

Neuroprotective

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Neuroprotection by *Spirulina platensis* protean extract and phycocyanin against iron-induced toxicity in SH-SY5Y neuroblastoma cells.

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We investigated the effect of *Spirulina platensis* protean extract and the biliprotein phycocyanin isolated from this microalga, on the activities of the antioxidant enzymes SOD, CAT, GPx, and GR, lipid peroxidation inhibitory activity and glutathione levels after the iron induced oxidative stress in SH-SY5Y neuroblastoma cells. Iron is one of the most important agents that produce oxidative stress and decline of neuronal functions. *S. platensis* protean extract and phycocyanin exert the antioxidant activity by protecting the activity of the cellular antioxidant enzymes total GPx, GPx-Se and GR and by increasing reduced glutathione in cells against oxidative stress induced by iron. These results suggested that *S. platensis* protean extract is a powerful antioxidant through a mechanism related to antioxidant activity, capable of interfering with radical-mediated cell death. *S. platensis* may be useful in diseases known to be aggravated by reactive oxygen species and in the development of novel treatments for neurodegenerative disorders as long as iron has been implicated in the neuropathology of several neurodegenerative disorders such as Alzheimer's or Parkinson diseases.

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Blueberry- and spirulina-enriched diets enhance striatal dopamine recovery and induce a rapid, transient microglia activation after injury of the rat nigrostriatal dopamine system.

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Neuroinflammation plays a critical role in loss of dopamine neurons during brain injury and in neurodegenerative diseases. Diets enriched in foods with antioxidant and anti-inflammatory actions may modulate this neuroinflammation. The model of 6-hydroxydopamine (6-OHDA) injected into the dorsal striatum of normal rats, causes a progressive loss of dopamine neurons in the ventral mesencephalon. In this study, we have investigated the inflammatory response following 6-OHDA injected into the striatum of adult rats treated with diet enriched in blueberry or spirulina. One week after the dopamine lesion, a similar size of dopamine degeneration was found in the striatum and in the globus pallidus in all lesioned animals. At 1 week, a significant increase in OX-6- (MHC class II) positive microglia was found in animals fed with blueberry- and spirulina-enriched diets in both the striatum and the globus pallidus. These OX-6-positive cells were located within the area of tyrosine hydroxylase (TH) -negativity. At 1 month after the lesion, the number of OX-6-positive cells was reduced in diet-treated animals while a significant increase beyond that observed at 1 week was now present in lesioned control animals. Dopamine recovery as revealed by TH-immunohistochemistry was significantly enhanced at 4 weeks postlesion in the striatum while in the globus pallidus the density of TH-positive nerve fibers was not different from control-fed lesioned animals. In conclusion, enhanced striatal dopamine recovery appeared in animals treated with diet enriched in antioxidants and anti-inflammatory phytochemicals and coincided with an early, transient increase in OX-6-positive microglia.

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Neuroprotective

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

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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-O suture for 60 min. The ligature was later removed to allow reperfusion 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.

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Neuroprotective

Diets enriched in foods with high antioxidant activity reverse age-induced decreases in cerebellar beta-adrenergic function and increases in proinflammatory cytokines.

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Antioxidants and diets supplemented with foods high in oxygen radical absorbance capacity (ORAC) reverse age-related decreases in cerebellar beta-adrenergic receptor function. We examined whether this effect was related to the antioxidant capacity of the food supplement and whether an antioxidant-rich diet reduced the levels of proinflammatory cytokines in the cerebellum. Aged male Fischer 344 rats were given apple (5 mg dry weight), spirulina (5 mg), or cucumber (5 mg) either in 0.5 ml water by oral gavage or supplied in the rat chow daily for 14 d. Electrophysiologic techniques revealed a significant decrease in beta-adrenergic receptor function in aged control rats. Spirulina reversed this effect. Apple (a food with intermediate ORAC) had an intermediate effect on cerebellar beta-adrenergic receptor physiology, and cucumber (low ORAC) had no effect, indicating that the reversal of beta-adrenergic receptor function decreases might be related to the ORAC dose. The mRNA of the proinflammatory cytokines tumor necrosis factor-alpha (TNFalpha) and TNFbeta was also examined. RNase protection assays revealed increased levels of these cytokines in the aged cerebellum. Spirulina and apple significantly downregulated this age-related increase in proinflammatory cytokines, whereas cucumber had no effect, suggesting that one mechanism by which these diets work is by modulation of an age-related increase in inflammatory responses. Malondialdehyde (MDA) was measured as a marker of oxidative damage. Apple and spirulina but not cucumber decreased MDA levels in the aged rats. In summary, the improved beta-adrenergic receptor function in aged rats induced by diets rich in antioxidants is related to the ORAC dose, and these diets reduce proinflammatory cytokine levels.

Spirulina maxima pretreatment partially protects against 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine neurotoxicity.

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Spirulina is an alga that has a high nutritional value and some of its biological activities are attributed to the presence of antioxidants. Oxidative stress is involved in Parkinson's disease. This study aims at evaluating the neuroprotective role of *Spirulina maxima* (Sp.) against 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) neurotoxicity, used as a model of Parkinson's disease. Ninety-six male C-57 black mice were pretreated with *Spirulina* for 14 days (25, 50, 100, 150 or 200 mg/kg, oral), followed by three MPTP administrations (30 mg/kg, intraperitoneal, i.p.). Animals were given Sp. for 8 additional days. After the treatment, the striatal dopamine (DA) content was analysed by high performance liquid chromatography, and lipid peroxidation was studied as an index of oxidative stress. Sp. pretreatment at 150 mg/kg partially prevented (51%) the DA-depleting effect of MPTP and blocked oxidative stress. *Spirulina* partially prevents MPTP neurotoxicity and oxidative stress, suggesting it could be a possible alternative in experimental therapy.

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- Research Support, Non-U.S. Gov't

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