

Blueberry

Antioxidant properties of prepared blueberry (*Vaccinium myrtillus*) extracts.

A blueberry extract (A) and two anthocyanin-derived extracts (B and C) were prepared. The contents of polyphenols, flavonoids, anthocyanins, and anthocyanin-derived pigments of the extracts were determined for the first time. The pigment profile of blueberry extract A corresponded to 15 anthocyanins, whereas extract B was mainly composed of anthocyanin-pyruvic acid adducts of the blueberry original anthocyanins and extract C was mainly composed of the respective vinylpyranoanthocyanin-catechins (portisins). The extracts' abilities to inhibit lipid peroxidation, induced by 2,2'-azobis(2-methyl-propanimidamide) dihydrochloride in a liposomal membrane system were examined. The antioxidant capacities of the extracts were evaluated through monitoring oxygen consumption and by measuring the formation of conjugated dienes. All of the extracts provided protection of membranes against peroxy radicals by increasing the induction time of oxidation. This effect increased with the polyphenol content and with the structural complexity of the anthocyanin-derived pigments of the extracts. The pigments present in extract C seemed to induce a higher protection of the liposome membranes toward oxidation. In addition, the antiradical properties and the reducing power of the extracts were determined by using DPPH and FRAP methods, respectively. The results from these assays were in agreement with those obtained with the liposome membranes.

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Phenolic compounds from blueberries can inhibit colon cancer cell proliferation and induce apoptosis.

Research has shown that diets rich in phenolic compounds may be associated with lower risks of several chronic diseases including cancer. This study systematically evaluated the bioactivities of phenolic compounds in rabbiteye blueberries and assessed their potential antiproliferation and apoptosis induction effects using two colon cancer cell lines, HT-29 and Caco-2. Polyphenols in three blueberry cultivars, Briteblue, Tifblue, and Powderblue, were extracted and freeze-dried. The extracts were further separated into phenolic acids, tannins, flavonols, and anthocyanins using an HLB cartridge and LH20 column. Some individual phenolic acids and

flavonoids were identified by HPLC with >90% purity in anthocyanin fractions. The dried extracts and fractions were added to the cell culture medium to test for antiproliferation activities and induction of apoptosis. Flavonol and tannin fractions resulted in 50% inhibition of cell proliferation at concentrations of 70–100 and 50–100 microg/mL in HT-29 and Caco-2 cells, respectively. The phenolic acid fraction showed relatively lower bioactivities with 50% inhibition at approximately 1000 microg/mL. The greatest antiproliferation effect among all four fractions was from the anthocyanin fractions. Both HT-29 and Caco-2 cell growth was significantly inhibited by >50% by the anthocyanin fractions at concentrations of 15–50 microg/mL. Anthocyanin fractions also resulted in 2–7 times increases in DNA fragmentation, indicating the induction of apoptosis. The effective dosage levels are close to the reported range of anthocyanin concentrations in rat plasma. These findings suggest that blueberry intake may reduce colon cancer risk.

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Blueberry supplemented diet reverses age-related decline in hippocampal HSP70 neuroprotection.

Dietary supplementation with antioxidant rich foods can decrease the level of oxidative stress in brain regions and can ameliorate age-related deficits in neuronal and behavioral functions. We examined whether short-term supplementation with blueberries might enhance the brain's ability to generate a heat shock protein 70 (HSP70) mediated neuroprotective response to stress. Hippocampal (HC) regions from young and old rats fed either a control or a supplemented diet for 10 weeks were subjected to an in vitro inflammatory challenge (LPS) and then examined for levels of HSP70 at various times post LPS (30, 90, and 240 min). While baseline levels of HSP70 did not differ among the various groups compared to young control diet rats, increases in HSP70 protein levels in response to an in vitro LPS challenge were significantly less in old as compared to young control diet rats at the 30, 90, and 240 min time points. However, it appeared that the blueberry diet completely restored the HSP70 response to LPS in the old rats at the 90 and 240 min times. This suggests that a short-term blueberry (BB) intervention may result in improved HSP70-mediated protection against a number of neurodegenerative processes in the brain. Results are discussed in terms of the multiplicity of the

effects of the BB supplementation which appear to range from antioxidant/anti-inflammatory activity to signaling.

