



## The Role of Citrus Juice in Supporting Cardiovascular Health

### Research Summaries

Published research studies suggest that regular consumption of citrus fruits and juices, such as orange juice and grapefruit juice and their nutrients, may play a role in helping to support healthy cholesterol levels and healthy blood vessels, lower blood pressure and reduce the risk of heart disease and stroke. These data support the inclusion of orange and grapefruit, and their juices, as part of a heart healthy diet and help individuals meet recommendations in the 2010 Dietary Guidelines for Americans.

### Citrus Juice and Its Nutrients in Cholesterol Management

A study published in [Nutrition Research](#)<sup>1</sup> examined the impact that approximately three 8-ounce servings of orange juice per day had on cholesterol levels in adults with either high or normal cholesterol levels. Following a 60-day trial, the high cholesterol group who consumed orange juice had a **12 percent decrease in LDL cholesterol**. Additionally, results showed that daily orange juice consumption may help maintain HDL levels and improve transfer of “free cholesterol” by HDL.

A study published in [Maturitas](#)<sup>2</sup> examined the effect of consuming approximately 2 cups per day of orange juice for 90 days, coupled with an aerobic training program, on cholesterol levels in overweight, middle-aged women. Women who consumed orange juice experienced a **15 percent decrease in LDL and an 18 percent increase in HDL cholesterol** compared to women who performed aerobic training but did not consume orange juice.

*In vitro* research that may support understanding of the mechanism of vitamin C and its role in microvascular biochemical activity was published in [Molecular and Cellular Biochemistry](#)<sup>3</sup> where researchers evaluated how vitamin C intake affects LDL oxidation in the cells that line human blood vessels. The data showed that **as concentration of vitamin C increased inside the cells, the amount of LDL decreased while oxidant-fighting elements in the cells were preserved**.

A study in [Alternative Therapies in Health and Medicine](#)<sup>4</sup> reported that of 120 adults with high cholesterol levels, participants who had taken a daily supplement for 12 weeks, containing **citrus fruit flavonoids, demonstrated significantly reduced total cholesterol by 30 percent, reduction of LDL cholesterol by 27 percent and reduction of triglycerides by 34 percent**, while participants taking a daily placebo pill demonstrated no significant changes. This study suggests that the flavonoids of the type provided naturally by orange juice may play a role in helping to support healthy cholesterol levels.

*In vitro* research providing support for understanding the mechanism of citrus juice components and their role in improving lipid profiles was published in the [Journal of Nutrition](#)<sup>5</sup>. The authors concluded that **two flavonoids reported in orange juice, hesperetin and nobiletin, likely contribute to the**

**decrease in plasma cholesterol** observed in previous studies, and that these contributions were associated with flavonoid's role in altering gene expression related to cholesterol regulation.

A study published in [Nutrition & Metabolism](#)<sup>6</sup> reported a randomized, controlled trial involving obese adults to evaluate the effect of consuming fresh grapefruit or grapefruit juice prior to meals as part of a weight loss diet plan. After 12 weeks, **individuals who consumed fresh grapefruit or grapefruit juice had a significant 6 to 8 percent increase in HDL cholesterol compared to baseline.** There was no significant change in HDL in the control group, who consumed water before meals.

A study published in [The American Journal of Clinical Nutrition](#)<sup>7</sup> involving 25 healthy individuals with elevated total cholesterol, reported that consumption of 3 cups (24 ounces) of orange juice daily for 4 weeks as part of the American Heart Association's Step 1 lipid lowering diet was associated with a **21 percent increase in HDL cholesterol and a 16 percent decrease in LDL/HDL ratio.**

In another clinical study published in the [Journal of Agricultural and Food Chemistry](#),<sup>8</sup> 72 patients ages 43-71 years, diagnosed with coronary artery disease and very high serum triglyceride levels, and having had previous coronary bypass surgery, were randomly divided into three experimental groups – a control group and two groups that consumed the juice of the grapefruit hybrid juice Oroblanco (also known as Sweetie). The grapefruit juice consumption groups consumed either 100 mL or 200 mL of fresh grapefruit juice, daily. After 30 days, the **total cholesterol, of the patients drinking 100 mL or 200 mL of grapefruit juice decreased by 9.5 percent, and 16.1 percent, respectively; low-density lipoprotein cholesterol decreased by 11.6 percent, and 21.0 percent, and total glycerides decreased by 11.5 percent, and 24.7 percent as compared to control.**

