

## *Summer's Harvest: Wild Blueberry!*

Larken Bunce

### *Awakening Our Innate Response*

Summer arrived on the heels of a riotous spring in the Green Mountains this year. The snow kept us on ice well into April, but then buds started popping and before we knew it, the scent of lilacs and apple blossoms filled the air. Not a person could be found who wasn't basking in the luminous green spreading across our hillsides. Visions of everything to be accomplished in these fleeting warm months occupied most minds. Now we're in the heat of summer's embrace and life is sweet.

While summer arrives uniquely all over the world, if we've accepted nature's invitations to reflect in fall, rest and dream in winter, and rejuvenate ourselves in spring, summer brings with it the opportunity to manifest our dreams for the year. Having conserved and renewed our reserves, we can be more productive and need less rest. We can give ourselves time to play more and connect with our community. We can experience the deep joy of accomplishment and connection. This is the juiciest part of the year, the time when our hearts open wide and spring inspirations can become the realities of summer.

For plants, summer means bursting forth in flower and fruit — literal fertility and juiciness! What better seasonal medicine for us than the luscious, colorful produce of the summer: berries of every kind, corn, tomatoes, squash, melons, peaches? The profusion of

such treats is a reminder to luxuriate in this warm, easy time when survival can be temporarily forgotten and the earth provides for us in abundance.

Here in the northeast, blueberries are a particular treat — they grow plump and sweet, begging pie-making, smoothies and of course, old-fashioned gorging oneself on fresh berries! Yes, blueberries are a delicious indulgence of summer — a pleasure remedy — yet, equally valuable is the potent medicine they provide for our bodies.

One of the richest sources of antioxidant polyphenols, blueberries, like other fruits and vegetables, may prevent, delay or reverse many chronic degenerative diseases, including cancer.<sup>1</sup> While “super-foods” seem to come and go, I continue to highly recommend blueberries as part of my clients' diet throughout the year. Many people, though they love berries, can't quite imagine eating them everyday (or simply can't afford to have berries in the house at all times). In this case, I recommend a blueberry product, such as Innate Formulas' **Wild Blueberry**, to maintain high polyphenol intake and thus, optimal health. Here, I'll discuss some of the many benefits of consuming blueberries regularly, carrying a little of summer's magic throughout the year.

### **POLYPHENOLS AND HEALTH**

Extensive epidemiological studies over the past fifteen years have demonstrated a correlation between



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polyphenol consumption and improved health.<sup>2</sup> The polyphenolic compounds particular to edible berries include the anthocyanins and flavonoid glycosides which give berries their color.<sup>1</sup> The polyphenols in blueberries have exhibited *in vitro* and *in vivo* antioxidant, anti-angiogenic, neuroprotective, cardioprotective, anti-inflammatory, antimicrobial, estrogen-modulating, antiproliferative and cytotoxic activities. Further, anthocyanins protect the integrity of genomic DNA and prevent lipid peroxidation.<sup>1,3</sup> In general, blueberries support healthy cellular function in diverse tissues, conferring system-wide resilience in the presence of normal endogenous oxidative stress, as well as resistance to degenerative processes and exogenous stressors.

Eating a “rainbow diet” — one that is rich in fruits and vegetables of a variety of colors — has been linked to numerous health benefits.<sup>2</sup> Such a full-spectrum diet ensures consumption of a diverse array of significant phytonutrients, such as polyphenols (blue/purple/red fruits and vegetables), carotenoids (red/orange/yellow), and isothiocyanates (white and green cruciferous vegetables). Blueberries can provide the necessary “blue element” in our diets, ensuring adequate polyphenol intake.

### BLUEBERRY CHEMISTRY

Anthocyanins are the primary polyphenol found in blueberry,<sup>4</sup> the wild (low bush) blueberry (*Vaccinium angustifolium*) exhibiting a higher polyphenol content and antioxidant capacity than its cultivated (high bush) cousin (*Vaccinium corymbosum*)<sup>5</sup>. Much study has been conducted on bilberry (*Vaccinium myrtillis*), the *Vaccinium* species more commonly used in Europe. One can extrapolate uses from bilberry to blueberry as they share identical anthocyanins, however dosing should be adjusted to reflect bilberry’s higher anthocyanin content. Though anthocyanins are poorly absorbed relative to other polyphenols, therapeutic levels can be reached in serum and tissue. Improved serum antioxidant status has been demonstrated in

humans after blueberry consumption<sup>6</sup> and studies in pigs (similar to humans in absorptive mechanisms) demonstrated significant accumulation of anthocyanins in liver, eye and brain tissues.<sup>7</sup> Anthocyanins have a particular affinity for connective tissue and have been found in skin in four-fold higher concentrations than in other tissues.<sup>2</sup>

