



Concord Grapes and Cardiovascular Health

In addition to a produce-rich diet and active lifestyle, Concord grapes may be one important ingredient in maintaining a healthy cardiovascular system by supporting healthy arteries, which helps promote healthy blood flow and blood pressure.^{1,2} A literature review outlining nearly 20 years of research shows that grapes and grape products promote heart health. The findings from this review highlight strong evidence for the heart-health benefits of grapes in low-density (LDL) oxidation, oxidative stress, and vascular function.³

Concord grapes may help support flexible arteries to promote healthy blood flow.⁴⁻¹²

- A study by Freedman et al. in 2001 (*Circulation*) investigated 20 healthy adults who drank Welch's Purple Grape Juice (7 mL/kg/d) for 14 days. Compared to baseline, after two weeks of juice consumption, platelet aggregation (clotting) was inhibited and superoxide (a free radical) release was decreased. In addition, drinking grape juice stimulated the production of nitric oxide by platelets – which promotes arterial relaxation and allows them to support healthy blood flow. While there was no significant change in the level of certain antioxidants within the plasma, an ORAC assay showed a significant increase in total plasma antioxidant capacity.⁷ See below for more on Concord grape juice's impact on antioxidant activity and platelet aggregation.
- Concord grape juice consumption appears to help widen arteries when necessary, specifically in individuals with coronary artery disease (CAD). In 1999, Stein et al. studied 15 participants with CAD who consumed Concord grape juice for two weeks (4 mL/kg/d twice daily) and saw increases in flow-mediated dilation of the brachial artery.⁸ Chou and colleagues performed a similar study over a longer time period. These researchers found that in two groups of 11 adults with CAD, supplemented with different levels of Concord grape juice (4 mL/kg/d and 8 mL/kg/d respectively), there were equivalent and significant increases in brachial dilation compared to baseline findings after 28 days.⁵
- A study completed and presented by Dorsey et al. suggests that drinking moderate amounts of Concord grape juice regularly supports healthy circulation in healthy overweight, older adults. This randomized, cross over, double blind, placebo-controlled study monitored 51 overweight men and women that were 50 years or older. Each group consumed 12 ounces (1 ½ cups) of Concord grape juice or a grape-flavored, sugar-sweetened drink daily during two continuous four week periods. Researchers found that drinking Concord grape juice daily significantly improved flow mediated dilation versus placebo, demonstrating a benefit to vascular function and blood vessel health.¹⁰
- In a study with young adult smokers who were otherwise considered healthy, Siasos et al. found that consumption of Concord grape juice increased flow mediated dilation (FMD) versus placebo. The 26 participants, average age 26 ± 5 years, consumed 7 mL/kg/d of Concord grape juice for two weeks and a placebo for two weeks with a four week washout

period in-between. The researchers also found that chronic consumption of Concord grape juice prevented an immediate smoking-induced decrease in FMD.¹¹

- When compared to nearly 50 other fruit juices, 100% grape juice made with Concord grapes, alongside blackcurrant juice and a red juice blend, had the most potent positive effect on blood vessel health. This laboratory research suggests that not only is it the polyphenol concentration, but also the type of polyphenols present in the grape juice, that supports blood vessel relaxation and healthy circulation.¹²
- In contrast, a study on grape juice and blood pressure of 64 subjects with pre-hypertension or stage 1 hypertension found that after eight weeks of consuming 100% Concord grape juice and a placebo beverage, there was no benefit of the grape juice on arterial stiffness and endothelial function. The authors suggest that no change was seen perhaps because the subjects were generally healthy and had only modestly elevated blood pressure.¹³
- Early research shows that Concord grape juice may work in a similar fashion to red wine to promote healthy, flexible arteries—but without the confounding effects of alcohol. For example, findings from a 2007 *Cardiovascular Research* study found that Concord grape juice was shown to stimulate the production of nitric oxide in cells that line the arteries, promoting arterial relaxation. In this laboratory study, Anselm and colleagues examined animal coronary arteries *ex vivo* to determine arterial endothelium production of nitric oxide following treatment with Concord grape juice. The researchers found nitric oxide production was stimulated more than the control not treated with Concord grape juice.⁴ Additional research has also illustrated that Concord grape juice produces this relaxation effect by stimulating the same reactions in the arteries that are activated by red wine.
- In a laboratory study by Schini-Kerth et al, the authors found that treating endothelial cells with Concord grape juice increased nitric oxide levels by 50%. And, for the first time, researchers showed that Concord grape juice boosted the levels of endothelial nitric oxide synthase (the protein that makes nitric oxide) for up to a full day. Specifically, Concord grape juice turned on proteins that signal the cell to make more endothelial nitric oxide synthase.⁹

