Curcum-Evail® 400 and 200

Highly Bioavailable Curcumin

By David M. Brady, ND, DACBN, IFMCP, FACN and Colleen Ambrose, ND, MAT

Curcum-Evail® is a highly bioavailable curcuminoid formulation containing three bioactive, extensively researched curcuminoids. Designs for Health's proprietary Evail™ emulsification technology is designed to enhance the bioavailability and absorption of bioactive ingredients. The Evail™ process uses quillaja extract, along with delta- and gamma-tocotrienols and medium-chain triglycerides to support absorption.

Formula Highlights

Curcum-Evail® contains a proprietary blend of the three main curcuminoid compounds: curcumin, demethoxycurcumin (DMC), and bisdemethoxycurcumin (BMC). It is available in two dosage forms depending on clinical need:

- Curcum-Evail® 400 provides 400 mg of curcuminoids per 1-softgel serving as a higher dosage option
- Curcum-Evail® 200 provides 200 mg of curcuminoids per 1-softgel serving as an option for individuals who have trouble swallowing softgels, improved patient compliance, and practitioner dosing flexibility

Role in Inflammation and Antioxidant Support

Turmeric (*Curcuma longa*) is a plant used both as a spice and medicinally. Turmeric contains 3% to 5% of the bioactive phenolic compounds of curcuminoids curcumin (77%), DMC (17%), and BMC (3% to 6%). Curcumin has a wide range of biological targets, including inflammatory mediators, cytokines, transcription factors, protein kinases, enzymes, and cellular pathways. It modulates cell signaling pathways associated with oxidative stress and inflammation, including mitogen-activated protein kinase (MAPK), nuclear factor κB (NF-kB), and nuclear factor erythroid 2-related factor 2 (Nrf2)-Kelch-like ECH-associated protein 1 (KEAP1).[1,2] Curcuminoids inhibit cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase, and pro-inflammatory cytokines interleukin-1 (IL-1), IL-6, IL-8, and tumor necrosis factor-alpha (TNF-α). Curcumin regulates apoptosis and suppresses neurotoxic factors in macrophages stimulated by lipopolysaccharides (LPS). It also inhibits the production of reactive oxygen species (ROS).[3]

Pharmacokinetic animal studies detected the presence of curcumin in the liver, kidney, and brain indicating that curcumin has the potential to pass through the blood-brain barrier. Metabolites of curcumin, namely tetrahydrocurcumin and dihydrocurcumin (DHC), were present in the liver and kidney. Conjugate enzyme activity for glucuronidation and sulfation of curcumin was detected in the liver, kidney, and intestinal mucosa. In vitro studies indicate that DHC upregulates Nrf2 to reduce oxidative stress and regulates the phosphatidylinositol 3-kinase (PI3K)/protein kinase B (Akt) pathway to modulate insulin resistance. DHC may also inhibit lipid biosynthesis, and it may have a stronger binding affinity to the active site of phospholipase A2 than curcumin. Tetrahydrocurcumin possesses similar properties to curcumin, but when compared to curcumin, tetrahydrocurcumin was shown to be more stable in physiological conditions. In animal studies, tetrahydrocurcumin was shown to have a neuroprotective effect after traumatic brain injury through its actions in mitochondrial apoptotic pathway inhibition, antioxidant activities, and autophagy increase. Tetrahydrocurcumin acts against mitophagy induced by hyperhomocysteinemia, a risk factor associated with some neurological pathologies. Tetrahydrocurcumin also attenuates hyperglycemia-induced oxidative stress through its modulation of sirtuin 1 and the transforming growth factor beta-1/SMAD3 pro-fibrotic pathway.[4]

Metabolic Support

In addition to its role in support of the body's response to oxidative stress and inflammation, curcumin supports healthy glucose and lipid metabolism through multiple pathways. Curcumin directly inhibits glucose transporter (GLUT) 1, thus lowering glucose uptake in cells that express GLUT1. It also inhibits the translocation of GLUT4 from the cytosol to the plasma membrane in adipocytes and hepatocytes.[2] Animal studies report improvements in glucose and insulin tolerance, likely due to its ability to modulate the AMPK pathway.[5]