### ANTIOXIDANT ACTIVITY

At the root of many degenerative diseases, including cancer, is oxidative damage to lipids and proteins caused by free radicals, as well as compromise of DNA integrity. Antioxidants protect cells from such damage and can intervene at various stages of tumor promotion. Powerful antioxidants, anthocyanins can improve tissue antioxidant status, reducing oxidative stress, and preventing premature aging and disease in tissues as varied as eye, skin, brain, and vasculature. In particular, wild blueberry extracts exhibit ORAC (oxygen-radical absorbing capacity) values, exceeding other phenol-rich berries tested (including cranberries, elderberry and raspberry), as well as grape seed proanthocyanidin extract, which itself is superior to the standard antioxidant vitamins C and E and beta-carotene.<sup>3</sup> These results highlight the fact that anthocyanins are more potent antioxidants than oligomeric proanthocyanidins (OPCs) and other flavonoids.<sup>1</sup>

As will be discussed below, antioxidant activity and the attending anti-inflammatory activity can positively impact numerous chronic conditions, including cardiovascular diseases, cancers of various organs, neurodegeneration, ocular degeneration and more.

### CARDIOVASCULAR SUPPORT

The relationship between oxidation and the etiology of cardiovascular diseases is commonly understood. It follows that antioxidant rich foods, such as blueberries, would contribute significantly to prevention and amelioration of such conditions. The affinity of antho-



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cyanins for connective tissue, present in much of the vasculature, further suggests a considerable impact in this system.

In chronic smokers, lipid hydroperoxides, a measure of oxidative stress, were significantly reduced by daily intake of blueberries. Researchers suggested that reduction of lipid hydroperoxides may be one mechanism by which blueberries provide antioxidant cardioprotection.<sup>8</sup> Vascular endothelial cells can incorporate anthocyanins into their membrane and cytosol, thus protecting themselves from oxidative stressors. Investigators have proposed that this may preserve endothelial function and prevent vascular disease.<sup>1</sup> Further, in a hamster model of atherosclerosis, berry anthocyanins reduced the percentage of aorta covered with foam cells, and reduced oxidation of LDL and VLDL;<sup>1</sup> additional studies have confirmed a reduction of LDL oxidation by anthocyanins *in vivo*.<sup>9</sup>

In addition to antioxidant protection, anthocyanins impact vascular permeability and relaxation,<sup>1</sup> as well as platelet aggregation,<sup>10</sup> suggesting support in conditions such as hypertension, atherosclerosis, thrombosis and stroke, varicosities and edema. Hypertension and atherosclerosis can reduce arterial wall flexibility, restricting blood flow and encouraging plaque formation. Anthocyanins may counteract these effects via nitric oxide-induced arterial relaxation<sup>1</sup> and normalization of vascular permeability.<sup>11</sup> Investigators suggested that modulation of permeability may be due to anthocyanin interaction with vascular collagen.<sup>11</sup>

### CHEMOPREVENTION

Anthocyanins have shown strong chemopreventive potential, due in part to their antioxidant capacity and ability to prevent inflammation, but also due to anti-angiogenic activity. Angiogenesis (formation of new blood vessels) is involved in tumor formation, feeding growth and metastasis. Tumor vascularization is largely mediated by vascular endothelial growth factor (VEGF). Two studies examined the ability of wild blueberry extract to inhibit expression of VEGF by human keratinocytes, where VEGF is generally inactive until induced. Each study demonstrated potent inhibition of both hydrogen peroxide-induced and tumor necrosis factor-alpha-induced expression.<sup>3</sup> Further, as mentioned earlier, bilberry extracts have been shown to reduce capillary permeability in several models, contributing to the reduction of blood supply to tumor cells.<sup>2</sup> These results suggest that blueberries may

play a significant role in preventing tumorigenesis.

Investigators have also proposed that anthocyanins may protect DNA from single strand breaks, interrupt cell cycle progressions involved in cell division<sup>2</sup> and prevent carcinogen-activated mutations.<sup>12</sup> Further, anthocyanins may act as either agonists or inhibitors at estrogen receptors, depending on the levels of endogenous estrogen present<sup>2</sup> which may be relevant in estrogen-dependent cancers.

