7.
- 18. Srivastava V, et al. Effect of Curcumin on Platelet Aggregation and Vascular Prostacyclin Synthesis. Arzneim Forsch/Drug Res. 1986;36:715-17.
- 19. Mehta K, et al. Antiproliferative Effect of Curcumin (Diferuloylmethane) against Human Breast Tumor Cell Line. Anticancer Drugs. Jun1997;8(5):470-81.
- 20. Rao CV, et al. Chemoprevention of Colon Carcinogenesis by Dietary Curcumin, a Naturally Occurring Plant Phenolic Compound. Cancer Res. Jan1995;55(2):259-66.
- 21. Ranjan D, et al. The Effect of Curcumin On Human B-Cell Immortalization by Epstein-Barr Virus. Am Surg. Jan1998;64(1):47-51.
- 22. Mazumder A, et al. Inhibition of Human Immunodefficiency Virus Type-I Integrase by Curcumin. Biochem. Pharmacol. 1995;49(11):1165-70.
- 23. Barthelemy S, et al. Curcumin and Curcumin Derivatives Inhibit Tat-mediated Transactivation of Type 1 Human Immunodeficiency Virus Long Terminal Repeat. Res Virol. Ian1998;149(1):43-52.
- 24. Kawamori T, et al. Chemopreventive Effect of Curcumin, A Naturally Occurring Anti-inflammatory Agent, During the Promotion/Progression Stages of Colon Cancer. Cancer Res. Feb1999;59(3):597-601.
- 25. Hidaka H, Ishiko T, Furuhashi T, Kamohara H, Suzuki S, Miyazaki M, et al. Curcumin inhibits interleukin 8 production and enhances interleukin 8 receptor expression on the cell surface:impact on human pancreatic carcinoma cell growth by autocrine regulation. Cancer. Sep2002;95(6):1206-14.
- 26. Soni KB, et al. Effect of Oral Curcumin Administration on Serum Peroxides and Cholesterol Levels in Human Volunteers. Indian J Physiol Pharmacol. Oct1992;36(4):273-75.
- 27. Sharma OP. Antioxidant Activity of Curcumin and Related Compounds. Biochem Pharmacol. 1976;46:1013.
- 28. Natarajan C, Bright JJ Curcumin inhibits experimental allergic encephalomyelitis by blocking IL-12 signaling through Janus kinase-STAT pathway in T lymphocytes. J Immunol. 2002 Jun 15;168(12):6506-1329 Kim SY, Jung SH.
- 29. Curcumin is a potent broad spectrum inhibitor of matrix metalloproteinase gene expression in human astroglioma cells. Biochem Biophys Res Commun. 2005 Nov 18;337(2):510-6. Epub 2005 Sep 21.
- 30. Danilenko M, Studzinski GP. Enhancement by other compounds of the anti-cancer activity of vitamin D(3) and its analogs. Exp Cell Res. 2004 Aug 15;298(2):339-58.
- 31. Sharma RA, McLelland HR, Hill KA, et al. Pharmacodynamic and pharmacokinetic study of oral Curcuma extract in patients with colorectal cancer. Clin Cancer Res 2001;7:1894-900
- 32. Zhang F, Altorki NK, Mestre JR, et al. Curcumin inhibits cyclooxygenase-2 transcription in bile acid- and phorbol ester-treated human gastrointestinal epithelial cells. Carcinogenesis 1999;20:445-51.
- 33. Surh YJ. Anti-tumor promoting potential of selected spice ingredients with antioxidative and anti-inflammatory activities: a short review. Food Chem Toxicol 2002;40:1091-7.
- 34. Miquel J, Bernd A, The curcuma antioxidants: pharmacological effects and prospects for future clinical use. A review. Arch Gerontol Geriatr. 2002 Feb;34(1):37-46.
- 35. Deeb D, Xu YX, Jiang H, et al. Curcumin (diferuloyl-methane) enhances tumor necrosis factor-related apoptosis-inducing ligand-induced apoptosis in LNCaP prostate cancer cells. Mol Cancer Ther 2003;2:95-103.
- 36. Thaloor D, Singh AK, Sidhu GS, et al. Inhibition of angiogenic differentiation of human umbilical vein endothelial cells by curcumin. Cell Growth Differ 1998;9:305-12.
