Blueberries can contribute both flavor and nutritional value to cereal-based foods, adding fiber, vitamins, and minerals and only low levels of sugars and fats. Most importantly, blueberries are rich in plant polyphenols that can complement cereals, which are rich in fiber but low in total phenolics (14). Consumption of blueberries in the United States has grown considerably, along with research on their health benefits. In a survey of the antioxidant capacity of common foods, blueberries ranked at the top (24) and, as a result, have been classified in the popular literature as a “super fruit” (39). Blueberries belong to the diverse Vaccinium genus of the plant family Ericaceae, which includes other familiar berries such as American cranberries, bilberries, and lingonberries, as well as many exotic species found in the neotropical region of the Americas (7).

**BLUEBERRY SPECIES**

Blueberries are one of the largest berry crops grown in the United States, with a total value of $871 million in 2011 (35). There are two main species of blueberries that are sold commercially in the United States: highbush (V. corymbosum) and lowbush (V. angustifolium).

**Highbush Blueberries.** Highbush blueberries (V. corymbosum) are widely available year-round in U.S. grocery stores due to widespread production in the United States, Canada, and South America (Fig. 1). Its large fruits and tall bushes make the highbush blueberry a favored crop of farmers in Michigan and New Jersey, which are the largest producers in the United States. Universally dispersed in the wild throughout the eastern United States, the highbush blueberry has been successfully hybridized with lowbush and rabbiteye blueberry species to create northern and southern varieties, respectively.

**Lowbush Blueberries.** Lowbush blueberries (V. angustifolium) are native to the northeastern United States and today are also grown commercially, especially in Maine. Due to their smaller size and intense flavor and aroma, lowbush blueberries are marketed as “wild blueberries.” These blueberries have a higher antioxidant capacity than highbush blueberries (24) and are often sold frozen after the harvest season is over. Indigenous to the southeastern United States, rabbiteye blueberries (V. ashei) have recently been hybridized and grown in southern states to produce berries that are much larger and firmer, which is an important quality for harvesting, storage, and marketability (11).

![Photo © David P. Smith / Shutterstock.com](http://dx.doi.org/10.1094/CFW-58-1-0013)

*Fig. 1. Blueberry production, import, and export in the United States, based on data from the U.S. Department of Agriculture (35).*
**Cranberries.** Another North American Vaccinium berry is the American cranberry (V. macrocarpon)—a berry utilized by Native Americans for its ability to delay lipid oxidation in meat preservation techniques (14). Cranberries naturally have little sugar, and most of it is in the form of glucose, which is considered a healthier alternative to fructose (32). However, because of its tartness, cranberries usually are consumed as juice or dried fruit with added sugar, offsetting their low sugar content. As an extract, cranberries ranked as the top-selling herbal dietary supplement in the United States in 2011 (6).

**Neotropical Blueberries.** The American tropics are home to many other blueberry species that have drawn the attention of scientists for their greater antioxidant capacity compared with the highbush blueberry (7). Some of the most bioactive species include Anthopeterus wardii, Cavendishia grandifolia, and Macleania coccoloboides. Although they are not yet commercially available in the United States, such species present valuable genetic and chemical diversity for further investigation.

**ACTIVE COMPOUNDS AND THEIR HEALTH BENEFITS**

Intake of plant polyphenols has been associated with decreased risk of cardiovascular disease (36), cancer (33), and obesity (3). Strong health benefit claims concerning plant polyphenols should be made only after information on their absorption, metabolism, and bioactivity has been matched to specific compounds and their respective quantities in food sources. Two of the polyphenol classes that may elucidate the health benefits of blueberries are flavonoids (e.g., anthocyanins and proanthocyanidins) and stilbenes (e.g., resveratrol and pterostilbene) (Fig. 2). These compounds are present in various amounts in different Vaccinium species and will be discussed further.

Plant polyphenols are a diverse group of organic secondary metabolites that contribute to the flavor, color, and nutritional properties of fruits. There are simple polyphenol molecules, such as phenolic acids and stilbenes, as well as more diverse and complex ones, such as lignins and flavonoids (Fig. 2). Various health benefits have been attributed to flavonoids because of their antioxidant and anti-inflammatory properties in vitro (14). Poor absorption and rapid degradation of some flavonoids suggest that they have an indirect health impact, such as activating enzymes that rid the body of toxins and improving gut microflora (16). The chemical structure of flavonoids usually consists of two aromatic rings linked by an oxygen-containing heterocycle, but chemical variation in bonds and functional groups subdivides them further into more categories, among which are the anthocyanins and the flavonols (e.g., catechins and proanthocyanidins) (Fig. 2).