In a clinical study published in [Preventive Medicine](#),<sup>9</sup> with patients suffering from coronary artery disease and very high cholesterol levels, 66 patients ages 47-68 years and that had previous coronary bypass surgery, were randomly divided into two experimental groups – a control group and a group that consumed one or two peeled grapefruit (Sweeties) per day. Grapefruit consumption involved the entire edible portion of the fruit and not just the juice. **After 30 days, the grapefruit consumption group demonstrated a decrease in plasma lipids levels as compared to the control group.** The results experienced by the control group, compared to the grapefruit consumption group were as follows: total cholesterol decreased by 8.7 percent and 16.1 percent respectively; low-density lipoprotein cholesterol (LDL-C) decreased by 1.6 percent, and 21.2 percent, respectively; and triglycerides by 11.5 percent, and 24.7 percent, respectively.

In a clinical study reported in the [Journal of Agricultural and Food Chemistry](#),<sup>10</sup> 57 patients ages 39-72 years, diagnosed with coronary artery disease and very high serum triglyceride levels, and having had previous coronary bypass surgery, were randomly divided into two experimental groups -- a control group and a group that consumed fresh red or white grapefruit daily for 30 days. Grapefruit consumption involved the entire edible portion of the fruit and not just the juice. It was reported that **serum lipid levels were reduced in patients of the red and white groups versus control (no grapefruit**

**consumption).** The authors noted that patients consuming red grapefruit experienced a greater lipid level reduction than patients consuming white grapefruit.

## **Citrus Juice Consumption and Blood Pressure Management**

A study published in [The American Journal of Clinical Nutrition](#)<sup>11</sup> reported that consuming about 2 cups of orange juice every day for one month **significantly lowered diastolic blood pressure** among men who were slightly overweight, but otherwise healthy. Other cardiovascular improvements included improved reactivity (vasodilatory response) in the lining of microvascular blood vessels. These results were observed when men drank 100 percent natural orange juice, and when they consumed a control drink plus juice equivalent amounts of purified hesperidin, a flavonoid found in oranges. These beneficial effects were not observed when the participants consumed an energy balanced placebo. This study also reported a **significant decrease in plasma uric acid** with orange juice consumption. Uric acid can be a marker of oxidative stress and associations between uric acid and cardiovascular diseases have been reported. The authors attributed these effects mainly to vitamin C.

A recent double-blind, cross-over study published in [Phytotherapy Research](#)<sup>12</sup> examined the effects of grapefruit and orange juice consumption on 40 volunteers 30 to 45 years old – half had normal blood pressures (normotensive) and half exhibited high blood pressure (hypertensive). Patients were randomized to receive 250 ml of freshly prepared grapefruit juice (GFJ), orange juice (OJ), milk (cow) or a vitamin C-supplemented beverage. **Forty minutes after the intake, normotensive subjects consuming GFJ demonstrated a statistically significant decrease in diastolic arterial pressure ( $65 \pm 10$  mmHg vs  $90 \pm 15$  mmHg (the normotensive control values) and systolic arterial pressure ( $90 \pm 10$  mmHg vs  $120 \pm 10$  mmHg). In hypertensive patients, the diastolic arterial pressure decreased from  $90 \pm 10$  mmHg to  $80 \pm 10$  mmHg, whereas the systolic arterial pressure decreased from  $140 \pm 15$  mmHg to  $115 \pm 10$  mmHg respectively.** The decrease in mean arterial pressure was even more pronounced in patients who received GFJ than with those subjects that consumed OJ. The authors concluded that the hypotensive effect could be associated with the flavonoids naringin and narirutin, and that this vasodilator effect could be mediated by the nitric oxide pathway.

Research published in [The American Journal of Clinical Nutrition](#)<sup>13</sup> reported that drinking **orange juice may positively impact pro-inflammatory responses to consumption of a high-fat, high-carbohydrate (HFHC) meal.** The study compared the effect of consumption of water, 300 calories of orange juice (about 3 cups), or 300 calories of a glucose drink on several inflammatory markers measured in healthy weight adults when a 900-calorie HFHC meal was consumed along with the three interventional drinks. The water and glucose drink groups demonstrated a significant increase in multiple inflammatory response markers, while the orange juice group demonstrated no similar changes.

