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COVER STORY

Antioxidant Power

Blueberries and bilberries slow brain aging and protect vision
by Ivy Greenwell

When it comes to antioxidant power, according to a measure called ORAC (oxygen radical absorbance capacity), blueberries are at the top of the USDA chart-ahead of blackberries, garlic, kale and strawberries, and far ahead of broccoli and spinach. Not only that, but they taste delicious. Here, nature has been gracious to us: a favorite food has been found to be a powerhouse of antioxidants. Talk about a miracle anti-aging food that is actually a treat!

Now, by all means keep eating spinach and kale-these vegetables contain the powerful carotenoids, lutein and zeaxanthin, as well as a sulfur-containing antioxidant, lipoic acid-nutrients that help protect us against macular degeneration and cataracts, and probably against cardiovascular disease and other aging-related disorders as well. Eating spinach, kale and other green leafy vegetables at least twice a week is highly recommended. But do consider consuming half a cup or more of blueberries every day in addition to all the vegetables and fruit you already consume. Yes, you've read that correctly: this article is urging you to eat blueberries every day. Why? Because adding blueberries to your daily diet could double your antioxidant intake from food.

Frozen blueberries are fine when fresh ones are out of season. Wild blueberries may be more potent than the larger, sweeter cultivated blueberries, but even the cultivated blueberries apparently can pack a ferocious punch against free radicals.



Why this sudden urgency about eating blueberries? It started with the scientists at the USDA Nutrition Research Center on Aging at Tufts University in Boston. They have discovered that the blueberry comes close to being a miracle food, considering the important health and anti-aging benefits it offers. It is rumored that the Tufts researchers themselves have begun to eat blueberries by the pint during the berry season; off-season, their freezers are stacked with frozen blueberries. Dr. James Joseph, a senior scientist at Tufts, admits that he started adding blueberries to his morning protein shake after he saw the results of his own research. This comes as no surprise: scientists have known for a long time that restoring and maintaining youthful brain function is key in slowing aging.

European bilberries (*Vaccinium myrtillus*) and North American blueberries (*Vaccinium corymbosum*) are closely related; cranberries (*Vaccinium macrocarpon*) are also close cousins to blueberries. Scientists think that the antioxidant and general anti-aging benefits of the *Vaccinium* species berries come from the compounds that give them their deep pigmentation. These compounds are a class of flavonoids (phenolic compounds) called anthocyanins, which often occur together with proanthocyanidins. Proanthocyanidins are the precursors of anthocyanins, and also excellent antioxidants in their own right.

Sometimes these complex flavonoids are referred to by an older term that seems to be regaining popularity, namely "condensed tannins." It is these tannins that give flowers, vegetables and fruit hues that include deep red, purple, mauve, blue, all the way to the extremely dark blue of Northern European bilberries, which can appear practically black. Thus, the redness of strawberries and raspberries and the blueness of blueberries are due to the same class of compounds. Elderberry, persimmon, tart red cherries (tartness indicates the presence of condensed tannins), red and purple grapes, beets, purple cabbage, and the peel of the purple eggplant also contain anthocyanins and proanthocyanidins.

So do many flowers-the very names of certain anthocyanins such as petunidine, malvidine, delphinidine, and peonidine indicate in which flowers these anthocyanins were first discovered. The anthocyanins in hydrangea have the interesting property of imparting mauve-pink color when the plant grows in acid soil, and blue color in alkaline soil. The red-mauve hues of autumn leaves are also due to these complex polyphenols. Those stunning scarlets of New England in October are the gift of anthocyanins. The astringent taste of wine and unripe fruit is also due to various condensed tannins.

In addition, one of the most potent flavonoids-quercetin-widely researched due to its powerful anti-cancer, anti-inflammatory, and cardioprotective properties, is chemically closely related to anthocyanins. Quercetin is present in wine, ginkgo, onions, apples, black tea and grapefruit. But berries appear to have something possibly even more potent in some ways than quercetin: a simple phenolic compound called ellagic acid, which has emerged as a star in natural chemoprevention.

