



# *The* Power *of* Blueberries

By Jasenka Piljac Zegarac, PhD







## *Evidence shows this fruit is jam-packed with antioxidants and phytochemicals that may help prevent and slow the progression of chronic diseases.*



**It's** rare to encounter a client or patient who doesn't enjoy the taste of blueberries (*Vaccinium spp.*). But beyond their tangy sweetness and the fact you can pop them into your mouth one by one or incorporate them into many recipes, blueberries offer a wealth of health benefits.

Blueberries are rich in antioxidants and phytochemicals that research has shown are associated with cardiovascular and cognitive health and cancer and diabetes prevention. And their popularity is on the rise in North America. The production of fresh and processed blueberries has grown steadily by an average of 20% every two years since 2008.<sup>1</sup> Between 2005 and 2012, North America's blueberry fields increased 74% from 71,075 to 123,635 acres. British Columbia has the most acres in cultivation, while Michigan has been a world leader in production volumes of both fresh and processed blueberries for many decades.

### **Nutritional Properties and Antioxidant Composition**

Dietitians have stressed the importance of incorporating low-fat, fiber-rich, and nutrient-dense foods into their clients' and patients' diets for decades. "Everyone should be aiming to reach their recommended amount of fruits and vegetables for optimal health, and blueberries are an easy and delicious way to help you reach your goal. Just ½ cup is considered one serving of fruit, and they require no slicing or peeling—plus there's no waste," says Joanne Tehrani, RD, communications manager for the US Highbush Blueberry Council. Blueberries are an excellent source of fiber, vitamins A and C, potassium, and folate.<sup>2</sup> One cupful contains 14% Daily Value of fiber. Moreover, blueberries are one of the richest sources of antioxidant phytonutrients.<sup>3</sup> Blueberries' diverse range of phenolic compounds, such as anthocyanins, quercetin, kaempferol, myricetin, and chlorogenic acid, contributes to their overall antioxidant capacity.<sup>4,5</sup> (Antioxidant capacity, measured by a chemical laboratory analysis technique called oxygen radical absorbance capacity is one of several methods that doesn't account for bioavailability, distribution, and metabolism of a product's ingredients.)

"Blueberries also have a rich diversity of different anthocyanin species—like 26 different anthocyanins—whereas some other berries may feature only two or three different anthocyanin species," says Mary Ann Lila, PhD, MS, director of the Plants for

Human Health Institute and a David H. Murdock distinguished professor at North Carolina State University, who has spent 18 years studying various *Vaccinium* species.

### **Health Benefits**

Because of the wide variety of bioactive compounds present in blueberries, studies conducted over the past decade have associated their consumption with preventing and slowing disease progression. The protective effects of cranberry and blueberry consumption have been recognized in certain cancers; cardiovascular diseases, such as atherosclerosis and ischemic stroke; and neurodegenerative diseases.<sup>6</sup> These protective effects have been attributed to the phytochemicals in *Vaccinium* species, such as flavonoids (anthocyanins, flavonols, and proanthocyanidins), cinnamic acid derivatives and stilbenes, and triterpenoids. Researchers suggest that the bioactive constituents in blueberries exert their effects by counteracting oxidative stress, decreasing inflammatory processes in the body, and modulating molecular interactions and expression of disease-related genes.<sup>6</sup> Positive effects of blueberry bioactives also have an impact on insulin sensitivity and type 2 diabetes, urinary tract disease, and acute and chronic inflammation.<sup>7-9</sup>

### **Heart Health**

According to the World Health Organization, cardiovascular diseases are the leading cause of death globally, and it's expected they'll account for 23.3 million deaths by 2030.<sup>10</sup> Cardiovascular diseases also are the leading cause of disability worldwide.

Blueberries have been the focus of several human and animal studies looking for associations between intake and improved heart health. One 10-week study looked at the effects of blueberry supplementation on blood pressure and vascular reactivity in rats fed a high-fat/high-cholesterol diet and a control diet.<sup>11</sup> Rats in the high-fat/high-cholesterol diet supplemented with 2% blueberries experienced a 14% reduction in systolic blood pressure at week 8, relative to rats fed the control diet. Rats fed the high-fat/high-cholesterol diet supplemented with 2% blueberries had the same 14% reduction in systolic blood pressure at week 10 compared with rats fed the high-fat diet alone. Vascular reactivity also improved in rats on the high-fat diet supplemented with blueberries.