Concord grapes may help promote healthy, clear arteries.^{8, 14-17}

- Although there is no evidence from human studies to suggest that Concord grape juice will lower total cholesterol levels, it may help manage the effects of LDL, or “bad,” cholesterol to help keep arteries free and clear of excess plaque build-up.^{8,14-17} If LDL particles are oxidized while in the arterial wall, this can initiate a cascade of events that can eventually lead to arterial blockage. Some,^{8,14} but not all¹⁸ research has shown that Concord grape juice is linked to an increase in serum antioxidant capacity as determined by ORAC. And studies have linked Concord grape juice to slowing of LDL oxidation, alone or with the addition of vitamin E.^{5, 8, 14-17}
- A 2002 study by O’Byrne et al., published in the *American Journal of Clinical Nutrition*, investigated the differences between Concord grape juice and vitamin E (alpha-tocopherol) on oxidative stress in healthy adults. Seventeen participants were randomized to a vitamin E (400 IU, alpha-tocopherol) group and 15 to a Concord grape juice (10 mL/kg/d) group.

Both groups experienced significant increases in serum antioxidant capacity and decreased LDL oxidation rate.¹⁴ Positive results on LDL-oxidation were also seen by Stein et al. (study also noted above), where CAD patients drinking Concord grape juice for two weeks experienced slowed LDL oxidation time versus baseline (117 v. 87 minutes).⁸ While these findings are promising, Chou and colleagues found that consuming Concord grape juice had no beneficial effect on LDL oxidation rate in CAD patients studied over a 28 day period.⁵ Additionally, in a recent study in healthy adults, Hollis and colleagues failed to find a significant increase in serum antioxidant capacity with chronic Concord grape juice consumption.¹⁸

Concord grapes have been shown to have an anti-clotting effect^{7,15,19} similar to red wine.²⁰

- Red wine has been shown to have an effect on inhibiting platelet aggregation.²⁰
- A crossover study by Keevil et al. compared the effects of consuming about two cups/day of either purple grape, orange or grapefruit juice in 10 healthy adults. 100% grape juice was the only juice to show anti-clotting effects through its ability to inhibit platelet aggregation.¹⁹ Freedman et al. published similar benefits of Concord grape juice on decreasing platelet aggregation in a study of 20 healthy, adults consuming 7 mL/kg/d for 2 weeks.⁷ Both authors attribute the anti-clotting effects to Concord grape juice's high content of proanthocyanins and other flavonoid polyphenols. While these clinical results are exciting, these outcomes were not replicated by Albers and colleagues who found Concord grape juice to have no beneficial effect on platelet aggregation in those who were already on aspirin therapy.²¹
- An animal study by Shanmuganayagam et al., published in *Atherosclerosis*, also supports the anti-clotting effects of Concord grape juice. Twenty animal subjects were fed the same high cholesterol diet for the first 48 days. For the second 48 days, half of the group received Concord grape juice and the other half of the group received a sugar water control. The animals drinking Concord grape juice experienced significantly reduced platelet aggregation by day 96.¹⁵

In certain populations, Concord grapes may play a role in healthy blood pressure.^{13,22,23}

- A double-blinded, placebo controlled study by Park et al., (*Biofactors*, 2004) of 40 adult Korean men with elevated blood pressure, found that daily consumption of Concord grape juice for 8 weeks (5.5 mL/kg/d) resulted in lower systolic and diastolic blood pressure versus baseline.²²
- Another study by Mark and Maki found that after 12 weeks of daily consumption of 12 oz. of Concord grape juice, both systolic and diastolic blood pressure responses were significantly decreased in men with a high baseline systolic blood pressure.²³
- It is healthy and normal for blood pressure to drop at night—giving the heart a rest. People who do not experience these nighttime (nocturnal) dips in blood pressure may be at increased risk for heart-related health issues over time.^{24,25} A recent double-blind, cross-over study, published in the *American Journal of Clinical Nutrition* by Dohadwala et al., of 64 adult men and women with pre-hypertension or stage 1 hypertension, found that drinking

Concord grape juice helped lower nocturnal blood pressure and had a beneficial effect on blood glucose levels compared to a placebo-matched control. This study also found that Concord grape juice consumption did not impact body weight. No significant decrease in 24-hour ambulatory blood pressure was found, so these findings should not be taken to mean that Concord grape juice treats high blood pressure.¹³

Bottom Line: Based on published research to-date, Concord grapes and grape-based products appear to play a positive role in promoting heart-health in certain population groups. With that said, findings from animal, both *in vivo* and *ex vivo*, and *in vitro* models need to be replicated in larger human studies in order to better understand the biomedical benefits of grapes and grape products in a more diverse population.