- 37. Shah BH, Nawaz Z, Pertani SA. Inhibitory effect of curcumin, a food spice from turmeric, on platelet-activating factor- and arachidonic acid-mediated platelet aggregation through inhibition of thromboxane formation and Ca2+ signaling. Biochem Pharmacol 1999;58:1167-72.
- 38. Thamlikitkul V, Bunyapraphatsara N, Dechatiwongse T, et al. Randomized double blind study of Curcuma domestica Val. for dyspepsia. J Med Assoc Thai 1989;72:613-20.
- 39. Rasyid A, Rahman AR, Jaalam K, Lelo A. Effect of different curcumin dosages on human gall bladder. Asia Pac J Clin Nutr 2002;11:314-8.
- 40. Leu TH, Maa MC. The molecular mechanisms for the antitumorigenic effect of curcumin. Curr Med Chem Anti-Canc Agents. 2002 May;2(3):357-70.
- 41. Antony S, Kuttan R, Kuttan G. Immunomodulatory activity of curcumin. Immunol Invest 1999;28:291-303.
- 42. Kuttan R, Sudheeran PC, Josph CD. Turmeric and curcumin as topical agents in cancer therapy. Tumori 1987;73:29-31.
- 43. Thapliyal R, Maru GB. Inhibition of cytochrome P450 isozymes by curcumins in vitro and in vivo. Food Chem Toxicol. 2001 Jun;39(6):541-7.
- 44. Lal B, Kapoor AK, Asthana OP, et al. Efficacy of curcumin in the management of chronic anterior uveitis. Phytother Res 1999;13:318-22.
- 45. Takada Y, Bhardwaj A, Potdar P, Aggarwal BB. Nonsteroidal anti-inflammatory agents differ in their ability to suppress NF-kappaB activation, inhibition of expression of cyclooxy genase-2 and cyclin D1, and abrogation of tumor cell proliferation. Oncogene 2004 Oct 18
- 46. Cole GM, Lim GP, Prevention of Alzheimer's disease: Omega-3 fatty acid and phenolic anti-oxidant interventions. Neurobiol Aging. 2005 Oct 30; [Epub ahead of print]
- 47. Wang Q, Sun AY, Neuroprotective mechanisms of curcumin against cerebral ischemia-induced neuronal apoptosis and behavioral deficits. J Neurosci Res. 2005 Oct 1;82(1):138-48.
- 48. Chan MM, Fong D. Inhibition of growth and sensitization to cisplatin-mediated killing of ovarian cancer cells by polyphenolic chemopreventive agents. J Cell Physiol. 2003 [an:194(1):63-70]
- 49. Zheng L, Tong QGrowth-inhibitory effects of curcumin on ovary cancer cells and its mechanisms. J Huazhong Univ Sci Technolog Med Sci. 2004;24(1):55-8.
- 50. Rajakrishnan V, Viswanathan P Neuroprotective role of curcumin from curcuma longa on ethanol-induced brain damage. Phytother Res. 1999 Nov;13(7):571-4.
- 51. Rajakrishnan V, Jayadeep A, Changes in the prostaglandin levels in alcohol toxicity: effect of curcumin and N-acetylcysteine. J Nutr Biochem. 2000 Oct;11(10):509-14
- 52. Satoskar RR, Shah SJ, Evaluation of anti-inflammatory property of curcumin (diferuloyl methane) in patients with postoperative inflammation. Int J Clin Pharmacol Ther Toxicol. 1986 Dec;24(12):651-4.
- 53. Baum L, Ng A. Curcumin interaction with copper and iron suggests one possible mechanism of action in Alzheimer's disease animal models. J Alzheimers Dis. 2004 Aug;6(4):367-77.
- 54. Rajakrishnan V, Jayadeep A, Changes in the prostaglandin levels in alcohol toxicity: effect of curcumin and N-acetylcysteine. J Nutr Biochem. 2000 Oct;11(10):509-14
- 55. Soni KB, Rajan A. Reversal of aflatoxin induced liver damage by turmeric and curcumin. Cancer Lett. 1992 Sep 30;66(2):115-21.
- 56. Schulze-Tanzil G. Effects of curcumin (diferuloylmethane) on nuclear factor kappaB signaling in interleukin-1beta-stimulated chondrocytes. Ann N Y Acad Sci. 2004 Dec;1030:578-86.