

## Monograph



### *Vaccinium myrtillus* (Bilberry)

#### Introduction

*Vaccinium myrtillus* (bilberry) is a member of the Ericaceae family, and is also known as European blueberry, huckleberry, whortleberry, or blueberry. It is a shrubby perennial plant one to two feet in height and can be found in the mountains and forests of Europe and the northern United States. Its branches contain alternating, elliptical, bright green leaves, and its flowers, which appear from April to June, are reddish or pink, and bell-shaped. The fruit of the bilberry plant is blue-black or purple and differs from the American blueberry in that the meat of the fruit is purple, rather than cream or white. Fruit is harvested July through September, and time of ripeness is somewhat dependent on plant elevation. Plants growing at higher elevations generally ripen later than those at lower elevations.

Bilberry has been used as food for centuries due to its high nutritive value, and today represents a precious wild delicacy. Bilberry's history of medicinal use dates back to the Middle Ages, but it did not become widely known to herbalists until the 16th century when its use was documented for treating bladder stones, biliary disorders, scurvy, coughs, and lung tuberculosis. More recently, bilberry fruit extracts have been used for the treatment of diarrhea, dysentery, and mouth and throat inflammations. Bilberry leaf decoctions have been used to lower blood sugar in diabetes.<sup>1</sup> Currently, bilberry research is focused on the treatment of ocular disorders, vascular disorders, and diabetes mellitus.

#### Active Constituents

Several active constituents have been isolated from the berries and leaves of the bilberry plant, including anthocyanoside flavonoids (anthocyanins), vitamins, sugars, and pectins, which are found in the berries, and quercetin, catechins, tannins, iridoids, and acids, which are found in the leaves.<sup>2,3</sup> The anthocyanosides are considered the most important of the pharmacologically active components. Anthocyanoside concentration in the fresh fruit is approximately 0.1 to 0.25 percent, while concentrated bilberry extracts are usually standardized to 25-percent anthocyanosides.<sup>3</sup> The berry's anthocyanoside content increases as the fruit ripens, while the reverse is true of its leaf constituents.<sup>4</sup>

## Pharmacology

Although bilberry constituents have multiple pharmacological actions, most of the research has focused on the anthocyanosides. Extracts containing anthocyanosides have been shown to possess strong antioxidant properties,<sup>5</sup> stabilize collagen fibers and promote collagen biosynthesis,<sup>6-8</sup> decrease capillary permeability and fragility,<sup>9</sup> and inhibit platelet aggregation.<sup>10</sup> Anthocyanosides and other bilberry leaf constituents prevent the release and synthesis of pro-inflammatory compounds such as histamine, prostaglandins, and leukotrienes.<sup>6-8,11</sup> In addition, bilberry leaf decoctions administered orally have been shown to lower blood glucose levels.<sup>12</sup>

## Clinical Applications

### *Ophthalmologic Disorders*

The mechanisms of action behind bilberry's beneficial effect on the eye are not completely understood. They include the ability to improve oxygen and blood delivery to the eye and to scavenge free radicals that can disrupt collagen structures and contribute to conditions such as cataracts and macular degeneration. In addition, the anthocyanosides have an affinity for the pigmented epithelium (visual purple) area of the retina, the portion of the retina responsible for vision and adjustments to light and dark.<sup>13,14</sup>

### *Vision Improvement*

Bilberry extract's visual enhancement properties were first studied by French researchers on Royal Air Force pilots during World War II. Administration of bilberry extract resulted in improved nighttime visual acuity, faster adjustment to darkness, and faster restoration of visual acuity after exposure to glare.<sup>15,16</sup> Later studies confirmed this effect,<sup>17,18</sup> although a subsequent double-blind, placebo-controlled, crossover study conducted on U.S. Navy SEAL personnel did not. Fifteen male subjects given 160 mg bilberry extract (standardized to 25-percent anthocyanosides) three times daily for three weeks, showed no significant improvement in either night visual acuity or night contrast sensitivity compared to placebo.<sup>19</sup> Conversely, studies of bilberry extract on individuals with retinitis pigmentosa and hemeralopia (inability to see distinctly in bright light) demonstrated a significant improvement in visual performance.<sup>18,20</sup> It may be the most significant effects will be observed in those with impaired visual acuity.

### *Glaucoma*

Consumption of bilberry extracts may offer significant protection against the development of glaucoma due to its collagen-enhancing and antioxidant properties. The reduced tensile strength and integrity of aging eye tissue may result in the increased intraocular pressure and loss of peripheral vision seen in glaucoma. In one study, eight patients with glaucoma were given a single oral dose of 200 mg *Vaccinium myrtillus* anthocyanosides and demonstrated improvement based on electroretinography.<sup>13</sup> A collagen-stabilizing effect on the trabecular meshwork, facilitating aqueous outflow, may provide a potential mechanism.