Bibliography

- ¹ Vislocky LM and Fernandez MLF. Biomedical Effects of Grape Products. *Nutr Rev.* 2010. 68(11): 656-670. onlinelibrary.wiley.com/doi/10.1111/j.1753-4887.2010.00335.x/abstract
- ² Vislocky LM, and Fernandez ML. Grapes and Grape Products: Their Role in Health. *Nutr Today.* 2013. 48(1):47-51. delivery.sheridan.com/downloads/original/196284_Vislocky_44393S_Marybeth.exe
- ³ Wightman JD and Heuberger RA. Effect of grape and other berries on cardiovascular health. *J Sci Food Agric.* 2015. 95(8):1584-1597. www.ncbi.nlm.nih.gov/pubmed/25171728
- ⁴ Anselm E, Chataigneau M, Ndiaye M, Chataigneau T and Schini-Kerth VB. Grape juice causes endothelium-dependent relaxation via a redox-sensitive Src- and Akt-dependent activation of eNOS. *Cardiovasc Res.* 2007. 73(2):404-413. www.ncbi.nlm.nih.gov/pubmed/16962569
- ⁵ Chou EJ, Keevil JG, Aeschlimann S, Wiebe DA, Folts JD and Stein JH. Effect of ingestion of purple grape juice on endothelial function in patients with coronary heart disease. *Am J Cardiol.* 2001. 88(5):553-555. www.ncbi.nlm.nih.gov/pubmed/11524068
- ⁶ Fitzpatrick DF, Hirschfield SL and Coffey RG. Endothelium-dependent vasorelaxing activity of wine and other grape products. *Am J Physiol.* 1993. 265(2 Pt 2):H774-778. www.ncbi.nlm.nih.gov/pubmed/8396352
- ⁷ Freedman JE, Parker C, 3rd, Li L, Perlman JA, Frei B, Ivanov V, Deak LR, Iafrafi MD and Folts JD. Select flavonoids and whole juice from purple grapes inhibit platelet function and enhance nitric oxide release. *Circulation.* 2001. 103(23):2792-2798. www.ncbi.nlm.nih.gov/pubmed/11401934
- ⁸ Stein JH, Keevil JG, Wiebe DA, Aeschlimann S and Folts JD. Purple grape juice improves endothelial function and reduces the susceptibility of LDL cholesterol to oxidation in patients with coronary artery disease. *Circulation.* 1999. 100(10):1050-1055. www.ncbi.nlm.nih.gov/pubmed/10477529
- ⁹ Alhosin M, Anselm E, Rashid S, Kim JH, Madeira SVF, Bronner C and Schini-Kerth VB. Redox-sensitive up-regulation of eNOS by purple grape juice in endothelial cells: role of PI3-kinase/Akt, p38 MAPK, JNK, FoxO1 and FoxO3a. *PLoS ONE.* 2013. 8(3):e57883. <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0057883>
- ¹⁰ Dorsey PG, Holbrook M, Carey M, Leleiko RM, Rodrigues I, Aasen J, Eberhardt RT, and Vita JA. Concord Grape Juice Improves Endothelial Function in Overweight, Older Adults. Presented at the 55th Annual Conference of American College of Nutrition. San Antonio, TX. October 15-18, 2014.
- ¹¹ Siasos G, Tousoulis D, Kokkou E, Oikonomou E, Kollia ME, Verveniotis A, Gouliopoulos N, Zisimos K, Plastiras A, Maniatis K and Stefanadis C. Favorable effects of Concord grape juice on endothelial function and arterial stiffness in healthy smokers. *Am J Hypertens.* 2014. 27(1):38-45. www.ncbi.nlm.nih.gov/pubmed/24061071

