

Cardio Control



Clinical Applications

- Supports Cardiovascular Health*
- Provides Antioxidant Support*
- Promotes the Maintenance of Healthy Blood Pressure Levels That Are Already Within the Healthy Range*

*Cardio Control combines three safe, standardized, food-derived extracts that have been shown to support antioxidant activity or nitric oxide synthesis or both. These mechanisms contribute to arterial health and the maintenance of blood pressure that is already within a healthy range.**

All The 3rd Opinion Inc Formulas Meet or Exceed cGMP Quality Standards

Discussion

Adequate functioning of the endothelium is critical to allow blood vessels to fully dilate in response to changes in blood flow and to deter constriction of vessels. Diminished nitric oxide (NO) availability and an imbalance of endothelium-derived relaxing and contracting factors contribute to endothelial dysfunction, which is linked to the development of numerous vascular conditions.^[1] Each of the food-derived extracts in Cardio Control have exhibited improvements in clinical markers of vascular health.*

Cordiant™

It has been suggested that hesperidin alters endothelial cells to permit natural dilation and control of blood flow and pressure. In isolated and cultured endothelial cells, hesperidin stimulates the production of endothelial NO synthase, the NO-producing enzyme that triggers arterial dilation which, in turn, increases healthy blood flow.^[2,3] A randomized, placebo-controlled, double-blind, crossover trial examined whether oral hesperidin administration (500 mg/day for three weeks) improved endothelial function in 24 individuals with metabolic syndrome. The results revealed a significant increase in flow-mediated dilation (FMD) in the metabolic syndrome patients compared to the patients on placebo.*^[4]

Another name for hesperidin is hesperetin 7-rutinoside. As discussed above, the rutinoside hesperidin is widely studied and has been linked to several major health-promoting effects. However, the low solubility and complex metabolism of rutinosides in the gastrointestinal system have limited their absorption. Each capsule of Cardio Control contains 250 mg of Cordiant, a unique pharmaceutical grade rutinoside orange peel extract that contains a high concentration of rutinoside-2S. The high ratio of the more active "S" form in Cordiant makes it unique. Compared to other rutinoside preparations, which contain nearly equal amounts of the "S" to "R" forms, Cordiant has shown greatly improved bioavailability.*^[5,6]

Cordiant has been studied for its effect in activating endothelial production of NO. In a randomized placebo-controlled trial, subjects received a three-week intervention of 500 mg/day of Cordiant resulting in an 18% higher FMD score, a direct marker of endothelial function, compared to those receiving placebo. Additionally, concentrations of high-sensitivity C-reactive protein (hs-CRP) and serum amyloid A (SAA) were reduced as was circulating E-selectin, indicating reduced obstruction of the endothelium.*^[4]

An additional randomized, double-blind, placebo-controlled study evaluated the effect of 450 mg of daily Cordiant on endothelial function in 68 overweight subjects for a six-week period. Although no significant changes in fasting or postprandial FMD were observed in a group of patients with a baseline FMD of less than 3%, those with a baseline greater than or equal to 3% showed significant improvement in endothelial function. Circulating adhesion molecules sVCAM-1 and sICAM-1 were reduced along with systolic and diastolic blood pressure in both groups regardless of baseline FMD. The findings suggested that Cordiant has a promising role in the preservation of endothelial function and healthy blood flow in overweight individuals.*^[7]

Grape Seed Extract

Grape seed extract is a rich source of oligomeric proanthocyanidins (OPCs), which donate electrons or protons to reactive oxygen species (ROS) and act as scavengers.^[8] Oxidative stress can increase vascular endothelial permeability, formation of oxidized LDL, and activation of phagocytic cells. Grape seed extract has been investigated for its ability to interfere with oxidative stress, benefiting cholesterol and blood pressure.*^[9,10]

When utilized as a dietary supplement, grape seed extract has been suggested for lowering blood pressure in individuals with mildly elevated levels. In a double-blind placebo-controlled study, supplementing with 300 mg per day of grape seed extract for eight weeks (n=66) resulted in a statistically significant decrease in both systolic (average reduction of 8 mmHg) and diastolic blood pressure (average reduction of 5mmHg) in adults with prehypertension (mildly elevated blood pressure). Levels in the placebo group were not reduced.*^[11]

In another double-blind placebo-controlled study, 27 subjects with metabolic syndrome were given 150 or 300 mg per day of grape seed extract for four weeks. Both systolic and diastolic blood pressures were lowered after treatment with grape seed extract as compared with placebo. A decrease in oxidation of LDL particles also occurred in the treatment group.*^[12]

