

Grape Seed Extract with MegaNatural-BP

**Doctor's
BEST**

Science-Based Nutrition™



Another study related to cardiovascular health investigated effects of a grape extract supplement containing resveratrol on stable patients with coronary artery disease (CAD) treated according to currently accepted guidelines for secondary prevention of cardiovascular disease. In a triple-blind, randomized, placebo-controlled, one-year follow-up, 3-arm pilot clinical trial, 75 stable-CAD patients received 350 mg/day of placebo, resveratrol-containing grape extract (grape phenolics plus 8 mg resveratrol) or conventional grape extract lacking resveratrol during 6 months, and a double dose for the following 6 months. Changes in circulating inflammatory and fibrinolytic biomarkers were analyzed. Moreover, the transcriptional profiling of inflammatory genes in peripheral blood mononuclear cells (PBMCs) was explored using microarrays and functional gene expression analysis. After 1 year, in contrast to the placebo and conventional grape extract groups, the resveratrol-containing grape extract group showed an increase of the anti-inflammatory serum adiponectin and a decrease of the thrombogenic plasminogen activator inhibitor type 1. In addition, 6 key inflammation-related transcription factors were predicted to be significantly activated or inhibited, with 27 extracellular-space acting genes involved in inflammation, cell migration and T-cell interaction signals presenting downregulation in PBMCs. No adverse effects were detected in relation to the study products. Chronic daily consumption of a resveratrol-containing grape nutraceutical could exert cardiovascular benefits in stable-CAD patients treated according to current evidence-based standards, by increasing serum adiponectin, preventing PAI-1 increase and inhibiting atherothrombotic signals in PBMCs ⁸.

Another randomized, double-blind, placebo-controlled, crossover study, used 22 healthy adults who received placebo and resveratrol (grape seed extract). After a 45-min resting absorption period, the participants performed a selection of cognitive tasks that activate the frontal cortex for an additional 36 min. Cerebral blood flow and hemodynamics, as indexed by concentration changes in oxygenated and deoxygenated hemoglobin,

INGREDIENTS

Doctor's Best Grape Seed Extract with MegaNatural®-BP (GSE) is made from California wine grape seeds.

BENEFITS

- Potent antioxidant
- Healthy blood pressure
- Cardiovascular health
- Heart health
- Brain health
- Excellent source of Resveratrol

Doctor's Best Grape Seed Extract with MegaNatural®-BP (GSE) is an extensively-studied antioxidant made from California wine grape seeds.

Grape Seed Extract is a potent, scientifically-proven antioxidant for healthy blood pressure and heart/brain cardiovascular health.

GSE with MegaNatural®-BP contains 90% phenolics. Phenolics are the potent health-promoting antioxidant compounds responsible for anti-inflammatory effects, healthy blood pressure and heart/brain cardiovascular health by relaxing blood vessels and reducing cardiovascular plaque ^{1, 2, 3, 4, 5, 6, 7, 8, 9}.

CLINICAL STUDIES

In one study, 287 patients diagnosed with asymptomatic carotid plaques or abnormal plaque free carotid intima-media thickness (CIMT) were randomly assigned to a GSE group (n = 146) or control group (n = 141). As anticipated, after treatment, GSE resulted in significant reduction in MMCIMT progression, while MMCIMT and plaque score were stable and even increased with the control group. The number of plaques and unstable plaques also decreased after treatment of GSE. Furthermore, the carotid plaque can disappear after treatment with GSE. The incidence rate for transitory ischemic attack (TIA), arterial revascularization procedure, and hospital readmission for unstable angina in GSE group was significantly lower compared with the control group ¹.

Supplement Facts

Serving Size 2 veggie softgels
Servings per container 60 servings

	Amount per serving	% Daily Value
MegaNatural®-BP Grape Seed Extract (from <i>Vitis vinifera</i> standardized to min. 90% polyphenols)	300 mg	†
† Daily Value not established.		

Other Ingredients: Sunflower oil, vegetarian soft-gel (modified food starch, glycerin, carrageenan, purified water, annatto), yellow beeswax, sunflower lecithin.

Suggested Adult Use: Take 2 softgels daily with or without food, or as recommended by a nutritionally-informed physician.

Non-GMO / Gluten Free / Soy Free / Vegetarian
Store in a cool dry place.

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* 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.

were assessed in the frontal cortex throughout the post treatment period with the use of near-infrared spectroscopy. Resveratrol administration resulted in dose-dependent increases in cerebral blood flow during task performance, as indexed by total concentrations of hemoglobin. There was also an increase in deoxyhemoglobin after both doses of resveratrol, which suggested enhanced oxygen extraction, that became apparent toward the end of the 45-min absorption phase and was sustained throughout task performance. Cognitive function was not affected. Resveratrol metabolites were present in plasma throughout the cognitive task period. These results showed that single doses of orally administered resveratrol can modulate cerebral blood flow variables ⁵.

Another study related to brain health showed that resveratrol (trans-3,4,5-trihydroxystilbene), a naturally occurring polyphenol in grape seed extract, markedly lowered levels of secreted and intracellular amyloid-beta (Abeta) peptides produced from different cell lines. Resveratrol did not inhibit Abeta production, because it had no effect on the Abeta-producing enzymes beta- and gamma-secretases, but promoted instead intracellular degradation of Abeta via a mechanism that involved the proteasome. These findings demonstrate anti-amyloidogenic activity of resveratrol and suggest that this natural compound has a therapeutic potential in Alzheimer's disease ⁶.