**Anthocyanins**

**Chemistry.** The flavonoid compounds responsible for the blue color in blueberries are called anthocyanins (25); however, these secondary metabolites can also be responsible for red and purple colors. They accumulate mainly in the skin of the berry, protecting the fruit from ultraviolet radiation and temperature stress. Anthocyanins are believed to help with depression (10) and lower the risk of obesity (25) even at low amounts. Their neuroprotection potential could stem from their ability to cross the blood-brain barrier, as shown in aged rats, and to trigger additional biological antioxidants in neural cells by inhibition of ASK1–JNK/p38 pathways (15). They have also been shown to enhance memory (1) and help with anxiety and depression (10). Dreiseitel et al. (10) showed that anthocyanins and their aglycons could inhibit the mitochondrial enzymes, raising the levels of groups, the compounds are called anthocyanidins (or anthocyanin aglycones).

**Absorption.** Anthocyanidins are much better absorbed in humans than their glycosylated forms. According to Yi et al. (40), more methoxy and fewer free hydroxyl groups in the aglycone core increased bioavailability, but some intact glycosylated anthocyanins were also transported through the intestinal cell monolayers in vitro. Furthermore, they showed that the glucose groups had a more favorable effect on absorption rates than other sugar moieties, pointing to malvidin glucoside as an example of a better absorbed anthocyanin (40). Low-bush blueberries contain the highest amounts of malvidin glucoside (26 mg/100 g of fresh fruit), while highbush blueberries and cranberries contain abundant amounts of delphinidin and cyanidin galactosides, respectively (21). Under physiological conditions, some anthocyanins are recovered as glucuro- and sulfon conjugates in human urine (12) or may be broken down into their phenolic acid and aldehyde constituents (38).

**Bioactivity.** In addition to their antioxidant and anti-inflammatory activities, anthocyanins are believed to help with depression (10) and lower the risk of obesity (25) even at low amounts. Their neuroprotection potential could stem from their ability to cross the blood-brain barrier, as shown in aged rats, and to trigger additional biological antioxidants in neural cells by inhibition of ASK1–JNK/p38 pathways (15). They have also been shown to enhance memory (1) and help with anxiety and depression (10). Dreiseitel et al. (10) showed that anthocyanins and their aglycons could inhibit the mitochondrial enzymes, raising the levels of

**Fig. 2.** Polyphenol classes, quantity of certain polyphenolic compounds in highbush blueberries and cranberries (based on fresh weight) (5,21,28), and their potential health benefits. “+” indicates the presence of the compound in minute amounts; superscript “a” denotes the presence of or activity due to A-type proanthocyanidins.
monoamines such as serotonin in brain tissues. As a result, a serving of anthocyanin-rich blueberries may help keep serotonin levels up and contribute to feelings of well-being and happiness (19). Another protective function of anthocyanins is related to obesity. Studies on mice showed decreased fasting serum glucose, leptin levels, and epididymal adipose tissue weights when anthocyanins were added to a high-fat diet (25). Additionally, anthocyanins may fight oxidative stress and inflammation, which play a role in the pathogenesis of many chronic diseases, such as chronic obstructive pulmonary disease (7).

**Proanthocyanidins**

**Chemistry.** Proanthocyanidins are some of the most abundant compounds in tea, apples, and berries. They are oligomeric flavonals, mainly dimers or oligomers of catechin and epicatechin and their gallic acid esters. The structural units of catechins are linked by a single bond in B-type procyanidins and by a double bond in the rare A-type procyanidins (Fig. 3). Whereas B-type procyanidins are present in most berries, the A-type procyanidins are found only in cultivated cranberries and wild lingonberries. Higher molecular weight polymeric proanthocyanidins are called condensed tannins.

**Absorption.** Polymerization has been shown to greatly impair intestinal absorption of proanthocyanidins in vitro and in vivo (2,8,9). Monomers are absorbed best, but their specific chemical structure also play a role; epicatechin is absorbed much more efficiently than catechin (3). Proanthocyanidin dimers B1 and B2 have been detected in human plasma but at much lower levels than flavanol monomers (31). Although polymers are not absorbed well, they may be degraded to simpler compounds in the gut.

