

## Anthocyanins

By Marilyn Sterling, R.D.

These plant pigments are more than coloring agents for fruit juices, wine, and other beverages. They also contain an array of health-promoting benefits.

Eaten in large amounts by primitive humans, anthocyanins are antioxidant flavonoids that protect many body systems. They have some of the strongest physiological effects of any plant compounds, and they are also things of beauty: anthocyanins provide pigment for pansies, petunias, and plums. (Anthocyanins are a separate class of flavonoids from [proanthocyanidins](#), discussed in *NSN* 2000;5(6):231-4.)

Anthocyanins are the active component in several herbal folk medicines such as bilberry (*Vaccinium myrtillus*), which was used in the 12th century to induce menstruation and during World War II to improve British pilots' night vision. Scientists are now discovering how such anthocyanins work and are beginning to appreciate their health benefits.

Anthocyanins link with sugar molecules to form anthocyanins; besides chlorophyll, anthocyanins are probably the most important group of visible plant pigments. Anthocyanins, a flavonoid category, were found in one study to have the strongest antioxidizing power of 150 flavonoids.<sup>1</sup> (Approximately 4,000 different flavonoids have been identified.)

The U.S. Department of Agriculture recently tested the abilities of berry varieties to protect against oxidative damage. In general, blackberries have the highest antioxidant capacity of any fruit. Different varieties of the same species have varying amounts of anthocyanins. The varietal cultivars with the highest antioxidative capacity against superoxide radicals, hydrogen peroxide, and other oxidants are hull, thornless, and jewel raspberries; early black cranberries; and Elliot blueberries.<sup>2</sup>

Anthocyanidins and their derivatives, many found in common foods, protect against a variety of oxidants through a number of mechanisms. For example, red cabbage anthocyanins protect animals against oxidative stress from the toxin paraquat.<sup>3</sup> Cyanidins, found in most fruit sources of anthocyanins, have been found to "function as a potent antioxidant in vivo" in recent Japanese animal studies.<sup>4</sup> In other animal studies, cyanidins protected cell membrane lipids from oxidation by a variety of harmful substances.<sup>5</sup> Additional animal studies confirm that cyanidin is four times more powerful an antioxidant than vitamin E.<sup>6</sup> The anthocyanin pelargonidin protects the amino acid tyrosine from the highly reactive oxidant peroxynitrite.<sup>7</sup> Eggplant contains a derivative of the anthocyanidin delphinidin called nasunin, which interferes with the dangerous hydroxyl radical-generating system—a major source of oxidants in the body.<sup>8</sup>

### Diverse Health Effects

Studies show anthocyanins' positive influences on a variety of health conditions. One reason is their anti-inflammatory properties, which affect collagen and the nervous system. Their ability to protect both large and small blood vessels from oxidative damage derives from a range of effects, including mitigating microvessel damage from high blood-sugar levels that cause complications in diabetics. By the same token, diabetic retinopathy, which damages eyesight, is caused by leaking, damaged capillaries.

**Inflammation And Collagen:** In the course of inflammation, enzymes damage connective tissue in capillaries, causing blood to leak into surrounding tissues. Oxidants are released and further damage blood-vessel walls. Anthocyanins protect in several ways. First, they neutralize enzymes that destroy connective tissue. Second, their antioxidant capacity prevents oxidants from damaging connective tissue. Finally, they repair damaged proteins in the blood-vessel walls. Animal experiments have shown that supplementation with anthocyanins effectively prevents inflammation and subsequent blood-vessel damage.<sup>9</sup>

Anthocyanins' anti-inflammatory ability has been shown to help dampen allergic reactions. In one study, Bulgarian researchers gave animals histamine and serotonin, both of which cause allergic reactions and increase capillary permeability. The animals were supplemented with a variety of flavonoids. Anthocyanins were found to have the strongest anti-inflammatory effect of any flavonoid tested.<sup>10</sup>

**The Nervous System:** Anthocyanins' effects on inflammation help explain many of their protective effects elsewhere in the body. The brain is particularly vulnerable to oxidative damage. Test-tube studies show that nasunin protects lipids in animal brain tissue from oxidation.<sup>11</sup> Peroxynitrite nitration of tyrosine residues in enzymes and proteins is believed to be a major cause of brain damage in neurodegenerative diseases and in brain trauma. Nitrated tyrosine blocks nerve growth-factor receptor sites, thus preventing new neural growth and inhibiting repair. By preventing tyrosine nitration, the anthocyanin pelargonidin may help protect against neurological diseases. Blueberry supplements have even been found to reverse age-related neurological deficits in animals.<sup>11</sup>

**Large Blood Vessels:** Anthocyanins' ability to counter oxidants makes them brawny atherosclerosis fighters. First, anthocyanins prevent a key step in atherogenesis: oxidation of low-density lipoproteins (LDL). Bilberry in even trace amounts effectively protects against LDL oxidation in test-tube studies. Researchers in a USDA-funded study concluded that bilberry is a "more potent" antioxidant than vitamin C or BHT, which is used as a preservative.<sup>2</sup> In a human study conducted in Europe, researchers found that 55 women with intrauterine growth retardation (which manifests as a decreased rate of fetal growth), who took anthocyanins, experienced decreased oxidated LDL levels from 1,104 mU/ml to 726 in two months. LDL levels rose in the control group.<sup>12</sup>