### *Cataracts*

Bilberry anthocyanosides may offer therapeutic benefit in prevention of cataracts. Animal studies show diets high in anthocyanoside flavonoids retard the development of cataracts in rats.<sup>21,22</sup> A clinical study, in which bilberry extract (180 mg twice daily of a 25-percent anthocyanoside extract) was given with vitamin E, demonstrated arrested cataract formation in 48 of 50 patients with senile cortical cataracts.<sup>23</sup>

### ***Diabetic Retinopathy***

In Europe, bilberry anthocyanoside extracts are recognized as highly effective in preventing diabetic retinopathy, with several clinical studies supporting its use.<sup>24-28</sup> In a double-blind study, 14 patients with diabetic and/or hypertensive retinopathy were supplemented with bilberry extract equivalent to 115 mg anthocyanosides daily (or placebo) for one month. Significant improvements were observed in the ophthalmoscopic parameters of 11 subjects receiving bilberry, and 12 patients showed improvement in angiographic parameters.<sup>27</sup> Additional clinical studies of bilberry's positive effects in treating retinopathy have been conducted in Europe but are not available in English.

### ***Vascular Disorders***

Bilberry extracts improve microcirculation. Animal studies have shown it to be of benefit in decreasing vascular permeability and improving vascular tone and blood flow.<sup>28,29</sup> Clinical trials in humans have yielded similar results. Fifteen patients with polyneuritis due to peripheral vascular insufficiency were given 480 mg/day of bilberry extract and significant improvement was noted in microcirculation.<sup>30</sup> In another study, the same dosage of bilberry extract given to 47 patients with various venous diseases resulted in reduced capillary flow as well as an elimination of microstagnation and blood stasis of the foot.<sup>31</sup> A review of uncontrolled trials from 1979 to 1985 on a total of 568 patients with venous insufficiency of the lower limbs showed bilberry extract was effective in rapidly decreasing symptomology and improving both venous microcirculation and lymph drainage.<sup>32</sup>

### ***Diabetes Mellitus***

Bilberry leaf decoctions have a long history of folk use as a hypoglycemic agent. Research demonstrates that oral administration of bilberry leaf decoctions reduce hyperglycemia in dogs, even in the presence of concurrently injected glucose.<sup>33,34</sup> This effect is attributed to the myrtillin anthocyanoside, apparently the most active hypoglycemic component.<sup>34</sup> In addition, bilberry anthocyanosides enhance collagen integrity, stabilize capillary permeability, and inhibit sorbitol accumulation, thus providing protection against vascular and neurological sequelae of diabetes.

### ***Other Effects***

Bilberry extracts have demonstrated anti-inflammatory properties in animals, and thus may be useful in the treatment of conditions such as rheumatoid arthritis.<sup>35</sup> Additionally, women with dysmenorrhea were given bilberry extract (115 mg anthocyanosides per day) for three days before and during menstruation. A significant improvement in pelvic/lumbosacral pain, mammary tension, nausea, and lower-limb heaviness was noted.<sup>36</sup> Bilberry extracts have also been shown to have strong antiplatelet aggregating activity in humans when given at doses of 480 mg daily for 30-60 days.<sup>37</sup> The antiulcer activity of one of bilberry's anthocyanosides (IdB 1027) has been demonstrated in various experimental models. Magistretti et al demonstrated that IdB 1027 decreased the incidence and severity of numerous forms of experimentally induced ulcers in Sprague Dawley and Wistar rats.<sup>38</sup> Another significant property of bilberry extracts is the capability to exert potent protective action on LDL particles during copper-mediated oxidation. This was accomplished using only trace amounts of *V. myrtillus* extract (15 to 20 mcg/mL); therefore, the extract may be even more potent than ascorbic acid in protecting LDL from oxidative stress.<sup>39</sup>

## Toxicology and Drug Interactions

As might be expected with a food, bilberry consumption is very safe. Dosages as high as 400 mg/kg body weight have been administered to rats without toxicity. Long-term oral administration in humans of doses equivalent to 180 mg/kg anthocyanosides per day for six months produced no toxic effects. No mutagenic or carcinogenic effects were observed.<sup>40</sup> Since bilberry extracts have antiplatelet aggregating properties, very high doses should be used cautiously in patients with hemorrhagic disorders and those taking anticoagulant or antiplatelet drugs. A review of studies comprising over 2,000 subjects taking bilberry extract reported only mild side effects affecting the gastrointestinal, cutaneous, or nervous system.<sup>40</sup>

## Dosage

Recommended dosages of bilberry depend on what form of the fruit is being consumed. If consuming fresh berries, 55-115 grams three times daily is recommended. Most bilberry is in the form of aqueous extract standardized to 25-percent anthocyanosides at a dose of 80-160 mg three times daily. The actual dosage of anthocyanosides is 20-40 mg three times daily.

## References

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