A randomized clinical trial involving more than 200 individuals with prediabetes explored the efficacy of supplementation with 250 mg of daily curcuminoids for 9 months. Study results showed decreases in homeostatic model assessment-insulin resistance (HOMA-IR) and C-peptide levels and improvements in beta-cell function.[5] Another randomized trial involved patients with type 2 diabetes mellitus (T2DM) showed improvements in low-density lipoprotein (LDL), very LDL, triglycerides, high-density lipoprotein, and postprandial improvements in glycemic control in the presence of supplementation with 475 mg of curcuminoids.[5]

Benefits*

- Supports a healthy inflammatory response
- Supports a normal response to oxidative stress
- Supports healthy metabolism
- Supports cardiovascular health
- Supports healthy cell proliferation and function
- Supports neurological health
- Supports a healthy immune system

Curcum-Evail® 400

Supplement Facts

Serving Size 1 softgel

Amount Per Serving		% Daily Value
Curcumin Extract Powder (*Curcuma longa*)(root) (containing 380 mg curcuminoids: curcumin, demethoxycurcumin, bisdemethoxycurcumin)	400 mg	*

*Daily Value not established.

Other Ingredients: Medium chain triglycerides, softgel ingredients (bovine gelatin, glycerine, purified water, annatto [color]), quillaja extract, beeswax, sunflower lecithin, turmeric oil, DeltaGold® tocotrienols.

Curcum-Evail® 200

Supplement Facts

Serving Size 1 softgel

Amount Per Serving		% Daily Value
Curcumin Extract Powder (*Curcuma longa*)(root)(containing 190 mg curcuminoids: curcumin, demethoxycurcumin, bisdemethoxycurcumin)	200 mg	*

*Daily Value not established.

Other Ingredients: Medium chain triglycerides, softgel ingredients (bovine gelatin, glycerine, purified water, annatto [color]), quillaja extract, beeswax, sunflower lecithin, turmeric oil, DeltaGold® tocotrienols.

In a randomized, double-blind, placebo-controlled trial, 100 individuals with type 2 diabetes mellitus (T2DM) were given 500 mg of curcuminoids plus 5 mg of piperine daily for 3 months. Fasting blood glucose, C-peptide levels, hemoglobin A1C, alanine aminotransferase, and aspartate aminostransferase all showed improvements in the treatment arm.[5] Another clinical trial involving 1,000 mg of supplementation with curcuminoids plus 10 mg of piperine daily for 12 weeks showed improvements in TNF-α, leptin, and the leptin-to-adiponectin ratio.[5]

Another study provided turmeric powder supplementation to hyperlipidemic individuals with T2DM for 8 weeks; the intervention was found to reduce complications from diabetes and atherosclerosis.[3] An additional clinical trial showed that supplementation with 1,000 mg of curcumin daily for 12 weeks in individuals with T2DM and coronary heart disease upregulated peroxisome proliferator-activated receptor-gamma in peripheral blood mononuclear cells and improved sleep quality.[3]

Cardiovascular Support
Curcumin has been shown in research to support the prevention of cardiovascular disease (CVD) in both healthy individuals and those with underlying CVD risk factors due to its range of antioxidant and anti-inflammatory properties. Curcumin contributes to increased LDL uptake through its activation of the expression of LDL receptors. In animal and laboratory studies, curcumin has also been shown to induce significant changes in aortic gene expression associated with monocyte adhesion to aortic endothelial cells. It also downregulates the expression of vascular cell adhesion molecule-1 (VCAM-1) and intercellular cell adhesion molecule-1 (ICAM-1). Both VCAM-1 and ICAM-1 play roles in the early formation of atherosclerosis. Curcumin has protective effects against cardiac hypertrophy and attenuates post-myocardial infarction (MI) cardiac fibrosis. Curcumin is also protective against MI-induced injury through its ability to reduce inflammatory status, oxidative stress, and cardiomyocyte apoptosis.[2]