In a study published in [The American Journal of Clinical Nutrition](#)<sup>14</sup> researchers reported that dietary vitamin C intake above 55 mg per day, a plasma concentration of vitamin C above 14.4 umol/L, and three servings or more of fruit per day were each **independently inversely associated with C-reactive**

protein and tissue plasminogen activator in study participants. C-reactive protein and tissue plasminogen activator are markers of inflammation and vessel dysfunction associated with heart disease.

Similarly, in a prospective case-control study published by the [British Journal of Nutrition](#)<sup>15</sup> individuals with the highest plasma concentration of vitamin C (77.1 umol/L mean) were reported to have a **one-third lower risk for coronary artery disease** than those with the lowest plasma concentration of vitamin C (27.6 umol/L mean). Eight ounces of orange juice provide at least 100 percent of the Daily Value (60 milligrams) for vitamin C. Citrus juice has been identified as a [primary contributor of natural vitamin C in the diet](#).<sup>16</sup>

### **Citrus Fruit and Juice Consumption and Cardiovascular Health**

A meta-analysis published in the [European Journal of Cardiovascular Prevention & Rehabilitation](#)<sup>17</sup> including 15 cohort studies and evaluating the relationship between the intake of antioxidant vitamins, such as vitamin C, and coronary heart disease (CHD) risk in almost 350,000 participants reported that **individuals with dietary vitamin C intake (not including supplements) in the top third had a 14 percent reduced risk for CHD compared to the bottom third of intake.**

A Finnish dietary history study of nearly 4,000 adults published in the [British Journal of Nutrition](#)<sup>18</sup> reported that those who consumed the most fruits had a 25 percent lower risk of cerebrovascular disease compared to those who consumed the least amount. **Citrus fruit had the strongest inverse association with cerebrovascular disease as compared to all other types of fruits.**

Researchers have shown that **consumption of orange juice and other dietary sources of vitamin C may be protective against stroke.** A study of more than 20,000 adults published in [The American Journal of Clinical Nutrition](#)<sup>19</sup> reported that men and women with plasma vitamin C concentrations greater than 66 umol/L had a 42 percent lower risk of stroke compared to participants with a plasma vitamin C concentration of less than 41 umol/L.

In a clinical study published in [The American Journal of Clinical Nutrition](#)<sup>20</sup> six men and six women consumed 500 mL orange juice per day for 14 days. Plasma vitamin C concentrations remained significantly higher and were maintained as long as the subjects were drinking the orange juice. Similarly after 14 days, a significant decrease in plasma uric acid was reported. **In general, uric acid concentrations were lower when the vitamin C concentration was higher, and an inverse association was observed between uric acid concentrations and plasma vitamin C concentrations across time in both men and women. Orange juice consumption was also associated with reduced oxidative stress in vivo by lowering the concentration of F2-isoprostanes. Total vitamin C was significantly and inversely correlated with 8-epi-PGF2, a marker for oxidative stress.** These effects were more accentuated among smokers than among nonsmokers. These findings suggest that the protective effect of vitamin C is

greater in persons with higher stress and that higher concentrations of vitamin C in tissues can be gained by drinking orange juice daily.

In a prospective cohort study reported in the [\*Journal of the American Medical Association\*](#)<sup>21</sup> utilizing data from the Nurses' Health Study and the Health Professionals Follow-Up Study, researchers reported that **each additional serving of citrus fruit, including juice, corresponded with a significantly reduced risk of ischemic stroke among participants.** The reduced risk observed with citrus fruit consumption was more significant than for all fruits combined.

In an epidemiological cohort study, published in the [\*British Journal of Nutrition\*](#),<sup>22</sup> researchers observed 2,105 men without coronary heart disease. In a five-year follow up, **men who consumed at least 0.5 servings per day of citrus fruit had a 36 percent lower risk of acute coronary events** than those who consumed very little citrus. No other fruit or vegetable group had a significant observed effect against coronary heart disease. One serving of citrus fruit is equal to one medium-sized orange.

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