Please note that green tea contains mainly catechins, which are relatively simple phenolic compounds. "Simple" doesn't mean that they are less beneficial. Black tea and many fruits and vegetables contain mainly complex polyphenols, also called polymeric polyphenols, or condensed tannins. Both simple and complex polyphenols, often present side by side, have been found to have a wide range of health benefits. Ellagic acid, for instance, a powerful anti-carcinogen, is also present in many kinds of berries, including blueberries and raspberries, as well as in cherries and pomegranates. Catechins are found not only in green tea, but also in red wine and dark chocolate (cocoa powder and bittersweet chocolate are good sources; "white chocolate" does not contain polyphenols). Likewise, coffee contains not only caffeine (an alkaloid; by the way, caffeine is also a strong antioxidant), but also catechins, as well as simple phenolic acids, such as chlorogenic acid, caffeic acid, and tannic acid. Hence, for instance, the well-established effectiveness of coffee in decreasing iron levels, or helping fight certain bacterial and viral infections.

Tannins are very common in the plant world. Apart from the sources already mentioned, they are also found in the bark of various trees-the best-known bark extract, Pycnogenol, comes from the bark of the French Maritime Pine, *Pinus maritima*. The wide distribution of tannins in the plant kingdom is probably related both to their antioxidant and antimicrobial properties. The presence of tannins in wood, for instance, is likely to be a key reason for the durability of wood. The fact that chocolate doesn't spoil in spite of its high fat content is also due to these fascinating polyphenols. Also, in spite of containing sugar, chocolate, like tea and other flavonoid-rich foods, appears to help prevent cavities. There is emerging evidence that thanks to their antimicrobial action, flavonoids can help prevent dental decay and oral diseases.

Bioflavonoids in general are amazingly bioactive with a wide range of benefits. Like many other powerful antioxidants, they show a biphasic action, depending on the dose. Lower doses, available from diet and supplements (even if you take several capsules per day of various flavonoid extracts, it is still a fairly low dose) act as antioxidants and raise the levels of reduced glutathione (GSH) and vitamin C. Negative effects such as pro-oxidant action and glutathione depletion become an issue only if huge megadoses are taken over a longer period of time. Again: neither blueberry eaters nor supplement takers need worry, since it would be very difficult and extremely expensive to reach the kind of tissue concentrations at which damage from flavonoids might occur. As Dr. Shukitt-Hale says, "You can't overdose on blueberries."

At the same, we badly need more research to investigate some unanswered questions about the dose range that produces optimum results. And of course, as usual, there are questions about in-vivo effects and complex interactions. Taking a single very potent flavonoid such as quercetin in megadoses (several grams a day, for instance) for an extended period of time should not be done without the supervision of an experienced clinician. We must remember that flavonoid research is still in infancy, and our knowledge is partial at best.

A lot of the benefits of phenolic compounds stem from their antioxidant properties. Flavonoids are powerful scavengers of free radicals. They also enter the body's antioxidant network, boosting the levels of vitamin C and of our chief endogenous antioxidant, glutathione. Higher levels of ascorbate and glutathione mean better protection of DNA and cell proteins against free radical damage. Higher levels of glutathione also mean better recycling of other antioxidant compounds, including, very importantly, estrogens, to their reduced (antioxidant) form so that these substances do not produce damage. Estrogens are excellent at protecting neural membranes from peroxidation and preventing neural death-but only if there is sufficient glutathione to keep recycling these powerful hormones to their antioxidant form. Thus, the ability of phenolic compounds such as anthocyanins to raise glutathione levels is extremely important. This, together with the inhibition of the enzymes needed for cell proliferation, such as tyrosine kinase and ornithine decarboxylase, leads to a longer cell cycle and a lower cellular turnover, since fewer damaged cells need to be replaced. The implications for anti-aging and cancer prevention are profound.

Hormone-like?

You may wonder why flavonoids have such a wide range of physiological effects, resembling those of hormones. Apparently this stems from the fact that flavonoids have chemical and structural similarities to steroid hormones, thyroid hormones, prostaglandins, retinoids, and fatty acids. Thus it should not be altogether surprising that flavonoids can even affect gene expression-both the expression of our own genes, and the genes of the various bacteria and viruses that may invade us.

Flavonoids can also attach themselves to proteins, modulating the action of enzymes. They inhibit certain digestive enzymes and also the kinase enzymes necessary for cell proliferation. This partly explains how flavonoids can serve as a valuable adjunct cancer therapy for many kinds of cancer. When very high doses of flavonoids are used, the proliferation of normal cells is also inhibited, but that generally doesn't hurt these cells, which just "sit." In fully developed cancer, however, tumor cells cannot survive in the resting state.

