



Quercetin Protects DNA from Oxidative Damage in Diabetics

Diabetics have reduced antioxidant defenses and an increased risk for free-radical mediated conditions such as heart disease and retinopathy. Quercetin, a dietary flavonoid with antioxidant properties, has been shown to protect retinal pigment epithelial and cortical cells during oxidative stress *in vitro*¹, and to inhibit tyrosine kinase, an enzyme that mediates vascular endothelial growth factor. Consumption of flavonoids, especially quercetin, has also been linked to a lower incidence of heart disease and stroke. In one clinical trial², diabetics were treated for 2 weeks on a low flavonoid diet followed by 2 weeks on one of 2 diets supplemented with flavonoids, one diet predominately quercetin. Oxidative damage to lymphocyte DNA was significantly lower after consuming the high quercetin diet, suggesting protection against oxidative stress at the tissue level. The finding was not accounted for by any change in diabetic control or changes in plasma levels of other known antioxidants.

1. Hanneken A, et al. Flavonoids protect human retinal pigment epithelial cells from oxidative stress-induced death. *Investigative Ophthalmology & Visual Science* 47:3164-77, 2006.
2. Lean MEJ, et al. Dietary flavonols protect diabetic human lymphocytes against oxidative damage to DNA. *Diabetes* 48:176-181, 1999.
3. Loke WM et al. Pure dietary flavonoids quercetin and epicatechin augment nitric oxide products and reduce endothelin-1 acutely in healthy men. *American Journal of Clinical Nutrition* 88:1018-25, 2008.

Magnesium Lowers Risk of Hypertension, Diabetes, Metabolic Syndrome

It is well known that diabetics with poor glucose control are often low in magnesium, a mineral that helps regulate cellular glucose metabolism and influences insulin secretion. Evidence also suggests that magnesium intake is inversely related to the risk of developing hypertension, type-2 diabetes, and metabolic syndrome both in young¹ and older² adults. In a meta-analysis³ of prospective cohort studies that included over 286,000 participants and nearly 11,000 cases of type-2, 6 of the 7 studies included showed a statistically significant inverse relationship between

magnesium intake and diabetes risk. The analysis found that every 100 mg per day increase in intake of the mineral was associated with a 15% decrease in risk.

1. He K, et al. Magnesium intake and incidence of metabolic syndrome among young adults. *Circulation* 113:1675-1682, 2006.
2. McKeown NM, et al. Dietary magnesium intake is related to metabolic syndrome in older Americans. *European Journal of Nutrition* 47:210-6, 2008.
3. Larsson A, et al. Magnesium intake and risk of type-2 diabetes: a meta-analysis. *Journal of Internal Medicine*, 2007.

Alpha Lipoic Acid Promotes Production of Glutathione; May Protect Retina

In addition to scavenging free radicals, alpha lipoic acid (ALA) modulates signal transduction pathways that increase production of important endogenous cellular antioxidants such as glutathione¹. Numerous well-controlled trials have shown that ALA reduces sensory symptoms in patients with diabetic neuropathy, and ALA has been reported to improve flow-mediated vasodilation in subjects with metabolic syndrome². Research in models of diabetic retinopathy suggests that ALA may protect the diabetic retina as well. In one such study³, early administration of ALA to diabetic mice prevented significant decreases of glutathione content and glutathione peroxidase activity, and normalized MDA concentration, a marker of oxidative stress. Further, ALA restored electroretinogram b-wave amplitude to control values.

1. Peterson, et al. Critical Review: Is alpha-lipoic acid a scavenger of reactive oxygen species *in vivo*? Evidence for its initiation of stress signaling pathways that promote endogenous antioxidant capacity. *Life*, 60: 362-367, 2008.
2. Singh U, et al. Alpha-lipoic acid supplementation and diabetes. *Nutrition Reviews* 66:646-57, 2008.
3. Johnsen-Soriano S, et al. Early lipoic acid intake protects retina of diabetic mice. *Free Radical Research* 4:613-7, 2008.

Proanthocyanidins Improve Microcirculation, Edema in Diabetics

In addition to acting as an antioxidant and anti-inflammatory, proanthocyanidins from pine bark selectively bind to collagen and elastin to strengthen blood vessel walls and improve capillary resistance.