While studies have examined anthocyanin effects on numerous cancer cell lines *in vitro*, particular activity has been noted in skin and colon cancers. For example, a model of photocarcinogenesis demonstrated prevention of UV-damage in bald mice fed a proanthocyanidin-rich extract (proanthocyanidins are non-glycosylated anthocyanins).<sup>2</sup> Again, the affinity for skin cells may explain some of the preferential effects.<sup>13-14</sup>

### NEUROPROTECTION

Motor skills, such as balance and coordination, as well as cognitive behavior, including short-term memory and information retrieval, can degenerate due to oxidative stress associated with aging. Studies suggest that supplementation with antioxidant-rich foods, such as blueberry, can decrease brain oxidative stress and alleviate age-related deficits in neuronal and behavioral functions. While antioxidant and anti-inflammatory activities are certainly involved, increases in cellular signaling and neuronal communication also play a role.

Age-related reductions in memory are caused in part by decreased hippocampal plasticity, indicated by reduced neurogenesis in the hippocampus and extracellular receptor kinase activation. Animal models examining spatial memory have demonstrated the beneficial effects of blueberries on hippocampal plasticity, which correlated with improvements in spatial memory.<sup>15</sup>

Not only may blueberry supplementation reverse age-related cognitive and motor behavior decline, but investigators using a transgenic animal model found that it may be possible to overcome genetic predispositions to Alzheimer's disease through diet — specifically including blueberry supplementation. Animals showed no expected deficits in Y-maze performance nor alterations in amyloid beta burden.<sup>16</sup>

### EYE HEALTH

Extensive research has been conducted on the use of bilberries—rich in the same anthocyanins as blueberries

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— to improve vision and eye health. A double-blind, placebo-controlled trial demonstrated that oral doses of anthocyanins are important for the generation of visual purple, which assists in converting light into electrical signals for the brain. Two further studies in patients with vascular retinopathy secondary to diabetes and/or hypertension and with senile cortical cataract both demonstrated significant improvement with bilberry anthocyanin therapy.<sup>1</sup>

### ANTI-MICROBIAL ACTIVITY: URINARY & GASTROINTESTINAL TRACT HEALTH

While blueberry's red cousin, cranberry (*Vaccinium macrocarpon*) is commonly employed in urinary tract infections,<sup>9</sup> we think less often of blueberry for this purpose. However, research has shown that proanthocyanidins from many *Vaccinium* species, including blueberries, also prevent mucus membrane adherence of p-fimbriated *E. coli*, the bacteria associated with urinary tract infections.<sup>17</sup>

Blueberry extract has also shown significant inhibition of *H. pylori* *in vitro*, suggesting a possible role in prevention and treatment of gastric and duodenal ulceration, and reduction in use of clarithromycin, to which *H. pylori* is developing resistance.<sup>1</sup> Further, *H. pylori* increases interleukin-8 (IL-8) (a potent angiogenic factor and mediator of inflammation) production in gastric cancer cells, and treatment with berry-derived anthocyanins inhibited IL-8 production, thus reducing inflammation and angiogenesis.<sup>1</sup>

### TRADITIONAL USES

Blueberries and their many cousins have been and remain part of traditional diets around the world, providing antioxidant and other support through seasonal consumption. As bilberry use has been more widely documented, we can look to that literature in considering the traditional uses of this family of berries sharing the anthocyanin polyphenols. Historically, bilberry's

astrigent activity was employed in diarrhea and gastrointestinal inflammation, hemorrhoids, excessive vaginal discharge and to dry up breast milk.<sup>18</sup>

In addition to these applications, herbalists now look to *Vaccinium spp.* for potent cardiovascular support. I often recommend blueberries to clients who have family or personal history of cardiovascular disease, especially vascular concerns. Blueberry's antioxidant activity can be depended on to protect vascular endothelium and reduce inflammation, while its impact on vascular permeability reduces edema, capillary fragility (useful in allergic rhinitis), vericosities and hemorrhoids. I have used it in post-operative healing and ongoing support of hemorrhoids with great success. Further, it can be counted on for a mild anti-platelet effect (which should be monitored if using high doses with other anti-platelet medications). Blueberry's affinity for connective tissue, and historical use in internal and external wound healing, suggest great benefit in dermal and gastrointestinal ulceration (not to mention its impact on *H. pylori*). Regarding use in diabetes, while bilberry has long been suggested in diabetic retinopathy, and blueberry leaf has been used as a hypoglycemic agent, new research suggests that anthocyanins may directly modulate adipocyte function in *in vitro* and *in vivo* systems, impacting



obesity and potentially contributing to prevention of metabolic syndrome.<sup>19</sup>

From blueberry's physiological activities in the cardiovascular system, brain and connective tissues, we can imagine the energetic impact of these fruits. They seem to me to help us keep our hearts and minds open and strong while maintaining appropriate boundaries, retaining our energy for self-nourishment. And of course, their sweet juiciness reminds me to enjoy small pleasures and to cultivate summer's joy in every season. May your summer be full of such contentment and the manifestation of this year's dreams.