On the other hand, very high levels of flavonoids are undesirable for women seeking to become pregnant, since these compounds are also known to decrease fertility, possibly by modulating hormone levels and even by interfering with the critical early stages of pregnancy. Soy and red clover phytoestrogens are a particular culprit here, acting as endocrine disruptors because of their high ability to bind to estrogen receptors. Less estrogenic flavonoids may have less impact on the menstrual cycle and other aspects of fertility. A lot remains to be explored.

We are barely beginning to research flavonoids and other phytochemicals in the kind of depth they deserve. For a long while it has been known that people who consume more vegetables and fruit showed significantly superior health compared to those eating the least, especially in regard to lower rates of cardiovascular disease and cancer. Now the reasons for this are emerging. While eating a wide variety of plant foods is highly recommended, due to the synergy of various phytochemicals, we are discovering that certain compounds are particularly valuable. The phytochemicals in blueberries and bilberries are now at the top of the list.

What is so special about blueberries and bilberries? They are the richest known source of anthocyanins. But it's possible that it is the synergy of the various compounds these berries contain that is responsible for the dramatic results recently obtained at Tufts University in Boston.

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Repairing the aging brain

The main reason there has been a recent flurry of articles and media reports on blueberries is the groundbreaking research at Tufts University in Boston, conducted under the direction of Dr. James Joseph.

Nineteen-month-old Fisher rats, the equivalent of 60- to 65-year-old humans, were fed dried aqueous blueberry extract in a dose assumed by the investigators to be the human equivalent of one-half cup of blueberries a day. Other experimental groups received either vitamin E, dried aqueous spinach extract, or strawberry extract. After eight weeks in which the rats were the equivalent of 70- to 75-year-old humans, the control rats and rats supplemented with strawberry, blueberry, and spinach extracts were subjected to various tests of memory and motor function. The latter included such challenging tasks as walking on a narrow rod and, most difficult of all, staying on an accelerating rotating rod (the researchers jocularly referred to these tests as the "rat Olympics").

While all supplemented rats showed some improvement on memory and learning tasks, only the rats fed blueberry extract showed a dramatic improvement in balance and motor coordination compared to unsupplemented rats. Rats fed blueberries could run faster and stay longer on the narrow rod and on the rotating rod. In fact, on the average they managed to stay on almost twice as long as all the other aged rats before falling off.

The blueberry-supplemented rats even came close to the youthful norm on maintaining balance while walking on the narrow rod. Young rats can stay on for 13 seconds; old rats fall off after five seconds. Rats in the groups receiving vitamin E, spinach extract, and strawberry extract fell off just as quickly as control rats. But the blueberry-supplemented old rats managed to stay on for 10 to 11 seconds.

All these feats show a reversal of the usual aging-related dysfunction in motor behavior, balance and coordination. Again, the blueberry-supplemented animals were the only group to show reversals in motor-behavioral deficits. Neither vitamin E, spinach extract or strawberry extract produced these rejuvenating effects on the motor function.

In his paper in the September 1999 issue of the Journal of Neuroscience, Dr. Joseph states, "This is the first study that has shown that dietary supplementation with fruit and vegetable extracts that are high in phytonutrient antioxidants can actually reverse some of the aging-related neuronal/behavioral dysfunction." The dryness and formality of this statement should not obscure the fact that something extraordinary has been discovered. We do not know of any other agent that can reverse the deterioration of motor function with aging. And yet daily doses of blueberry extract have done just that.

An impaired sense of balance is one of the telltale signs of aging. For instance, a young person can usually stand on one leg, even with eyes closed, much longer than an older person, who begins to sway and quickly needs to put down the raised leg in order to prevent a fall. The elderly are also notorious for falling down for no apparent reason. We maintain our posture by automatically correcting against swaying motion; when the conduction of neural signals slows down due to aging, we easily lose our balance. The phytochemicals in the blueberry extract appear to have speeded up neural communication.

The next project is to start feeding blueberry extract to very young rats, to see to what extent the age-related deterioration in both cognitive and motor function can be prevented. Previous Tufts studies have already shown that if rats are fed antioxidants beginning at six months of age, their aging process is partly slowed down (in animal studies, various antioxidants have been found to extend the average life span by 10% to 30%). It would be interesting to see if any of the fruit- or vegetable-extract supplemented diets also extend longevity. The fact that blueberry extract resulted in greater ability to release dopamine may be significant for longevity. Several nutrients that increase dopamine (and thus also growth hormone) have been shown to increase the average life span.