- ¹² Auger C, Pollet B, Arnold C, Marx C and Schini-Kerth VB. Great Heterogeneity of Commercial Fruit Juices to Induce Endothelium-Dependent Relaxation in Isolated Porcine Coronary Arteries: Role of Phenolic Content and Composition. *J Med Food*. 2015.18(1):128-136 www.ncbi.nlm.nih.gov/pubmed/25009961
- ¹³ Dohadwala MM, Hamburg NM, Holbrook M, Kim BH, Duess M, Levit A, Titas M, Chung WB, Vincent FB, Caiano T, Frame AA, Keaney Jr JF, and Vita JA. Effects of Concord grape juice on ambulatory blood pressure in prehypertension and stage 1 hypertension. *Am J Clin Nutr*. 2010. 92(5):1052-1059. www.ncbi.nlm.nih.gov/pubmed/20844075
- ¹⁴ O'Byrne DJ, Devaraj S, Grundy SM and Jialal I. Comparison of the antioxidant effects of Concord grape juice flavonoids alpha-tocopherol on markers of oxidative stress in healthy adults. *Am J Clin Nutr*. 2002. 76(6):1367-1374. www.ncbi.nlm.nih.gov/pubmed/12450905
- ¹⁵ Shanmuganayagam D, Warner TF, Krueger CG, Reed JD and Folts JD. Concord grape juice attenuates platelet aggregation, serum cholesterol and development of atheroma in hypercholesterolemic rabbits. *Atherosclerosis*. 2007.190(1):135-142. www.ncbi.nlm.nih.gov/pubmed/16780846
- ¹⁶ Vinson JA, Teufel K and Wu N. Red wine, dealcoholized red wine, and especially grape juice, inhibit atherosclerosis in a hamster model. *Atherosclerosis*. 2001. 156(1):67-72. www.ncbi.nlm.nih.gov/pubmed/11368998
- ¹⁷ Vinson JA, Yang J, Proch J and Liang X. Grape juice, but not orange juice, has in vitro, ex vivo, and in vivo antioxidant properties. *J Med Food*. 2000. 3(4):167-171. www.ncbi.nlm.nih.gov/pubmed/19236173
- ¹⁸ Hollis JH, Houchins JA, Blumberg JB and Mattes RD. Effects of Concord Grape Juice on Appetite, Diet, Body Weight, Lipid Profile, and Antioxidant Status of Adults. *J Am Coll Nutr*. 2009. 28(5):574-582. www.ncbi.nlm.nih.gov/pubmed/20439553
- ¹⁹ Keevil JG, Osman HE, Reed JD and Folts JD. Grape juice, but not orange juice or grapefruit juice, inhibits human platelet aggregation. *J Nutr*. 2000. 130(1):53-56. www.ncbi.nlm.nih.gov/pubmed/10613766
- ²⁰ Folts JD. Antithrombotic potential of grape juice and red wine for preventing heart attacks. *Pharmaceutical Biology*. 1998. 36(Suppl. 1):21-27. www.ingentaconnect.com/content/tandf/phbi/1998/00000036/A00100s1/art00005
- ²¹ Albers AR, Varghese S, Vitseva O, Vita JA and Freedman JE. The antiinflammatory effects of purple grape juice consumption in subjects with stable coronary artery disease. *Arterioscler Thromb Vasc Biol*. 2004. 24(11):e179-180. www.ncbi.nlm.nih.gov/pubmed/15528483
- ²² Park YK, Kim JS and Kang MH. Concord grape juice supplementation reduces blood pressure in Korean hypertensive men: double-blind, placebo controlled intervention trial. *Biofactors*. 2004. 22(1-4):145-147. www.ncbi.nlm.nih.gov/pubmed/15630270
- ²³ Mark D and Maki K. Concord grape juice reduces blood pressure in men with high systolic blood pressure. Presented at Experimental Biology. San Diego, CA. April 11-15, 2003.
- ²⁴ Ben Dov IZ, Kark, JD, Ben Ishay D, Mekler J, Ben Arie L and Bursztyn M. Predictors of all-cause mortality in clinical ambulatory monitoring: unique aspects of blood pressure during sleep. *Hypertension*. 2007. 49(6):1235-1241. www.ncbi.nlm.nih.gov/pubmed/17389258
- ²⁵ Sayk F, Becker, C, Teckentrup C, Fehm HL, Struk J, Wellhoener JP and Dodt C. To dip or not to dip: on the physiology of blood pressure decrease during nocturnal sleep in healthy humans. *Hypertension*. 2007. 49(5):1070-1076. www.ncbi.nlm.nih.gov/pubmed/17353512

Rev. 08/15