



What's New In BLUEBERRY HEALTH RESEARCH

Blueberries are a healthy fruit: Blueberries are a healthy fruit: A serving (a handful or a cup) contains just 80 calories and only naturally occurring sugars, and contributes essential nutrients, including dietary fiber, vitamin C, vitamin K and phytonutrients called polyphenols. The group of polyphenols includes anthocyanins (163 mg/100 g), which are compounds that give blueberries their blue color. Following are summaries of recent studies investigators are currently pursuing to better understand the role that blueberries may play in promoting good health. These studies address four tracks: cardiovascular health, diabetes management, brain health and the gut microbiome. For more information, visit the Health Professionals section of blueberryCouncil.org.

Cardiovascular Health



Cardiovascular disease is a major public health concern in the United States and currently the leading cause of death for both men and women ("Heart Disease Facts," 2019). Conditions that in combination significantly increase an individual's risk for developing cardiovascular disease include high blood sugar, high blood pressure, obesity and high blood-lipid levels. The name given to this cluster of symptoms is metabolic syndrome ("Metabolic Syndrome").

In a 2010 study of 48 obese human subjects with metabolic syndrome, those who consumed a blueberry beverage over an eight-week period experienced a slight decrease (- 6 and - 4%) in their systolic and diastolic blood pressure compared to those who consumed a placebo beverage (- 1.5 and - 1.2%). During the study, participants maintained their usual diets and physical activity patterns, but were asked to avoid consuming flavonoid-rich foods such as any other berries, green tea, cocoa and soy (Basu, 2010). The results warrant further investigation and provide some evidence for including blueberries as part of healthy dietary practices.

A 2015 double-blind, placebo-controlled human study out of Florida State University investigated the effects of blueberry consumption on 40 postmenopausal women with pre- and stage 1 hypertension (Johnson, 2015). Conducted over an eight-week period, the participants were advised to maintain their usual diet and physical activity levels during the duration of the study. The results showed that the 20 participants who consumed blueberries given as blueberry powder experienced 5.1% and 6.3% reductions in mean systolic blood pressure and diastolic blood pressure, respectively, whereas there were no significant decreases in the control group. From baseline to eight weeks, there was a significant ($P < 0.01$) reduction in ankle-brachial pulse wave velocity, and there was a group-time interaction ($P < 0.05$) in the blueberry group, whereas there were no changes in the control group. Reduced bioavailability of nitric oxide is thought to be one of the central factors common to cardiovascular disease, though it is unclear whether this is a cause of, or a result of, endothelial dysfunction (Naseem, 2015). While more research is needed, this initial study provides insight on the role that blueberries may play in the area of blood pressure and cardiovascular health.

In another human study, 44 adults with metabolic syndrome who consumed a blueberry smoothie twice daily for six weeks exhibited significant improvement in vascular endothelial function versus those who consumed a placebo (Stull, 2015). Vascular endothelial function is thought to play a pivotal role in the development, progression and clinical complications of atherosclerosis (Landmesser, 2005). There was not a significant change in blood pressure; however, many of these subjects were on antihypertensive medications, which may have masked any effect from the blueberries. There was also no difference in insulin sensitivity between the blueberry and placebo groups. Although more trials are needed, this study does suggest blueberries have a favorable effect on vascular health

over a six-week period in adults with metabolic syndrome. Clinical trials with a larger sample size and longer duration are warranted to explain the potential role blueberries have in improving endothelial function and blood pressure in a population at high risk for developing cardiovascular disease.

Another research study out of the University of East Anglia in the United Kingdom investigated if blueberries improve biomarkers of cardiometabolic function in participants with metabolic syndrome in a six-month, double-blind, randomized controlled trial. One hundred and fifteen (115) participants between the ages of 50 and 75 with metabolic syndrome were randomly assigned to receive one of three daily treatments: 26 g freeze-dried blueberries (the equivalent of one U.S. cup/day); 13 g freeze-dried blueberries (the equivalent of one-half U.S. cup/day fresh blueberries); or a placebo powder matched for color, taste and consistency. The study found that daily intake of the equivalent of one U.S. cup of blueberries (given as 26 g freeze-dried blueberries) resulted in clinically significant improvements in heart health measures, particularly markers of vascular function. Improved endothelial function and reduced arterial stiffness are associated with a reduced risk of cardiovascular events such as heart attack and stroke. Intake of one cup of blueberries per day also resulted in significantly increased HDL-C levels compared to the placebo. Additional lipid biomarkers researched in the study support these findings, such as significant increases in HDL particle number and APO-A1 levels, which are other predictors of heart disease risk (Curtis, 2019). Insulin resistance, pulse wave velocity, blood pressure and other lipid levels (including total cholesterol) were unaffected by any of the interventions. There were also no observed clinical benefits from the intake of one-half cup of blueberries in this at-risk participant group. While the conclusions drawn are from a single study that cannot be generalized to all populations, the data add weight to the evidence that a dietary intervention with a realistic serving of blueberries may be an effective strategy to decrease important risk factors for heart disease.