**Bioactivity.** A proanthocyanidin monomer, (+)-epigallocatechin-3-gallate, identified in cranberry is the strongest inducer of endogenous detoxifying phase II gene expression (18). The phase II enzymes protect tissues from damaging toxins, and declining levels of these enzymes are associated with aging, chronic conditions, and cancer. Therefore, proanthocyanidin monomers may play a protective role against such age-related illnesses.

The oligomeric proanthocyanidins found in red wine have been correlated with good vascular health in the regions of France that produce wines with the highest amounts of these compounds (35). The A-type oligomer proanthocyanidins, which are unique to cranberries and lingonberries, act as potent bacterial inhibitors in urinary tract infections (13,17). Polymeric proanthocyanidins, although not efficiently absorbed, may directly affect the intestinal mucosa and protect it against oxidative stress and toxins (37). The gut microbiota can hydrolyze proanthocyanidins, increasing their bioavailability: their metabolites in the colon have been shown to result in small phenolic acids that can be absorbed more easily and can reduce inflammation. Therefore, proanthocyanidins when metabolized may have implications for chronic inflammatory or autoimmune diseases such as inflammatory bowel disease (20).

Proanthocyanidins in apples have a direct effect on carbohydrate fermentation by gut microbiota, inhibiting metabolic degradation of short-chain fatty acid production (4). When carbohydrate fermentation is inhibited in the proximal colon, short-chain fatty acid production may be extended to the distal colon, thereby reducing the harmful effects of amino acid catabolites there.

Tuohy et al. (34) suggested that polyphenol-rich beverages consumed at meal times can directly affect starch digestion by inhibiting starch-degrading enzymes in the upper gut and, therefore, blunt postprandial glucose peaks. Blueberries added to whole grain cereal foods, therefore, could help regulate spikes in glucose levels and synergistically affect the human gut microbiota by modulating both species composition and the profile of metabolites absorbed from the colon (34).

**Stilbenes**

**Chemistry.** Stilbenes make up a class of polyphenolic compounds that consists of aromatic groups bonded with a carbon-carbon double bond. They are antimicrobial substances synthesized by the plant at the site of infection. Resveratrol and pterostilbene are two structurally similar stilbenes that have been recognized for their health-promoting properties.

**Bioavailability.** Resveratrol is similar to pterostilbene except for its two hydroxy

![Fig. 3. Chemical structures of selected polyphenolic compounds.](image-url)
groups, which in pterostilbene are methoxy groups. This structural difference makes pterostilbene more bioavailable and slows its metabolization compared with resveratrol. Low quantities of both stilbenes have been detected in foods: resveratrol is found in red wine, grapes, and many of the *Vaccinium* berries, with higher amounts found in cranberries, while pterostilbene has been identified in several blueberry species (27,28,30).

**Bioactivity.** Resveratrol is thought to be the active compound that creates the French paradox—the observation that the French, despite their generally high-fat diet, have lower rates of coronary heart disease. Resveratrol's anti-aging and anti-diabetic mechanisms of action are associated with increased cAMP levels, leading to its proposed potency in preventing obesity and elevating glucose tolerance and physical stamina in mice (22). Both resveratrol and pterostilbene have positive implications for cardiovascular health because of their actions as proteasome inhibitors, suppressing pro-inflammatory cytokines and iNOS genes in mice (26). Pterostilbene has suppressed colon cancer, cell proliferation, and key inflammatory markers in vitro and in vivo (23). Moreover, it lowered lipid and glucose levels in vivo by activating endogenous peroxisome proliferator-activated receptor-alfa (PPAR-alfa), suggesting it may have potential as an antiobesity agent (29).

**CONCLUSIONS**

The polyphenols contained in blueberries offer several health advantages that can supplement the nutritional benefits of cereal-based foods. The absorption, metabolism, and bioactivity of individual polyphenolic compounds should be considered when linking potential health-promoting properties with polyphenol-rich foods. Polyphenol content varies depending on blueberry species and food processing methods, and further studies tracking their metabolites and effects in vivo are needed to assess the synergy between various food groups. Still, there is scientific evidence suggesting polyphenols have protective potential against cancer, diabetes, and neurodegenerative diseases. Normal amounts of blueberries combined with whole grain cereals have been suggested to extend fiber metabolism through the end sections of the digestive tract and to improve gut microbiota. The synergistic combination of blueberries and cereal-based foods can lead to novel products that aim to provide lasting nutrition without sugar spikes, as well as to activate protective detoxifying enzymes in the human body and enhance focus, memory, and feelings of well-being and happiness.

**References**


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