Pine bark extract has been tested in over 1200 people with retinopathy and diabetic retinopathy in open and controlled trials, with results generally supporting a delay of progression according to one review¹. One double-masked, placebo-controlled trial investigated the effect of 150 mg day of pine bark extract (Pycnogenol®) on objective parameters in patients with retinopathies associated with diabetes, atherosclerosis and hypertension^{2,3}. Examination of the ocular fundus showed a significant improvement in those treated with Pycnogenol®, as well as improvements in electrophysiology and fluoroangiography measures. The group taking Pycnogenol® also experienced a significant reduction in vascular permeability and an improvement in the blood-retinal barrier.

1. Schönlau F, et al. Pycnogenol for diabetic retinopathy: A review. *International Ophthalmology* 24:161-71, 2002.
2. Bartlett HE and Eperjesi F. Nutritional supplementation for type 2 diabetes: a systematic review. *Ophthalmic Physiology Optometry* 28: 503-523, 2008.
3. Spadea L and Balestrazzi E. Treatment of vascular retinopathies with Pycnogenol. *Phytotherapy Research* 15:219-223, 2001.

Low Vitamin D Levels Prevalent in Diabetics; May Counter Inflammation

It has been reported that low levels of vitamin D are highly prevalent in type-2 diabetics, and are independently and strongly associated with increased thickness of the carotid artery lining¹. Seventy-five percent of young people with type-1 have also been observed to be deficient in vitamin D². Since inflammation plays a role in the etiology of atherosclerosis, researchers examined the immune modulating effects of vitamin D in type-2 diabetics³. Monocytes from type-2 patients exhibited a pro-inflammatory profile compared to healthy controls. Further, vitamin D was shown to down-regulate the expression of pro-inflammatory mediators TNF-alpha, IL-1, IL-6 and IL-8 in monocytes from the diabetic subjects.

1. Targher G, et al. Serum 25-hydroxyvitamin D3 concentrations and carotid artery intima-media thickness among type 2 diabetic patients. *Clinical Endocrinology (Oxf)* 65:593-7, 2006.
2. Svoren BM, et al. Significant vitamin D deficiency in youth with type-1 diabetes mellitus. *Journal of Pediatrics* 514:132-34, 2009.
3. Giuletti A, et al. Monocytes from type 2 diabetic patients have a pro-inflammatory profile; 1-25-dihydroxyvitamin D(3) works as an anti-inflammatory. *Diabetes Research and Clinical Practice* 77:47-57, 2007.

Low Thiamin Plasma Levels Common in Type 1 and 2 Diabetics

Researchers report that plasma concentrations of the B-vitamin thiamin were decreased by about 75% in type-1 and -2 diabetics with and without microalbuminuria compared to levels in healthy controls. Plasma thiamin concentration correlated negatively with renal clearance of thiamin, which was increased 24-fold in type-1 diabetic patients and 16-fold in type-2 diabetic patients. This marked deficiency of plasma thiamin also correlated negatively with soluble vascular adhesion molecule, a marker of endothelial dysfunction and increased risk of atherosclerosis. Previous studies in animals have reported that low thiamin levels can lead to kidney & vascular disease.

Thornally PF, et al. High prevalence of low plasma thiamine concentration in diabetes linked to a marker of vascular disease. *Diabetologia* 50:2164-70, 2007.

Proanthocyanidins Promote Blood Pressure Control in Diabetics

Type-2 diabetics are at higher risk for cardiovascular disease. Pine bark extract is a concentrated source of proanthocyanidins, compounds with antioxidant and anti-inflammatory properties. In a recent double-blind study of diabetics with hypertension taking ACE inhibitors, 58% achieved blood pressure control at ½ their pretrial medication dose during three months of pine bark extract supplementation (Pycnogenol®). Statistically significant effects on other cardiovascular disease risk factors such as decreased plasma endothelin-1 and LDL cholesterol were also noted in the pine bark group compared to placebo.

Zibadi S, et al. Reduction of cardiovascular risk factors in subjects with type 2 diabetes by Pycnogenol supplementation. *Nutrition Research* 28:315-20, 2008.

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