Each capsule of Cardio Control contains 75 mg of Enovita®, a grape seed extract standardized to 95% proanthocyanidins. Enovita has shown efficacy in maintaining healthy blood pressure when associated with diet and lifestyle modification. A four-month duration study evaluated two dosages (150 mg/day and 300 mg/day) of Enovita in 119 subjects with borderline hypertension (defined as pre-hypertension) (120-139 mmHg/80-





Supplement Facts

Serving Size: 1 Capsule
Servings Per Container: 60

	Amount Per Serving	%Daily Value
Cordiant™ Rutinoside (from <i>Citrus sinensis</i>)(fruit)	250 mg	**
Arthricor® Olive Extract Blend (<i>Olea europaea</i>)(fruit) (9% hydroxytyrosol, 4% oleuropein, 1% tyrosol)	125 mg	**
Enovita® Grape Extract (<i>Vitis vinifera</i>)(seed) (95% proanthocyanidins)	75 mg	**

**Daily Value not established.

Other Ingredients: HPMC, dicalcium phosphate, maltodextrin, ascorbyl palmitate, and silica.

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Cordiant is a trademark of BioActor B.V.

89 mmHg) and stage 1 hypertension (140-159 mmHg/90-99 mmHg).^[13] The participants utilized nondrug dietary (reduction in salt, alcohol, and caffeinated drinks) and lifestyle (regular exercise, sleep time improvement, relaxation, and smoking reduction) interventions. Blood pressure and heart rate were the primary endpoints, with blood pressure normalization being significantly higher in the Enovita supplementation groups compared to control starting from the fourth week of supplementation.^{*[14]}

Olive Extract

The evidence linking the Mediterranean diet to cardiovascular health has grown substantially in recent years^[15-17] with specific research suggesting that olive oil and its phenolic constituents are primary beneficial contributors.^[18-22] Phenolic compounds have been shown to have a protective effect against LDL oxidation,^[20,23,24] and additional studies have demonstrated the ability of olive leaf extracts to significantly reduce blood pressure measurements.^[25] Olive polyphenolic compounds have also been linked to an increase in the production of NO.^{*[26,27]}

Each capsule of Cardio Control provides 125 mg of Arthricor® olive extract blend with three polyphenols—hydroxytyrosol, oleuropein, and tyrosol at levels supportive of vascular health.*