Second, anthocyanins protect the integrity of the endothelial cells that line blood-vessel walls. Damage to these cells stimulates white blood cell migration to the area, initiating atherosclerosis and stimulating red blood cell migration. A study by the USDA at Tufts University in Boston found elderberry anthocyanins are quickly taken up into endothelial cell membranes where they prevent oxidation from hydrogen peroxide and other oxidants. The researchers concluded that elderberry has "important implications on ... vascular diseases."<sup>5</sup>

In addition, anthocyanins relax blood vessels. In one experiment, French researchers treated animal aortas with norepinephrine, which constricts blood vessels. Presence of the anthocyanin delphinidin relaxed the aorta by 89 percent, whereas another anthocyanin, malvidin, was ineffective. The researchers concluded that delphinidin may "be involved in reduction of cardiovascular mortality related to the presence of wine, fruits, and vegetables in the diet."<sup>13</sup>

**Small Blood Vessels:** Anthocyanins help maintain microcapillary integrity by stabilizing capillary walls. Blocked or reduced oxygen followed by reestablishment of normal supplies is called ischemia-reperfusion. Ischemia-reperfusion creates oxidants that result in white blood cell adhesion to microcapillary walls, increases capillary wall permeability, reduces blood flow, and often causes permanent capillary damage.

One of the classic experiments on anthocyanins was conducted on hamsters in Italy. Ischemia-reperfusion was created in their cheeks by a brief clamping, causing white cells to clump onto the capillary wall and damage it. After several weeks of bilberry supplementation, scientists repeated the tests. This time, normal blood supply through the capillaries was restored, fewer white blood cells stuck to the vessel walls, and permeability was significantly reduced after reperfusion.<sup>9</sup>

**Diabetes:** Microvessel damage from high blood-sugar levels causes most of the complications in diabetes. Collagen proteins become linked with sugars, resulting in abnormal polymeric blood vessel collagen. In one German study, 12 adult diabetics took 600 mg anthocyanins daily for two months. Samples of their gum tissue were taken before and after treatment. After supplementation, abnormal collagen production was significantly decreased.<sup>14</sup> Diabetes renders capillaries more permeable to large molecules than they should be. For instance, the protein albumin migrates into the space between cells and is not adequately taken up by the lymphatic system. In a recent French

study, researchers using an animal diabetic model found that those treated with bilberry maintained normal microcirculatory function including normal capillary filtration of albumin and its uptake by the lymphatic system.<sup>15</sup>

One of the most serious diabetic complications is retinopathy, which can cause blindness. Retinopathy occurs when the body attempts to repair leaking, damaged capillaries, but does so by overproducing abnormal proteins. Not only do anthocyanins prevent capillaries from leaking in the first place, but they also prevent abnormal protein proliferation. In one Italian study, 30 out of 40 people with retinopathy showed significant improvement after taking 120 mg anthocyanin daily for several weeks. None of the control subjects improved.<sup>16</sup>

**Eyesight:** Anthocyanins may also improve eyesight by other mechanisms. In a French study conducted in 1964, researchers vision-tested 36 people for their ability to adapt to light and dark both before and after taking bilberry anthocyanins. For several hours after supplementation, their eyesight improved significantly, although the effect wore off within 24 hours.<sup>17</sup> A recent Japanese study found that people taking 50 mg, but not 20 mg, black currant anthocyanins adapted better to the dark and had less eye fatigue than those in the placebo group.<sup>18</sup>

Two recent tests on anthocyanins and vision have produced negative results. In 1999, Israeli researchers found that supplementation with 24 mg and 48 mg anthocyanins daily did not improve three measures of night vision: scotopic retinal threshold, dark adaptation rates, and mesopic contrast sensitivity.<sup>19</sup> Researchers in a NASA study found that using 40 mg bilberry anthocyanins had no effect in night vision, visual acuity, or contrast sensitivity compared with placebo.<sup>20</sup>

#### Other Effects

Anthocyanins may have other potential benefits for humans. In the laboratory, they have been found to inhibit some human tumor cells. Cyanidin and delphinidin inhibit epidermal growth factor receptor in cancer cells, while malvidin is less effective.<sup>21</sup>

Bilberry, traditionally used for ulcers, may increase the production of stomach mucus and protect the stomach from injury. In one uncontrolled Italian study, 10 men took 1,200 mg anthocyanins for 10 days. This increased their gastric juice secretion and mucus, while stomach acid production remained constant.<sup>22</sup>

A recent Austrian pilot study, in conjunction with the U.S. Air Force, found a proprietary, standardized, elderberry extract reduced stress-related parameters such as blood glucose levels induced by stress.<sup>23</sup>

Anthocyanins have received less attention than other flavonoids, despite their far-reaching effects. Because berries were such a large part of early diets, our ancestors probably ate far more anthocyanins than we do. Some researchers feel that, by comparison, we are deficient in anthocyanins. When people become aware of the antioxidant power of these compounds, perhaps we can remedy that deficiency. In the process, some of our popular foods may become even more enjoyable.