The anthocyanins in blueberries and strawberries also have been associated with a lower risk of myocardial infarction in young and middle-aged women. A study published in 2013 followed 93,600 women aged 25 to 42 for 18 years.<sup>12</sup> The women were healthy at baseline, but in the 18-year study period researchers observed 405 cases of myocardial infarction. However, the women who consumed more than three servings of blueberries and strawberries per week experienced significant protective effects against myocardial infarction.

## Types of Blueberries

Blueberry varieties are classified as two main types: the cultivated highbush (*Vaccinium corymbosum*) form and the wild lowbush (*Vaccinium angustifolium*) form. There also are hybrid blueberries that exhibit intermediate properties of the two main forms. Highbush blueberry shrubs grow significantly taller than the lowbush shrubs (up to 8 ft), and their berries are larger and more abundant. Lowbush shrubs typically reach only about 1 ft in height and bear smaller but more flavorful fruit. Northern highbush varieties thrive in cool climates with long and cold winters. Southern highbush varieties are frost-resistant and ideally suited for mild southern climates. In some blueberry-growing states, such as Michigan and Maine, pick-your-own farms are local tourist attractions, offering visitors the opportunity to pick, taste, and purchase a variety of blueberry products on the spot.

Europeans and North Americans have been consuming blueberries (*Vaccinium sp*) for centuries. Today, they're grown commercially throughout the world. Northern highbush varieties, such as Patriot, Duke, and Jersey, are the most widely planted. North America is the world's largest production region, accounting for approximately 60% of the global highbush crop, according to the North American Blueberry Council's 2012 World Blueberry Acreage and Production Report. The blueberry season in North America typically starts in mid-May and ends in late summer.

— JPZ

## Anticancer Properties

Evidence from preclinical and clinical studies suggests that the active substances in blueberries also may serve as anticancer agents through a variety of biological mechanisms.<sup>13</sup> The mechanisms involved include inhibition of cancer cell proliferation and metastasis, increased apoptosis, reduction of oxidative stress products and damage to macromolecules, and prevention of proinflammatory molecule production. Studies examining cancer cell lines have shown positive effects of blueberries and individual blueberry compounds on breast and oral cancer cells.<sup>14-17</sup> Pterostilbene, a natural stilbene isolated from blueberries and a resveratrol analogue, is especially considered an anticancer agent based on its antineoplastic properties in several common malignancies.<sup>18</sup> This compound has been studied for its ability to suppress breast cancer stem cell generation; prevent prostate cancer growth, progression, and metastasis; and inhibit cell proliferation and induce apoptosis in human gastric carcinoma cells.<sup>14,19,20</sup> Although the exact pharmacologic mechanism of pterostilbene still is unknown, its greater bioavailability is an advantage over other stilbene compounds.<sup>18</sup> The full anticancer potential of pterostilbene and other blueberry bioactives may be determined in future studies.

## Neurocognitive Effects

In addition to anticancer properties, several animal and human studies have shown that a blueberry-rich diet can have positive neurocognitive effects. The first study on this subject, published in 1999 in the *Journal of Neuroscience*, demonstrated that a diet rich in blueberry extract improved short-term memory loss and reversed some loss of balance and coordination in aging rats.<sup>21</sup> The research was expanded in 2003 with an experiment on transgenic mice in an Alzheimer's disease model, which indicated for the first time that a genetic predisposition to Alzheimer's disease possibly could be prevented through diet.<sup>22</sup>

In 2010, a preliminary study investigating the effects of daily wild blueberry juice consumption in nine older adults with memory changes was published in the *Journal of Agricultural and Food Chemistry*.<sup>23</sup> After the 12-week intervention, researchers noted improvements in paired associate learning and word list recall among participants. The third study, published in 2011, presented evidence that consuming a blueberry-enriched diet for one and two months can prevent and reverse age-related object memory decline in aged rats to a certain degree.<sup>24</sup> The rats fed the blueberry-rich diet for two months maintained improved performance through the following month while receiving a standard laboratory diet. These studies have sparked interest in the neurocognitive benefits of blueberry consumption and may serve as the basis for more thorough clinical trials in the future.