Directions

Take one capsule twice daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

Does Not Contain

Wheat, gluten, yeast, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

References

- Hadi HA, Carr CS, Al Suwaidi J. Endothelial dysfunction: cardiovascular risk factors, therapy, and outcome. *Vasc Health Risk Manag.* 2005 Sep; 1(3):183-198. [PMID: 17319104]
- Chiou CS, Lin JW, Kao PF, et al. Effects of hesperidin on cyclic strain-induced endothelin-1 release in human umbilical vein endothelial cells. *Clin Exp Pharmacol Physiol.* 2008 Aug;35(8):938-43. [PMID: 18430059]
- Liu L, Xu DM, Cheng YY. Distinct effects of naringenin and hesperetin on nitric oxide production from endothelial cells. *J Agric Food Chem.* 2008 Feb 13;56(3):824-9. [PMID: 18197618]
- Rizza S, Muniyappa R, Iantorno M, et al. Citrus polyphenol hesperidin stimulates production of nitric oxide in endothelial cells while improving endothelial function and reducing inflammatory markers in patients with metabolic syndrome. *J Clin Endocrinol Metab.* 2011 May;96(5):E782-92. [PMID: 21346065]
- Hua S, Song C, Geczy CL, et al. A role for acute-phase serum amyloid A and high-density lipoprotein in oxidative stress, endothelial dysfunction and atherosclerosis. *Redox Rep.* 2009;14 (5): 187-96. [PMID: 19843373]
- BioActor. Cordiant™ Formulation Has a >100% Improved Bioavailability Compared to Standard Rutinoside. Bioavailability Study Report. Maastricht, Netherlands: Bioactor B.V.; 2013. [available on request]
- Salden BN, Bouke N, Troost FJ, et al. Randomized clinical trial on the efficacy of hesperidin 2S on validated cardiovascular biomarkers in healthy overweight individuals. *Am J Clin Nutr.* 2016 Dec;104(6):1523-1533. [PMID: 27797708]
- Cook NC, Samman S. Flavonoids – chemistry, metabolism, cardioprotective effects, and dietary sources. *J Nutr Biochem.* 1996;7:66–76. doi: [http://dx.doi.org/10.1016/S0955-2863\(95\)00168-9](http://dx.doi.org/10.1016/S0955-2863(95)00168-9).
- Lum, H., Roebuck, KA. Oxidant stress and endothelial cell dysfunction. *Am J Physiol Cell Physiol.* 2001 Apr;280(4):C719-C741. [PMID: 11245588]
- Shi J, Yu J, Pohoryl JE, et al. Polyphenolics in grape seeds—biochemistry and functionality. *J Med Food.* 2003 Winter;6(4):291-9. [PMID: 14977436]
- Robinson M, Lu B, Edirisinghe I, et al. Effect of grape seed extract on blood pressure in subjects with pre-hypertension. *J Pharm Nutr Sci.* 2012;2(2):155-159. <http://www.lifescienceglobal.com/pms/index.php/jpans/article/view/916/411>. Published May 11, 2012. Accessed May 7, 2017.
- Sivaprakasapillai B, Edirisinghe I, Randolph J, et al. Effect of grape seed extract on blood pressure in subjects with the metabolic syndrome. *Metabolism.* 2009 Dec;58(12):1743-1746. [PMID: 19608210]
- Pimenta E, Oparil S. Management of hypertension in the elderly. *Nat. Rev Cardiol.* 2012 Mar 13;9(5):286-96. [PMID: 22411292]
- Belcaro G, Ledda A, Hu S, et al. Grape seed procyanidins in pre-and mild hypertension: a registry study. *Evid Based Complement Alternat Med.* 2013;2013:313142. [PMID: 24171039]
- Estruch R, Ros E, Salas-Salvado J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med.* 2013 Apr 4;368(14):1279-90. [PMID: 23432189]
- Mayor S. Mediterranean diet reduces cardiovascular events in people with heart disease, study shows. *BMJ.* 2016 Apr 24;353:i2348. [PMID: 27114468]
- Chiva-Blanch G, Badimon L, Estruch R. Latest evidence of the effects of the Mediterranean diet in prevention of cardiovascular disease. *Curr Atheroscler Rep.* 2014 Oct;16(10):446. [PMID: 25115436]
- Fitó M, Cladellas M, de la Torre R, et al. Anti-inflammatory effect of virgin olive oil in stable coronary disease patients: a randomized, crossover, controlled trial. *Eur J Clin Nutr.* 2008 Apr;62(4):570-74. [PMID: 17375118]
- Ruano J, López-Miranda J, de la Torre R, et al. Intake of phenol-rich virgin olive oil improves the postprandial prothrombotic profile in hypercholesterolemic patients. *Am J Clin Nutr.* 2007 Aug;86(2):341-46. [PMID: 17684203]
- Gimeno E, de la Torre-Carbot K, Lamuela-Raventós RM, et al. Changes in the phenolic content of low density lipoprotein after olive oil consumption in men. A randomized crossover controlled trial. *Br J Nutr.* 2007 Dec;98(6):1243-50. [PMID: 17617938]
- Bogani P, Galli C, Villa M, et al. Postprandial anti-inflammatory and antioxidant effects of extra virgin olive oil. *Atherosclerosis.* 2007 Jan;190(1):181-86. [PMID: 16488419]
- Guasch-Ferré M, Hu FB, Martínez-González MA, et al. Olive oil intake and risk of cardiovascular disease and mortality in the PREDIMED Study. *BMC Med.* 2014 May 13;12:78. [PMID: 24886626]
- Castañer O, Covas MI, Khymenets O, et al. Protection of LDL from oxidation by olive oil polyphenols is associated with a downregulation of CD40-ligand expression and its downstream products in vivo in humans. *Am J Clin Nutr.* 2012 May;95(5):1238-44. [PMID: 22440854]
- Raederstorff D. Antioxidant activity of olive polyphenols in humans: a review. *Int J Vitam Nutr Res.* 2009 May;79(3):152-65. [PMID: 20209466]
- Cherif S, Rahal N, Haouala M, et al. A clinical trial of a titrated Olea extract in the treatment of essential arterial hypertension. *J Pharm Belg.* 1996 Mar-Apr;51(2):69-71. [PMID: 8786521]
- Visioli F, Bellocchio S, Galli C. Oleuropein, the bitter principle of olives, enhances nitric oxide production by mouse macrophages. *Life Sci.* 1998;62(6):541-6. [PMID: 9464466]
- Rocha BS, Gago B, Barbosa RM, et al. Dietary polyphenols generate nitric oxide from nitrite in the stomach and induce smooth muscle relaxation. *Toxicology.* 2009 Nov 9;265(1-2):41-8. [PMID: 19778575]

***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.**

