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## REPORT

### Blueberries

Colorful Protection For a Healthier Heart, Sharper Brain, and Cancer Defense

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#### COLORFUL PROTECTION FOR A HEALTHIER HEART, SHARPER BRAIN, AND CANCER DEFENSE

While an apple a day has long been recommended to help keep the doctor away, new research suggests that if you're looking to simultaneously ward off the oncologist, the neurologist, and the cardiologist, you would do well to consider increasing your intake of powerful disease-fighting blueberries.



Once touted by Native Americans for its mythical ability to boost stamina, the tiny but mighty blueberry is quickly becoming the stuff of modern-day legend as emerging research suggests that it can do everything from combating cancer, diabetes, and cardiovascular disease to safeguarding against age-related declines in mental acuity and motor function.

#### DIVERSE BENEFITS OF BLUEBERRIES

Unlocking the mystery of how such a diminutive fruit is capable of working so many miracles has spawned a frenzy of scientific investigation. Over the past years, the results of ongoing work indicate that the remarkable concentration of phytonutrients—particularly phenolic compounds—unique to blueberries boasts an astounding range of health benefits. Although researchers are only beginning to unravel the precise, biochemical mechanisms of action of these compounds, the antioxidant and anti-inflammatory attributes of blueberry phytonutrients are increasingly well established with just about every new berry study to hit the journals.



More specifically, the many subclasses of *phenols* and *polyphenols* (plant compounds comprising hydroxyl groups attached to aromatic rings) that exist in abundance in blueberries and blueberry leaves represent some of the most powerful, naturally occurring antioxidants and anti-inflammatory agents found in vegetation. By neutralizing free radicals and quelling maladaptive inflammatory responses, these compounds protect cells and tissues against the oxidative damage and inflammation believed to initiate, mediate, or accelerate conditions ranging from diabetes, heart disease, and Alzheimer's disease to numerous forms of cancer. And that may be just the beginning of the health boons of blueberries!

#### BLUEBERRIES: THE NEW BRAIN FOOD

The best-studied aspects of the blueberry as a functional food pertain to its utility as an agent of neurological support. This is great news for everyone—especially the 80 million of us who will be over 65 by 2040 when the US population is expected to peak.<sup>1</sup> Experts agree that unless we find ways to reduce the age-related declines in brain function, health care costs will continue to skyrocket over the coming decades. As it so happens, cutting-edge research indicates that blueberry phytonutrients can attenuate age-related declines in cognitive and motor function.<sup>2</sup> Compared with pharmaceutical therapies, blueberries and their extracts may represent a much safer and more cost-effective approach to treating—and possibly even preventing—neurodegenerative disorders and dementia.

In a recent study, 12 weeks of a diet that included 2% blueberries by weight restored cognitive performance and improved spatial memory in “senior” rats exhibiting early symptoms of senescence (brain aging).<sup>3</sup> Similarly, compared with control animals that did not receive blueberry extract, rats whose brains were injected with an inflammatory neurotoxin known to cause learning impairment demonstrated marked improvement in cognition and spatial memory when fed a blueberry-supplemented diet for eight weeks prior to injection.<sup>4</sup> Plus, at least one study suggests that blueberry extracts limit brain injury caused by ischemic (lack of blood flow) stroke.<sup>5</sup> Based on these and other findings, investigators hypothesize that blueberry supplementation protects against the neuronal damage and subsequent cognitive impairment brought about by oxidative stress.<sup>6,7</sup>



In addition to their well-documented antioxidant activity,<sup>8</sup> ongoing research from the Human Nutrition Research Center on Aging suggests that blueberry polyphenols may exert neuroprotective effects by indirectly increasing brain cell receptor sensitivity, thereby improving neuronal signaling.<sup>2,9,10</sup> There is further evidence that blueberry polyphenols promote the formation of new synaptic connections between neurons,<sup>11</sup> a mechanism that could theoretically augment brain plasticity—i.e., learning capacity—even in the elderly.

What does the future hold for blueberries and brain research? Believe it or not, blueberry phytonutrients may soon play a pivotal role in brain tissue transplantation, an exciting area of investigation that could one day help prevent or even reverse neurodegenerative disorders like Parkinson’s disease. A handful of recent studies indicate that inclusion of blueberry extract in the diets of rats undergoing brain-grafting procedures significantly increased not only the survival of implanted neurons, but also their subsequent growth and the ultimate dimensions of the grafted tissue.<sup>12,13</sup>

### HEART-HEALTHY BENEFITS OF BLUEBERRIES

Improving brain function within an aging population would certainly be a lofty accomplishment. However, the fact remains that the number one cause of morbidity and mortality in the industrialized world is heart disease, not dementia. Fortunately, emerging research indicates that blueberry phytonutrients may also be effective at safeguarding cardiovascular health. Although scientists have only just begun to explore this field of inquiry, a range of blueberry’s heart-healthy effects have already been identified.