### Antidiabetes Properties

In 2008, researchers conducted a study published in the *Journal of Medicinal Food* that focused on quantifying phenolic compounds and their antioxidant properties in blueberry leaf infusions, which have been shown to contain antidiabetes properties.<sup>25</sup> This in-vitro study compared phenolic content with antioxidant action among several highbush blueberries and the wild European blueberry, also known as the bilberry (*Vaccinium myrtillus*). Researchers found that the wild blueberry infusion exhibited the highest antioxidant capacity and free radical-scavenging ability.

Wild blueberry leaf infusions were used in traditional medicine practices of Europe and North America, and the antidiabetes properties of polyphenol-rich leaves of wild *Vaccinium* species were noted earlier.<sup>26,27</sup> A study conducted in vitro on ethanol extracts from the roots, stems, leaves, and fruits of wild blueberry, using a variety of cell-based bioassays, found that different parts of the plant contain several active constituents with insulinlike antidiabetes properties.<sup>27</sup> The data on the effects in humans are limited, with beneficial effects observed mostly in middle-aged and elderly patients and in mild cases of diabetes.<sup>28</sup> In a preclinical study, daily dietary supplementation with whole blueberries over six weeks resulted in improved insulin sensitivity in obese, insulin-resistant men and women without diabetes.<sup>29</sup>

In a recent animal model, researchers evaluated the effect of an orally administered phenolic extract and an anthocyanin-enriched fraction from *Vaccinium angustifolium* Aiton berries, with the added bio-enhancing agent Labrasol, for lowering

hyperglycemia in mice with diabetes.<sup>30</sup> Treatment (500 mg/kg of body weight) with both the phenolic-rich extract and the anthocyanin-enriched fraction reduced elevated blood glucose levels by 33% and 51%, respectively. The effects of these formulations were comparable to the antidiabetes drug metformin (27% at 300 mg/kg).<sup>31</sup> The effect of the anthocyanin-enriched fraction largely was attributed to malvidin-3-O-glucoside, the primary anthocyanin contained in the extract. However, the authors noted that the effect wasn't significant without Labrasol, which most likely increased the bioavailability of the administered preparations. When asked whether future research efforts should be focused on the antidiabetes potential of malvidin-3-O-glucoside, Lila says, "We do believe there is particular potential there. However, in general, we really advocate eating the whole fruit, not an extract isolated from any fruit. There are solid reasons that the interacting mélange of phytochemicals within a fruit have been put together. Some of the phytochemicals are bioactive, others that co-occur in the same fruit may not have bioactive potential themselves, but when codelivered with the phytoactive, they'll help bioavailability and entry into the bloodstream. In repeated research throughout the nation and the globe, it is the mélange of co-occurring phytochemicals that prove to be more efficacious than single isolated compounds. That is how plants work—through synergies and phytochemical teamwork."

### Get Your Blues

Wild or cultivated, blueberries have plenty of health benefits dietitians can tell clients and patients about. Their phytochemical and antioxidant makeup can help promote heart and brain health, stabilize blood sugar and improve insulin sensitivity, and prevent and slow disease progression. "All blueberries are in a class by themselves among fruits," Lila says. "They contain a plethora of phytoactive compounds—anthocyanins, proanthocyanidins, cinnamic and other phenolic acids, and other flavonoids—that because of their potentiating interactions, are particularly powerful interacting with human therapeutic targets to ward off chronic diseases. There are synergies and additive interactions between the phytoactive chemicals that are unusually powerful against diseases."

"Pop a handful into your mouth, top off a favorite dish, or fold them into a recipe," Tehrani says. "They are an easy and healthful ingredient that enhances just about any dish."

—Jasenka Piljac Zegarac, PhD, is a scientist and freelance writer based in Okemos, Michigan ([www.thescientistwriter.com](http://www.thescientistwriter.com)). She has coauthored more than 30 peer-reviewed scientific journal articles and the popular science book *Zinfandel: A Croatian-American Wine Story*.



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