The supplemented rats also showed improved learning and short-term memory, performing closer to youthful levels in tests such as navigating mazes and finding an underwater platform. One possible explanation is vision improvement, since flavonoids and other compounds found in berries and spinach are known for their benefits to the eyes. However, an improvement in memory and cognition in general is also likely to be involved. This is to be expected when the levels of neurotransmitters, which typically decline with advancing age, are raised through a powerful antioxidant intervention. In separate studies, it has also been found that

phytochemicals contained in blueberry, strawberry and spinach extracts prevented cell death and the loss of nerve growth factors.

When the brain tissue from the blueberry-supplemented rats was subjected to various in-vitro tests, it was discovered that it showed the greatest dopamine release, and the best ability to handle calcium ions. "It appears that blueberry supplementation may be effective in reversing the deleterious effects of aging on calcium homeostasis," Dr. Joseph states in his paper. Other changes also confirmed that the neurons from blueberry-supplemented rats had the best ability to communicate with other cells. Dr. Joseph speculates that mechanisms other than the antioxidant protection may be involved here, mainly an increase in membrane fluidity and lower levels of inflammatory compounds. An increase in glutathione was also found, but it did not reach statistical difference.

A co-author of the study, Barbara Shukitt-Hale, said in an interview, "People are told once you're old, there's nothing you can do. That might not be true." You may chuckle at this truism. Coming from the scientific establishment, however, the suggestion that nutrients easily obtained from the diet might at least partially reverse aging-related impairment is quite revolutionary. Up to now, the belief has been that the decline in brain function, both the cognitive and motor aspects, is inevitable and irreversible. Now, more and more evidence points the opposite way.

If simply eating one-half cup of blueberries a day might produce dramatic changes (though of course this is yet to be documented in humans), then a more aggressive and multi-factorial approach might yield even more profound results. For instance, we know that certain hormones have a profound impact on brain function. In terms of motor function, coordination has been shown to improve when the levels of estradiol and progesterone are high. Likewise, postmenopausal women have shown faster reaction time and improved manual dexterity when put on hormone replacement. A popular old definition of flavonoids used to be "weak plant estrogens." These compounds often bind to the newly discovered human Type II estrogen receptors. A great deal of exploration remains to be done.

Are there yet other possible mechanisms through which blueberries might work to protect and repair neural tissue? One interesting property of polyphenols is their ability to modulate the production of nitric oxide. In correct amounts, nitric oxide is extremely useful. In excess, it is neurotoxic. Phenolic compounds seem particularly effective in terms of keeping nitric oxide within the correct range, thus improving circulation and reducing free-radical damage from nitrogen peroxides.

Another important property of flavonoids is their ability to raise the levels of glutathione. Glutathione is arguably the most important neuroprotector, being not only our primary antioxidant defense, but also an effective suppressor of chronic inflammation, known to be a significant factor in all the major diseases related to aging. Victims of Parkinson's disease show low levels of glutathione in brain tissue. It's interesting to speculate that perhaps compounds that raise glutathione, such as lipoic acid, NAC, and the potent phenolics found in berries, cherries and walnuts, might be able to help prevent the development of Alzheimer's disease and Parkinson's disease, two of the most feared and disabling degenerative disorders of old age. Both could be called "death in life" and are a tragedy for both the victim and the nearest family members. What if it turned out that simply eating half a cup of blueberries every day could largely prevent an enormous amount of suffering later! (For even better prevention, one needs to boost the entire antioxidant network-see the review of Packer's Antioxidant Miracle in the June 1999 issue of Life Extension magazine. -Eds.)

Flavonoids also tend to lower blood sugar, and thus glycation. An extract of blueberry leaves has been a traditional folk remedy against diabetes. Glycation and its toxic end product, known as AGEs (a singularly apt acronym for "advanced glycation end products"), are regarded as one of the important factors in the development and progression of brain diseases such as Alzheimer's disease.

In addition, bilberry extract has been shown to enhance the blood-brain barrier, which tends to become impaired with aging, showing a decrease in vascular density, increased permeability and other abnormalities. The normal functioning of blood-brain barrier is important not only for keeping out toxins and undesirable compounds, but also for glucose transport to the brain. Anthocyanins and related compounds seem able to decrease capillary permeability (possibly by stabilizing membrane phospholipids). Animal studies have also shown that if the blood-brain barrier becomes damaged and too permeable, anthocyanins help restore normal permeability.