Using a pig model, investigators found that dietary supplementation with blueberries resulted in a significant decrease in total serum cholesterol as well as a reduction in detrimental low-density lipoprotein (LDL), thus favorably modifying two important cardiovascular risk factors.<sup>14</sup>

The multitasking blueberry leaf may also possess anti-hypertensive properties. One laboratory study demonstrated that the phytonutrients in blueberry leaves have a marked inhibitory effect on angiotensin-converting enzyme (ACE) activity.

This is an intriguing finding, since ACE-inhibiting pharmaceuticals are an important tool in the medical management of hypertension. Additionally, supplementation with blueberry leaf extract helped prevent the development of high blood pressure in rats susceptible to the condition.<sup>15</sup>



### BENEFITS FOR DIABETES AND BLOOD SUGAR CONTROL

In addition to their cholesterol-lowering prowess, blueberry phytonutrients are rapidly building a reputation for possessing antidiabetic properties. In a recent *in vitro* study, extracts of the Canadian lowbush blueberry were fermented with the *Serratia vaccinii* bacterium, a process known to modify the phenolic content and increase antioxidant activity. Results indicated that the fermented blueberry juice dramatically increased glucose uptake into muscle cell cultures while decreasing triglyceride formation in adipocytes (fat cells).<sup>16</sup>

One promising area of future research involves the phytonutrients found in the leaf of the blueberry plant. Among them are polyphenols that demonstrate alpha-amylase inhibitor activity. By reducing the rate of carbohydrate breakdown after ingestion, alpha-amylase inhibitors effectively lower blood glucose levels and insulin response following a meal, making these compounds an encouraging adjunctive treatment for type 2 diabetes.<sup>17</sup> In fact, one study found that diabetic test subjects who supplemented with a commercially available formulation of blueberry leaves three times daily for four weeks were able to lower their average fasting plasma glucose from 143 to 104 mg/dL. The investigation also revealed a correlation between the reduction of fasting glucose and a correspondingly significant reduction in several well-established markers of inflammation including alanine aminotransferases (ALT), aspartate aminotransferases (AST), glutamyltransferase (GGT), and C-reactive protein (CRP).<sup>18</sup>

## WHAT YOU NEED TO KNOW: BLUEBERRIES

- Blueberry phytonutrients exert their health-promoting effects via complex biochemical mechanisms that counteract oxidative stress, decrease inflammation, and modulate genes associated with a myriad of disease processes.
- Blueberry is best studied as an agent of neurological support. Research suggests that blueberry phytonutrients attenuate age-related declines in cognitive and motor function, augment brain plasticity, limit brain damage after ischemic stroke, and may one day play a role in the prevention and treatment of neurodegenerative disorders like Parkinson's disease and dementia.
- Blueberry phytonutrients may also safeguard cardiovascular health by decreasing total serum cholesterol and fighting high blood pressure.
- Fermented blueberry extracts can function as insulin potentiators. Diabetics taking a commercial preparation of blueberry and other extracts significantly lowered their fasting plasma glucose levels. Blueberry leaves contain polyphenols that demonstrate alpha-amylase inhibitor activity and may represent an encouraging adjunctive treatment for type 2 diabetes.
- The juice of blueberries, as well as a number of other berry fruits, significantly inhibits in vitro proliferation of prostate, breast, intestinal, and gastric cancer. Pterostilbene, a phenolic compound found in blueberries, shows promise against colon cancer in animal and laboratory models.
- Low molecular-weight phenols found in blueberries boost colon health by altering bacterial metabolism. Blueberry consumption was shown to improve several parameters of disease activity in a model of colitis.
- Emerging research also indicates that blueberry phytonutrients may help combat liver inflammation, vascular disease, and osteoporosis.

### BLUEBERRIES BATTLE CANCER

If shielding your heart from the ravages of LDL, hypertension, and diabetes whilst simultaneously boosting your brain power isn't enough to make you want to increase your consumption of blueberries, here's one more reason: *blueberries fight cancer*. And not just a single type of cancer, but a variety of today's most malignant types.

Investigators at the Charles-Bruneau cancer research center in Montreal, Quebec examined the effects of a diversity of berries on different cancer cell lines. Their remarkable findings were that the juice of blueberries, as well as a number of other berry fruits including raspberries, black and white currants, gooseberries, and cranberries, all significantly inhibit in vitro proliferation of prostate, breast, intestinal, and gastric cancer. Surprisingly, however, study authors found no direct relationship between antioxidant capacity and anti-proliferative activity, suggesting that other factors, such as the anti-inflammatory phytonutrients inherent to berry juices, play an even more important role in their ability to combat malignancy.<sup>19</sup>



One such anti-inflammatory phytonutrient is *pterostilbene*, a phenolic compound found in extremely high concentrations in blueberries and grapes. A recent study demonstrated that pterostilbene induced apoptosis (cell death) in human gastric carcinoma cell cultures.<sup>20</sup> In related work, administration of either isolated pterostilbene or blueberries suppressed the occurrence of pre-cancerous lesions in the colons of rats exposed to *azoxymethane*, a carcinogenic compound known to induce colonic adenomas and cancer.<sup>21,22</sup> Other promising research suggests that blueberry may help limit tumor growth by inhibiting angiogenesis, the process by which cancers develop their own blood supply in order to fuel their growth.<sup>23,24</sup>

### GASTROINTESTINAL HEALTH BENEFITS

Fighting colon cancer isn't the only gastrointestinal health benefit of blueberries—studies suggest the berries may help fight inflammation and infection in the lower gastrointestinal tract.