Neurobiol Aging. 2005 Apr 30

Anthocyanins in aged blueberry-fed rats are found centrally and may enhance memory.

Research has shown that fruits and vegetables containing high levels of polyphenolics (flavonoids) display high total antioxidant activity. Our laboratory found that various fruit and vegetable extracts, particularly blueberry (BB), were effective in reversing age-related deficits in neuronal signaling and behavioral parameters following 8 weeks of feeding, possibly due to their polyphenolic content. However, it was unclear if these phytonutrients were able to directly access the brain from dietary BB supplementation (BBS). The present study examined whether different classes of polyphenols could be found in brain areas associated with cognitive performance following BBS. Thus, 19 month old F344 rats were fed a control or 2% BB diet for 8–10 weeks and tested in the Morris water maze (MWM), a measure of spatial learning and memory. LC-MS analyses of anthocyanins in the diet and subsequently in different brain regions of BBS and control rats were carried out. Several anthocyanins (cyanidin-3-O-beta-galactoside, cyanidin-3-O-beta-glucoside, cyanidin-3-O-beta-arabinose, malvidin-3-O-beta-galactoside, malvidin-3-O-beta-glucoside, malvidin-3-O-beta-arabinose, peonidin-3-O-beta-arabinose and delphinidin-3-O-beta-galactoside) were found in the cerebellum, cortex, hippocampus or striatum of the BBS rats, but not the controls. These findings are the first to suggest that polyphenolic compounds are able to cross the blood brain barrier and localize in various brain regions important for learning and memory. Correlational analyses revealed a relationship between MWM performance in BBS rats and the total number of anthocyanin compounds found in the cortex. These findings suggest that these compounds may deliver their antioxidant and signaling modifying capabilities centrally.

Nutr Neurosci. 2005 Apr;8(2):111–20

Dietary supplementation with blueberries, spinach, or spirulina reduces ischemic brain damage.

Free radicals are involved in neurodegenerative disorders, such as ischemia and aging. We have previously demonstrated that treatment with diets enriched with blueberry, spinach, or spirulina

have been shown to reduce neurodegenerative changes in aged animals. The purpose of this study was to determine if these diets have neuroprotective effects in focal ischemic brain. Adult male Sprague–Dawley rats were fed with equal amounts of diets (blueberry, spinach, and spirulina) or with control diet. After 4 weeks of feeding, all animals were anesthetized with chloral hydrate. The right middle cerebral artery was ligated with a 10–0 suture for 60 min. The ligature was later removed to allow reperfusional injury. Animals were sacrificed and brains were removed for caspase–3 enzymatic assays and triphenyltetrazolium chloride staining at 8 and 48 h after the onset of reperfusion. A subgroup of animals was used for locomotor behavior and biochemical assays. We found that animals which received blueberry, spinach, or spirulina enriched diets had a significant reduction in the volume of infarction in the cerebral cortex and an increase in post–stroke locomotor activity. There was no difference in blood biochemistry, blood CO₂, and electrolyte levels among all groups, suggesting that the protection was not indirectly mediated through the changes in physiological functions. Animals treated with blueberry, spinach, or spirulina had significantly lower caspase–3 activity in the ischemic hemisphere. In conclusion, our data suggest that chronic treatment with blueberry, spinach, or spirulina reduces ischemia/reperfusion–induced apoptosis and cerebral infarction.

Exp Neurol. 2005 May;193(1):75–84

Blueberry extract enhances survival of intraocular hippocampal transplants.