In general, we have plenty of evidence that Dr. Packer is right when he says, "Flavonoids are a brain booster." But their action goes beyond mere "boosting." At least some flavonoids can apparently repair the age-related damage to the neurons-and here the anthocyanins and proanthocyanidins in blueberries, bilberry extract and grape seed extract (or red wine and purple grape juice) are the best candidates for this starring new role in the anti-aging regimen.

Berries, true eye-openers

The public became interested in bilberry extract after the news about its vision-improving benefits. Bilberry flavonoids appear to protect the retina and enhance the production of rhodopsin, also called the visual purple. Rhodopsin is a protein necessary for near vision. Exposure to light, particularly bright daylight, high-contrast lights or even computer screens deplete rhodopsin, resulting in poor night vision. A sufficient dose of bilberry anthocyanins apparently leads to an increase in rhodopsin.

The first anecdotal reports about the effectiveness of bilberries came from British pilots who consumed bilberry jam in order to improve their night vision. This story became so widely known to the readers of popular alternative health magazines that unfortunately for quite a while the public assumed that the only benefits of bilberry extract relate to night vision. Later on we learned about bilberry in relation to enhanced microcirculation in the retina. Even now, many people assume that the benefits of bilberry extract are confined to vision. This is reminiscent of a similar development in regard to glutathione. Because glutathione is present in especially high levels in the lens of the eye, early research focused on the role of glutathione in vision; the understanding of glutathione's primary role as the body's main antioxidant, detoxifier, anti-inflammatory and possibly the key anti-aging compound came only later.

This is not to deny that the protection of the retina is indeed extremely important. Interestingly, it was not in England, but in Italy that most studies on bilberry extract and vision were performed, mostly in the late 1980s. One study achieved an unprecedented 97% success in halting cataract progression using bilberry extract and vitamin E. In another exciting study, bilberry extract improved vision in 75% of nearsighted subjects. A German study using a combination of vitamin E and anthocyanins found either a stabilization of myopia or an actual improvement in visual acuity in the majority of patients, whereas the control group showed further deterioration. The progressive nature of myopia is one of axioms of traditional ophthalmology: once you become near-sighted, the older you get, the more near-sighted you get, requiring a stronger prescription every couple of years. Hence, it is truly revolutionary to note that a group of naturally occurring flavonoids has been shown to either arrest or even reverse the progression of myopia.

Please note: those who wish to experiment with bilberry extract for reversing myopia should understand that there is no guarantee of this benefit. On the other hand, there is nothing to lose, since it is likely that at least the progressive deterioration of vision can be arrested. In addition, bilberry extract has many other health benefits, typical for phenolic antioxidants.

Of special interest in various ophthalmic pathologies are the anti-angiogenic properties of certain flavonoids, when these phytonutrients are used in the correct dosage range. Catechins, anthocyanins and proanthocyanidins have been found to inhibit the growth of abnormal blood vessels. This happens to be one of the mechanisms through which phenolic compounds can inhibit the growth and spread of tumors. But it also applies to the growth of abnormal blood vessels involved in the "wet," or advanced macular degeneration.

But perhaps the greatest enemy of good eye health is elevated blood glucose. You do not need to be diagnosed with diabetes to suffer some degree of damage to the tiny blood vessels of the retina (microvascular damage) due to the destructive action of glucose. Serum glucose levels typically rise with age. Apart from a low-carbohydrate diet combined with exercise, can anything be done? Here again the finding that various kinds of polyphenols lower blood sugar is of great relevance.

Interestingly, Chinese medicine recommends raspberries for vision improvement. Close enough: raspberries contain many of the same flavonoids as blueberries and bilberries. For vision improvement, think in terms of deeply colored berries (and probably cherries and plums as well). Red wine may also help: one study found that red wine drinkers were 20% less likely to develop macular degeneration. And since we have mentioned Oriental medicine, ginkgo too has been shown to have benefits for the retina, thanks to its antioxidant properties, its ability to raise glutathione levels, and its enhancement of the blood-retinal barrier. To put it simply, various potent flavonoids have similar effects, whether on the brain, eyesight or the vascular system.