Investigators from the Rowett Research Institute in Aberdeen, UK believe they may have identified a fundamental component of the anticancer, anti-inflammatory activity of blueberry phytonutrients in the colon. Because low molecular-weight phenols exist attached to non-digestible portions of the berry and are therefore able to reach the large bowel intact, they are the predominant phenolic compounds detected in the colon. Research from the Rowett Institute suggests that these low molecular weight phenols boost colon health by altering local bacterial metabolism.<sup>25</sup> This hypothesis is supported by the findings from another recent study of an animal model of colitis (inflammation of the colon), in which blueberry consumption was shown to improve several parameters of disease activity by reducing local inflammation and preventing bacterial translocation, a process by which pathogenic bacteria migrate from inside the colon to nearby lymph nodes and other extra-intestinal sites.<sup>26</sup>



One common cause of diarrhea in both the developed and developing worlds is the pesky protozoan parasite known as *Giardia duodenalis*. In vitro assays indicate that blueberry extracts can kill *Giardia duodenalis* during the activated/feeding stage of the parasite's life cycle.<sup>27</sup>

## WHAT CAN BLUEBERRIES DO FOR YOU?

The recent eruption of scientific inquiry has only begun to scratch the surface of blueberry's vast health-promoting potential. In addition to the work discussed throughout this article, currently there are studies linking the consumption of berries and berry extracts to protection against estrogen-induced breast cancer,<sup>28</sup> osteoporosis,<sup>29</sup> liver inflammation,<sup>30</sup> vascular disease,<sup>31</sup> urinary tract infections,<sup>32-34</sup> and more.

It sort of makes you wonder how such a ubiquitous food item that is a treasure-trove of good health has, until very recently, managed to elude scientific detection. After all, prior to 10,000 years ago, when the advent of agriculture introduced the widespread cultivation of grains and obviated the caloric need to gather wild vegetation for survival, berry fruits represented a significant portion of modern man's energy intake. In terms of our evolutionary history, it should then come as no surprise that berry phytonutrients constitute such a panacea.

As studies continue to explore their expansive health benefits, berry fruits seem destined to assume their rightful place as veritable powerhouses of antioxidant and anti-inflammatory activity, "discovered" during an era when the perils of modern living, and especially the declining quality of our food supply, have rendered the human race more inflamed and prone to chronic disease than ever before.

If you have any questions on the scientific content of this article, please call a Life Extension Health Advisor at 1-800-226-2370.

### AURORABLUE®: NOT ALL BLUEBERRIES ARE CREATED EQUAL

While all blueberries are undoubtedly good for you, some are apparently better than others. According to recent studies, organically grown blueberries appear to yield significantly more phytonutrients and demonstrate greater antioxidant activity than blueberries grown conventionally.<sup>35</sup> Perhaps even more impressive is what scientists are discovering about how geography and climate affect the nutritional properties of wild blueberries.

One bioprospector has turned the quest for the ultimate blueberry into a personal crusade. NIH researcher Maureen McKenzie, PhD, spent 15 years exploring the Alaskan frontier and building a relationship of mutual trust and respect with the native Eskimo, Aleut, and American Indians dwelling in these remote areas. The fruits of her labors include the identification of 17 different blueberry sub-species that are not only unique to Alaska, but are uniquely powerful sources of phytonutrients. The Alaskan blueberry is able to thrive in the harsh geo-climactic conditions of the tundra thanks to genetic adaptations that augment its antioxidant production by several-fold, compared with wild blueberries grown in more temperate regions like Maine.<sup>36</sup>

Armed with her extraordinary blueberries, Dr. McKenzie founded the only company in Alaska dedicated to pharmaceutical and nutraceutical discovery from boreal territories. One of her proprietary formulations, AuroraBlue®, is touted as the next generation in natural blueberry supplementation. Made from four of the predominant sub-species of Alaskan blueberry, AuroraBlue® boasts an oxygen radical absorbance capacity (ORAC, a measure of free radical-scavenging capacity) score of 1,205 micromoles trolox equivalents per gram ( $\mu\text{mol TE/g}$ )—nearly four times the ORAC of wild Maine blueberries (314  $\mu\text{mol TE/g}$ ) and more than seven times the ORAC of conventionally cultivated blueberries (155  $\mu\text{mol TE/g}$ ).<sup>36,37</sup>

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