Sidebars:

#### [Anthocyanin Content Of Common Fruits](#)

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#### References

1. Elliot. Inhibition of glutathione reductase by flavonoids. A structure-activity study. *Biochem Pharmacol* 1992;44(8): 1603-8.

2. Wang SY, Jiao H. Scavenging capacity of berry crops on superoxide radicals, hydrogen peroxide, hydroxyl radicals, and singlet oxygen. *J Agric Food Chem* 2000 Nov;48(11):5677-84.
3. Igarashi K, et al. Preventive effects of dietary cabbage acylated anthocyanins on paraquat-induced oxidative stress in rats. *Biosci Biotechnol Biochem* 2000 Aug;64(8):1600-7.
4. Tsuda T. The role of anthocyanins as an antioxidant under oxidative stress in rats. *Biofactors* 2000;13(1-4):133-9.
5. Tsuda T. Dietary cyanidin 3-O-beta-D-glucoside increases ex vivo oxidative resistance of serum in rats. *Lipids* 1998 Jun;33(6):583-8.
6. Rice-Evans CA. The relative antioxidant activities of plant-derived polyphenolic flavonoids. *Free Radical Res* 1995 Apr;22(4):3785-93.
7. Tsuda T. Mechanism for the peroxynitrite scavenging activity by anthocyanins. *FEBS Lett* 2000 Nov 10;484(3):207-10.
8. Noda Y. Antioxidant activity of nasunin, an anthocyanin in eggplant peels. *Toxicology* 2000 Aug 7;148(2-3):119-23.
9. Bertuglia S, et al. Effect of *Vaccinium myrtillus* anthocyanosides on ischemia reperfusion injury in hamster cheek pouch microcirculation. *Pharmacol Res* 1995;31(3/4):183-7.
10. Borissova P, et al. Anti-inflammatory effects of flavonoids in the natural juice from *Aronia melanocarpa*, rutin, and rutin-magnesium. Complex on an experimental model of inflammation induced by histamine and serotonin. *Acta Physiol Pharmacol Bulg* 1994;20(1):25-30.
11. Joseph JA. Reversals of age-related declines in neuronal signal transduction, cognitive, and motor behavioral deficits with blueberry, spina strawberry dietary supplementation. *J Neurosci* 1999 Sep 15;19(18):8114-21.
12. Pawlowicz, P. Administration of natural anthocyanins derived from chokeberry retardation of idiopathic and preeclamptic origin. Influence on metabolism of plasma oxidized lipoproteins: the role of autoantibodies to oxidized low-density lipoproteins. *Ginekol Pol* 2000 Aug;71(8):848-53.
13. Andriambelison E. Natural dietary polyphenolic compounds cause endothelium-dependent vasorelaxation in rat thoracic aorta. *J Nutr* 1998 Dec;128(12):2324-33.
14. Boniface R. Effect of anthocyanins on human connective tissue metabolism in the human. *Klin Monatsbl Augenheilkd* 1996 Dec;209(6):368-77.
15. Cohen-Boulakia F. In vivo sequential study of skeletal muscle capillary permeability in diabetic rats: effect of anthocyanosides. *Metabolism* 2000 Jul;49(7):880-5.
16. Perossini M. Diabetic and hypertensive retinopathy therapy with *Vaccinium myrtillus* anthocyanosides (Tegens) double blind placebo controlled clinical trial. *Ann Ottalmol Clin Ocul* 1987;12:1173.
17. Jayle GE, et al. Action des glucosides d'anthocyanes sur la vision scotopique et mesopique du sujet normal. *Therapie* 1964:19171-85.
18. Nakaishi H. Effects of black current anthocyanoside intake on dark adaptation and VDT work-induced transient refractive alteration in healthy humans. *Alt Med Rev* 2000 Dec;5(6):553-62.
19. Zadok D. The effect of anthocyanosides in a multiple oral dose on night vision. *Eye*

1999 Dec;13(Pt 6):734-6.

20. Muth ER. The effect of bilberry nutritional supplementation on night visual acuity and contrast sensitivity. *Alt Med Rev* 2000 Apr;5(2):164-73.

21. Meiers S. The anthocyanidins cyanidin and delphinidin are potent inhibitors of the epidermal growth-factor receptor. *J Ag Food Chem* 2001 Feb 19;49(2):958-62.

22. Magistretti MJ, et al. Antiulcer activity of an anthocyanadin from *Vaccinium myrtillus*. *Arzneimittel Forschung* 1988;38(5):686-90.

23. Letiner G, et al. Stress induced electrolyte and blood gas changes with and without a six-day oral treatment with elderberry (*Sambucus nigra* L.) concentrate. *Magnesium-Bulletin* 2000;22(3):72-6.