Curcum-Evail® 400

Highly Bioavailable Curcumin

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Curcum-Evail® 400 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

- Contains a proprietary blend of the three main curcuminoid compounds: curcumin, demethoxycurcumin (DMC), and bisdemethoxycurcumin (BMC)
- Provides 400 mg of curcuminoids per 1-softgel serving
- Uses proprietary Evail™ technology to promote the bioavailability and absorption of curcumin extract
- Gluten-free, dairy-free, soy-free; non-GMO

Benefits*

- Supports a healthy immune and inflammatory response[1-3,5,6,8,10]
- Supports a normal response to oxidative stress[1-4,6,11,12]
- Supports healthy metabolism[2-5]
- Supports cardiovascular health[2-6]
- Supports healthy cell proliferation and function[1-4,8,9,10]
- May support neurological health according to preclinical studies [3,4,6,7]

Promoting Healthy Inflammatory Responses and Antioxidant Status*

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] Mechanistically, 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]

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. CE4030-1

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 supporting healthy inflammatory responses and helping protect cells from the effects of oxidative stress, 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 individuals with prediabetes investigated the efficacy of supplementing with 250 mg/day of curcuminoids for nine months. The 120 individuals receiving the supplementation exhibited decreases in Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) and C-peptide levels, along with improvements in beta-cell function.[5] Another

randomized trial with 100 overweight or obese type 2 diabetes mellites (T2DM) patients observed that those receiving 300 mg/day of curcuminoids for three months had a significant reduction in fasting glucose, hemoglobin A1C, and a decrease in serum triglycerides and total free fatty acids, suggesting curcumin may also help support healthy lipid metabolism.[5]

A systematic review of 16 randomized, double-blind, placebo-controlled clinical trials (N = 1,309) concluded that curcumin can be a clinically helpful adjunct for individuals with diabetes. Individuals who received curcumin supplementation displayed significantly reduced fasting blood glucose, HbA1c, body mass index, triglycerides, total cholesterol, low-density lipoprotein (LDL)-cholesterol, high-density lipoprotein (HDL)-cholesterol, very LDL-cholesterol, C-reactive protein, and plasma malondialdehyde. The use of curcumin varied widely, ranging from 80 mg/day to 2,100 mg/day, and the duration of intervention spanned 8 weeks to 16 weeks.[3]

Cardiovascular Support*
Curcumin administration has been associated with a lower risk of cardiovascular disease (CVD) in both healthy individuals and those with underlying CVD risk factors due to its range of functional benefits.[2] Curcumin has mechanistically been shown to contribute 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 eight 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 healthy neuroinflammatory responses and antioxidant status.[6,7] Curcumin has been shown in animal studies to significantly increase superoxide dismutase activity, elevate catalase plasma activity, and modulate specific pathways, such as PI3K/Akt, activated protein kinase, MAPK, and Akt/Nrf2.[6] Individuals who received curcumin supplementation in clinical studies exhibited improved vascular endothelial function, resulting from a reduction in oxidative stress, which also supports enhanced blood flow and oxygen delivery to the brain, benefiting neurological function. Tetrahydrocurcumin, a metabolite of curcumin, has been found in in vitro studies to modulate neuroinflammatory responses, reduce the level of reactive oxygen species (ROS) related to beta-amyloid fibers, and improve neurobehavioral function by upregulating the Nrf2 pathway. Animal studies show that tetrahydrocurcumin increases dopamine status and inhibits the activity of monoamine oxidase in the presence of Parkinson's disease.[6] In animal models, 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, 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 in vitro.[7]

Cellular Health Support*

Research across laboratory (in vitro), animal, and clinical studies indicates that curcumin demonstrates a wide range of actions to support cellular health.[8] In vitro studies have shown that curcumin promotes healthy cellular processes by activating caspase enzymes, upregulating genes associated with cellular maintenance and repair (e.g., p53), and modulating genes that influence cell turnover.[8] A systematic review of in vitro studies further revealed that curcumin enhances markers of regulated cell processes, such as balancing cell survival and turnover by modulating specific cellular markers.[9]

Additionally, curcumin has demonstrated the ability in animal and in vitro studies to promote balanced cellular growth by influencing growth factors, matrix metalloproteases, and signaling molecules such as NF-κB, activator protein-1, and TNF-α. It has also been shown in in vitro and animal studies to support cellular environments by modulating angiogenesis-related pathways and reducing signaling molecules such as IL-6, IL-23, and IL-1-beta.[8] Further findings from animal studies suggest that curcumin aids in maintaining cell cycle balance by regulating the activity of cyclin-dependent kinases and modulating signal transduction pathways like STAT3 phosphorylation.[9]

Additional Applications
DMC supports a healthy inflammatory process through its ability to inhibit nitric oxide and TNF-α generation in microglia activated by LPS in vitro. 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 in vitro and animal 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-tech-sheet-references

Dosing recommendations are given for typical use based on an average 150-pound healthy adult. Health-care 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.**

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