A placebo-controlled clinical trial involving 121 individuals undergoing coronary artery bypass grafting explored the efficacy of supplementation with 4 g of curcuminoids daily for 8 days. The incidence of in-hospital MI was decreased in the treatment group. Postoperative levels of C-reactive protein, plasma malondialdehyde, and N-terminal pro-B-type natriuretic peptide levels were also lower in the treatment arm as compared to a placebo.[2]

Neurological Support
Curcumin supports a healthy response to neuroinflammation and oxidative stress.* It also significantly increases superoxide dismutase activity, elevates catalase plasma activity, and modulates specific pathways, such as PI3K/Akt, activated protein kinase, MAPK, and Akt/Nrf2.[6] Supplementation with curcumin improves vascular endothelial function through the reduction of oxidative stress. Tetrahydrocurcumin modulates neuroinflammation, reduces the level of ROS related to beta-amyloid fibers, and improves neurobehavioral function by upregulating the Nrf2 pathway. An animal study showed that tetrahydrocurcumin increased dopamine levels and inhibited the activity of monoamine oxidase in the presence of Parkinson's disease.[6] Curcumin also decreases the number of glial fibrillary acidic protein and ionized calcium-binding adaptor protein-1 positive cells. In the presence of Alzheimer's disease in the in vitro studies, curcumin decreased messenger RNA levels of NF-kB, beta-secretase 1, and toll-like receptors, and upregulated the vitamin D receptor and mannosylglycoprotein N-acetyl-glucosaminyltransferase 3, which can result in diminished amyloid-beta aggregates.[7]

Cellular Health Support
Research at the laboratory, animal, and clinical levels indicate that curcumin exhibits a wide range of actions to promote cellular health. Some studies suggest that, curcumin may suppress the proliferation of certain cancer cells by activating caspase, upregulating cancer-suppressive genes (e.g., p53), and modulating anti-apoptotic genes.[8] A meta-analysis showed that curcumin-induced apoptosis in many types of cancer cell lines through its ability to downregulate anti-apoptotic marker B-cell lymphoma (Bcl-2), upregulate pro-apoptotic marker Bcl2-associated X protein, modulate poly-adenosine diphosphate ribose polymerase-1, and release cytochrome C in the cytoplasm.[9]

Curcumin has demonstrated the potential to inhibit tumor invasion by influencing growth factors (human epidermal growth factor receptor 2 and estimated glomerular filtration rate), matrix metalloproteases, NF-kB, activator protein-1, TNF-α, oxidized low-density lipoprotein receptor, COX-2, N-terminal activity, tyrosine kinase protein, and angiogenic cytokines, such as IL-6, IL-23, and IL-1-beta.[8] Curcumin also inhibits signal transducer and activator of transcription 3 (STAT3) phosphorylation and interferes with cell cycle progression by reducing cyclin-dependent kinases expression. Curcumin has been shown to attenuate angiogenesis by inhibiting hypoxia-inducible factor 1.[8]

Additional Applications
DMC supports a healthy inflammatory process through its ability to inhibit nitric oxide and TNF-α generation in microglia activated by LPS. It also helps modulate NF-kB and COX-2 activity, and it attenuates TNF-α, IL-1, and IL-6.[10] In a laboratory study to assess the efficacy of BMC in the presence of Parkinson's disease, BMC enhanced cellular survival, supported antioxidant activity, and modulated the phosphorylation levels of Janus kinase/STAT3 in cells treated with rotenone.[11] Another study assessed the cardioprotective qualities of BMC and showed that it significantly inhibited myocardial apoptosis, diminished ROS production, improved cell survival, and activated Nrf2 and Heme oxygenase-1 signaling.[12]

Recommended Use: Take 1 softgel per day with a meal or as directed by your health-care practitioner.

For a list of references cited in this document, please visit:
https://www.designsforhealth.com/api/library-assets/literature-reference---curcum-evail-400-200-tech-sheet-references

Dosing recommendations are given for typical use based on an average 150 pound healthy adult. Healthcare practitioners are encouraged to use clinical judgement with case-specific dosing based on intended goals, subject body weight, medical history, and concomitant medication and supplement usage.

***These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.**

To contact Designs for Health, please call us at (860) 623-6314, or visit us on the web at www.designsforhealth.com.