Diabetes Management



According to the National Institute of Diabetes and Digestive and Kidney Diseases, insulin resistance is a condition in which cells do not fully respond to the action of insulin, a hormone that regulates blood glucose ("Insulin Resistance & Prediabetes," 2018). As a result, cellular uptake of glucose is impaired and blood glucose levels become abnormally high. Insulin resistance is commonly seen in obese individuals and can lead to type 2, or adult-onset diabetes, the most common form of diabetes in the United States, which continues to rise at a rapid rate ("Diabetes Report," 2017).



Brain Health

In a human clinical trial, 32 individuals who were already diagnosed with metabolic syndrome consumed similar-tasting smoothies either with or without blueberries twice daily for six weeks. The researchers found that those who consumed the blueberry-containing smoothie were more able to lower their blood glucose in response to insulin than those who consumed the smoothie without blueberries (Stull, 2010). While the study is not conclusive, it strongly suggests that more research is needed to evaluate blueberries and their potential role in improving insulin sensitivity in an insulin-resistant population.

In another study out of the Stratton Veterans Affairs (VA) Medical Center in Albany, New York, the effect of blueberry consumption on cardiometabolic health parameters was investigated in men with type 2 diabetes in a double-blind, randomized, placebo-controlled trial. Over the eight-week period, researchers studied 52 overweight male participants between the ages of 51 and 75 who had a medical diagnosis of type 2 diabetes for at least six months as indicated by hemoglobin A1c (HbA1c) > 6.5 and < 9 and BMI > 25 kg/m². Along with their regular diet, participants were randomly assigned one of two daily interventions: either 1) 22 g of freeze-dried blueberries (the equivalent of one U.S. cup/day fresh blueberries) or 2) 22 g of a placebo powder (matched in energy and carbohydrate content to the freeze-dried blueberries). Of note, fiber was not controlled in the study, which is known to influence glycemic response. The study found that intake of the equivalent of one U.S. cup of fresh blueberries (given as 22 g freeze-dried blueberries) resulted in clinically significant improvements in measurable indicators of type 2 diabetes – HbA1c and fructosamine – compared to a placebo. The results also showed significantly decreased levels of serum triglycerides after blueberry consumption compared to placebo (Stote, 2020). Fasting plasma glucose, serum insulin, total cholesterol, LDL cholesterol, HDL cholesterol, CRP concentrations, blood pressure and body weight were not significantly different after eight weeks of consumption of freeze-dried blueberries, compared with placebo.

Epidemiological studies that have looked at the diets of large groups of people over a long period of time, such as the Nurses' Health Study and the Health Professionals Follow-Up Study, have shown that a high intake of fruit – particularly fruits high in anthocyanins, like blueberries – is associated with a decreased risk of developing type 2 diabetes (Wedick, 2012; Muraki, 2013). It is possible that these findings reflect other dietary components that co-exist in anthocyanin-rich foods. Randomized trials will be needed to establish the effects that can be specifically attributed to anthocyanins.

Scientists at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University have been studying the beneficial effects of blueberries on brain function in animal models for over a decade and are now studying the effects on humans. In a recent human study on healthy subjects, 13 men and 24 women between the ages of 60 and 75 were randomly selected to receive a diet supplemented daily with blueberries or a placebo for 90 days. The results found that the blueberry-supplemented group showed significantly fewer errors compared to the placebo group in tests used to assess verbal memory and task switching. There was no improvement in mobility in either the blueberry or the placebo group (Miller, 2017). While more evidence is needed, results of this study add to the growing body of research on blueberry-supplemented diets and positive outcomes on age-related cognitive decline.

Dr. Robert Krikorian and his team at the University of Cincinnati investigated the effects of a blueberry-supplemented diet in 37 older adults with mild cognitive impairment. They assessed cognitive function using measures of speed of processing, working memory, lexical access, and verbal and nonverbal long-term memory. Participants were randomly selected to consume freeze-dried blueberry powder or a placebo (daily with their morning and evening meals). After 16 weeks of consuming either blueberries or the placebo, the blueberry group demonstrated an improvement in semantic access (p=0.01) and visual-spatial memory (p=0.05).

Dr. Krikorian also assessed changes in regional brain activation using functional magnetic resonance imaging (fMRI) in a subset of the participants (n=16) while the participants were undergoing a working memory test. Although there was no clear indication of working memory enhancement during the scan, the group that consumed blueberries exhibited increased BOLD (blood oxygen level-dependent) activation in certain parts of the brain (Boespflug, 2017).



Gut Microbiome

Research into blueberries' role on the gut microbiome is still in its early stages. However, a recent study showed that blueberry supplementation in the high-fat diets fed to male rats resulted in changes in the gut microbiota associated with improvements in inflammation and insulin signaling. Further research is needed, and these results cannot be directly extrapolated to humans due to differences in gut microbiota and physiology (Lee, 2018).



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