Again, a reminder that vegetables and/or supplements containing lutein and zeaxanthin are also a must if you wish to protect your vision against aging-related deterioration. Egg yolks are a rich source of lutein, as is spinach. Vitamins E and C (800 mg/d), as well as zinc, have also been documented to help prevent cataracts. In addition, antioxidant hormones such as estrogens and DHEA may also be protective. Finally, the alkaloid vinpocetine (an extract of the lesser periwinkle, *Vinca minor*) is a promising new addition to the growing arsenal of compounds that can help protect our eyesight. The omega-3 fatty acid known as DHA (docosahexaenoic), richly present in fish oil, also appears to be important for protecting vision. When you use a variety of protective supplements are used, you lower your chances of developing the "inevitable" senile cataracts and other age-related eye problems.

References

Asgary S et al. Antioxidant effect of flavonoids on hemoglobin glycosylation. *Pharma Acta Helv* 1999; 73:223-6.

Atkins R. *The Vita-Nutrient Solution*. Simon and Schuster, 1999, pp. 310-311.

Bagchi D et al. Protective effects of grape seed proanthocyanidins and selected antioxidants against TPA-induced hepatic and brain lipid peroxidation and DNA fragmentation, and peritoneal macrophage activation in mice. *Gen Pharmacol* 1998; 30: 771-6.

Baker ME. Flavonoids as hormones. A perspective from an analysis of molecular fossils. *Adv Exp Med Biol* 1998;439:249-67.

Bickford PC et al. Diets high in antioxidants can reverse age-related declines in cerebellar beta-adrenergic receptor functions and motor learning. Paper presented at the 1999 AGE Annual Meeting, Seattle.

Buee L. Cerebrovascular aging. *Therapie* 1999; 54:155-65.

Cao G et al. Hyperoxia-induced changes in antioxidant capacity and the effect of dietary antioxidants. J Appl Physiol 1999; 86:1917-22.

Chung KT et al. Tannins and human health: a review. Crit Rev Food Sci Nutr 1998; 38:421-64.

Hampson E, Kimura D. Reciprocal effects of hormonal fluctuations on human motor and perceptual-spatial skills. Behav Neurosci 1988; 102:456-9.

Joseph JA et al. Membrane and receptor modifications of oxidative stress vulnerability in aging. Nutritional considerations. Ann NY Acad Sci 1998; 854:268-76.

King A, Young G. Characteristics and occurrence of phenolic phytochemicals. J Am Diet Assoc 1999; 99:213-8.

Li JJ et al. Age-dependent accumulation of advanced glycosylation end products in human neurons. Neurobiol Aging 1995; 16:69-76.

Mian E et al. Anthocyanosides and the walls of the microvessels: further aspects of the mechanism of action of their protective effect in syndromes due to abnormal capillary fragility. Minerva Med 1977; 68:3565-81.

Nagata H et al. Antioxidant action of flavonoids, quercetin and catechin, mediated by the activation of glutathione peroxidase. Tokai J Exp Clin Med 1999; 24:1-11.

Paasche G et al. The glutathione content of retinal Muller (glial) cells: the effects of aging and of application of free-radical scavengers. Ophthalmic Res 1998;30:351-60.

Packer L and Colman C. The Antioxidant Miracle. John Wiley and Sons, 1999.

Packer L et al. Antioxidant activity and biologic properties of a procyanidin-rich extract from pine bark, Pycnogenol. Free Radic Biol Med 1999; 27:704-24.

Politzer M. Experiences in the medical treatment of progressive myopia. Klin Monatsbl Augenheilkd 1977; 17:616-9.

Robert AM et al. Action of anthocyanins of Vaccinium myrtillus on the permeability of blood-brain barrier. J Med 1977; 8:321-32.

Sakagami H et al. Prevention of oral diseases by polyphenols. In Vivo 1999; 13:155-7.

Sasaki N et al. Advanced glycation end products in Alzheimer's disease and other neurodegenerative disorders. Am J Pathol 1998; 153:1149-55.

Shukitt-Hale B et al. Prevention and reversal of age-related motor and cognitive behavioral deficits with antioxidant diets. Paper presented at the 1999 AGE Annual Meeting, Seattle.

Thompson, LU et al. Relationship between polyphenol intake and blood glucose response of normal and diabetic individuals. Am J Nutr 1984;39:745-51.

Winter JC. The effects of an extract of ginkgo biloba on cognitive behavior and longevity in the rat. Physiol Behav 1998; 63:425-33.

Quotations by Shukitt-Hale - "A berry good nutrition tip," AARP Bulletin, November 1999, p.15; Reuters Health News, September 12, 1999.

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