Similarly, a randomized, placebo-controlled, double-blind, multicenter 52-week phase 2 trial of resveratrol in individuals with mild to moderate Alzheimer disease (AD) examined its safety and tolerability and effects on biomarker (plasma A β 40 and A β 42, CSF A β 40, A β 42, tau, and phospho-tau 181) and volumetric MRI outcomes (primary outcomes) and clinical outcomes (secondary outcomes). Participants (n = 119) were randomized to placebo or resveratrol 500 mg orally once daily (with dose escalation by 500-mg increments every 13 weeks, ending with 1,000 mg twice daily). Brain MRI and CSF collection were performed at baseline and after completion of treatment. Detailed pharmacokinetics were performed on a subset (n = 15) at baseline and weeks 13, 26, 39, and 52. Resveratrol and its major metabolites were measurable in plasma and CSF. CSF A β 40 and plasma A β 40 levels declined more in the placebo group than the resveratrol-treated group, resulting in a significant difference at week 52. Brain volume loss was increased by resveratrol treatment compared to placebo. Resveratrol was safe and well-tolerated. Resveratrol and its major metabolites penetrated the blood-brain barrier to have CNS effects ⁹.

A study relevant to healthy blood pressure was undertaken to determine whether grape seed extracts (GSE) that contain powerful vasodilator phenolic compounds lower blood pressure in subjects with the metabolic syndrome. The subjects were randomized into 3 groups-(a) placebo, (b) 150 mg GSE per day, and (c) 300 mg GSE per day-and treated for 4 weeks. Serum lipids and blood glucose were measured at the beginning of the study and at the end. Blood pressure was recorded using an ambulatory monitoring device at the start of the treatment period and at the end. Both the systolic and diastolic blood pressures were lowered after treatment with GSE as compared with placebo. There were no significant changes in serum lipids or blood glucose values. These findings suggest that GSE could be used as a nutraceutical in a lifestyle modification program for patients with the metabolic syndrome ⁷.

In another study, two groups (10 each) of normal-weight healthy subjects were randomized to placebo or GSE daily for 6 wk. Fasting blood samples were obtained prior to and after treatment at 1, 3, and 6 wk. Mononuclear cells were prepared for reactive oxygen species generation, RNA isolation, nuclear extract, and total cell homogenate preparation. Indices of oxidative and inflammatory stress, suppressor of cytokine signaling-3, phosphotyrosine phosphatase-1B, jun-N-terminal kinase-1, and inhibitor of kappaB-kinase-beta were measured by RT-PCR and Western blotting. GSE induced a significant reduction in reactive oxygen species generation, the expression of p47(phox), intranuclear nuclear factor-kappaB binding,

and the expression of jun-N-terminal kinase-1, inhibitor of kappaB-kinase-beta, phosphotyrosine phosphatase-1B, and suppressor of cytokine signaling-3 in mononuclear cells when compared with the baseline and the placebo. PCE intake also suppressed plasma concentrations of TNF-alpha, IL-6, and C-reactive protein. There was no change in these indices in the control group given placebo³.



Similarly, another study measured urine redox potential in forty-six healthy volunteers given GSE. All forty-six showed a reduction of the urine redox potential after treatment with grape seed extract. This simple dietary intervention significantly reduced (33 %) the urine redox potential, reflecting an overall increase in antioxidant status. Incorporation of plant-derived phenols in the diet may increase anti-oxidative status ⁴.

SAFETY

Grape Seed Extract is Generally Recognized as Safe (GRAS) by the United States Food and Drug Administration (FDA).

SCIENTIFIC REFERENCES

1. Cao, Ai-Hong et al. Beneficial clinical effects of grape seed proanthocyanidin extract on the progression of carotid atherosclerotic plaques. *Journal of Geriatric Cardiology* (2015) 12: 417-423.
2. Edirisinghe, Indika et. al. Mechanism of the endothelium-dependent relaxation evoked by a grape seed extract. *Clinical Science* (2008) 114, 331-337.
3. Ghanim, Husam et al. An antiinflammatory and reactive oxygen species suppressive effects of an extract of *Polygonum cuspidatum* containing resveratrol. *J Clin Endocrinol Metab.* 2010 Sep;95(9):E1-8.
4. Grases, Felix et al. Effect of consuming a grape seed supplement with abundant phenolic compounds on the oxidative status of healthy human volunteers. *Nutrition Journal* (2015) 14:94.
5. Kennedy, DO et al. Effects of resveratrol on cerebral blood flow variables and cognitive performance in humans: a double-blind, placebo-controlled, crossover investigation. *Am J Clin Nutr.* 2010 Jun;91(6):1590-7.
6. Marambaud, Philippe et al. Resveratrol Promotes Clearance of Alzheimer's Disease Amyloid- β Peptides. *The Journal of Biological Chemistry* (2005) 280, 37377-37382.
7. Sivaprakasapillai, Brahmesh et al. Effect of grape seed extract on blood pressure in subjects with the metabolic syndrome. *Metabolism Clinical and Experimental* 58 (2009) 1743-1746.
8. Tomé-Carneiro, João et al. Grape Resveratrol Increases Serum Adiponectin and Downregulates Inflammatory Genes in Peripheral Blood Mononuclear Cells: A Triple-Blind, Placebo-Controlled, One-Year Clinical Trial in Patients with Stable Coronary Artery Disease. *Cardiovasc Drugs Ther.* 2012, Dec 8.
9. Turner, Scott R. et al. A randomized, double-blind, placebo-controlled trial of resveratrol for Alzheimer disease. *Neurology* (2015) Sept. 11, 2015.

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