Transplantation of neural tissue has been explored as a potential therapy to replace dead or dying cells in the brain, such as after brain injury or neurodegenerative disease. However, survival of transplanted tissue is poor, especially when the transplant recipient is of advanced age. Recent studies have demonstrated improvement of neuronal deficits in aged animals given a diet supplemented with blueberry extract. The present study focuses on the survival of fetal hippocampal transplants to young (4 months) or middle–aged (16 months) animals with or without dietary supplementation with blueberry extract. Results indicate that fetal hippocampus transplanted to middle–aged host animals exhibits poor survival characterized by reduced growth and compromised tissue organization. However, when middle–aged animals were maintained on a diet supplemented with 2% blueberry extract, hippocampal

graft growth was significantly improved and cellular organization of grafts was comparable to that seen in tissue grafted to young host animals. Thus, the data suggest that factor(s) in blueberries may have significant effects on development and organization of this important brain region.

Cell Transplant. 2005;14(4):213–23

Fatty acid composition and antioxidant properties of cold-pressed marionberry, boysenberry, red raspberry, and blueberry seed oils.

Cold-pressed marionberry, boysenberry, red raspberry, and blueberry seed oils were evaluated for their fatty acid composition, carotenoid content, tocopherol profile, total phenolic content (TPC), oxidative stability index (OSI), peroxide value, and antioxidant properties. All tested seed oils contained significant levels of alpha-linolenic acid ranging from 19.6 to 32.4 g per 100 g of oil, along with a low ratio of n-6/n-3 fatty acids (1.64–3.99). The total carotenoid content ranged from 12.5 to 30.0 micromoles per kg oil. Zeaxanthin was the major carotenoid compound in all tested berry seed oils, along with beta-carotene, lutein, and cryptoxanthin. Total tocopherol was 260.6–2276.9 micromoles per kg oil, including alpha-, gamma-, and delta-tocopherols. OSI values were 20.07, 20.30, and 44.76 h for the marionberry, red raspberry, and boysenberry seed oils, respectively. The highest TPC of 2.0 mg gallic acid equivalents per gram of oil was observed in the red raspberry seed oil, while the strongest oxygen radical absorbance capacity was in boysenberry seed oil extract (77.9 micromol trolox equivalents per g oil). All tested berry seed oils directly reacted with and quenched DPPH radicals in a dose- and time-dependent manner. These data suggest that the cold-pressed berry seed oils may serve as potential dietary sources of tocopherols, carotenoids, and natural antioxidants.

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Wild blueberry-rich diets affect the contractile machinery of the vascular smooth muscle in the Sprague-Dawley rat.

Weanling male Sprague-Dawley rats were randomly fed a control diet (AIN-93) (C) or a blueberry diet (B) for 13 weeks, or a reverse diet (R) (C diet for 13 weeks, switched to the B diet for 8 weeks). Aortas were excised, and two intact and two endothelium-denuded rings were immersed in tissue baths containing physiological salt solution at 37 degrees C and aerated with 95% O₂ and 5% CO₂

(pH 7.4). Following equilibration and preconditioning under 1.5-g preload, cumulative dose-response curves were generated with six doses of the alpha1-adrenergic receptor-selective agonist L-phenylephrine (L-Phe, 10^{-8} – 3×10^{-6} M) and relaxed with one dose of acetylcholine (3×10^{-6} M) to assess intact endothelium. The maximum force of contraction (Fmax) and vessel sensitivity (pD(2)) were determined in intact and endothelium-denuded rings. A two-way analysis of variance test revealed that blueberry-fed animals (B and R diets) developed a significantly lower F (max) (0.873 ± 0.0463 and 0.9266 ± 0.0463 g, respectively) when contracted with L-Phe, compared with the animals on the C diet (1.109 ± 0.0463 g) ($P < .05$). The pD(2) of the intact rings was not significantly different among diet groups. Additionally, diet did not significantly affect the mean F (max) or pD(2) of endothelium-denuded rings. Our results indicate for the first time that wild blueberries incorporated into the diet affect the vascular smooth muscle contractile machinery by suppressing the alpha1-adrenergic receptor agonist-mediated contraction while having no effect on membrane sensitivity of the endothelial or vascular smooth muscle cell layer. Furthermore, their mechanism of action seems to be accomplished through an endothelium-dependent pathway.

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