



Neuroprotective and Cardioprotective Effects of Pyrroloquinoline Quinone (PQQ)

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Pyrroloquinoline quinone (PQQ) was first identified in 1979 as an enzyme cofactor in microorganisms.⁽¹⁾ This unique compound has since been characterized as an important growth factor in bacteria and plants and is widely distributed in nature. Significant dietary sources of PQQ include tea, green peppers, parsley and beans. PQQ is found naturally in human organs and tissues, with the highest levels in the spleen, pancreas, lung, kidney and breast milk.⁽²⁻⁴⁾ The chemistry and stability of PQQ enable it to efficiently catalyze successive oxidation and reduction reactions (redox cycles), which are essential to the function of many enzymes.⁽⁵⁾ The same properties lend PQQ powerful antioxidant activity, which has been demonstrated in a variety of experimental models. Although PQQ shares functional similarities with essential B-vitamins, it is not classified as such. However, significant physiological roles of PQQ are evident in studies of mice with PQQ deficiency, which exhibit growth impairment, immunosuppression, reduced fertility and mitochondrial dysfunction.^{(2,6,7)*}

PQQ and mitochondrial function

In recent years, a substantial body of evidence has underscored the importance of mitochondrial function in maintaining energy homeostasis, minimizing oxidative stress and promoting longevity. Mitochondrial homeostasis has been examined in many contexts including metabolic, neural and age-related conditions. PQQ deficiency decreases the size, number and function of mitochondria in rodents, and supplementation reverses these effects.⁽⁷⁻⁹⁾ The underpinnings of mitochondrial support by PQQ likely involve the activation of a key transcription factor known as CREB (cAMP response element binding protein). CREB induces the expression of the genomic cofactor PGC-1 α (PPAR γ coactivator 1 α). In turn, PGC-1 α orchestrates a coordinated molecular genetic program directing the synthesis of mitochondria.^{(10)*}

Cardiac and neurovascular effects of PQQ

As disruptions in cellular respiration and oxidative stress contribute to ischemia-reperfusion injury, mitochondrial function is an important therapeutic target to support cardiac health.⁽¹¹⁾ Although the mechanisms have not been delineated, several studies suggest that PQQ may reduce cellular stress and promote myocardial and cerebral tissue health in models. In isolated cardiomyocytes, PQQ protects the mitochondrial membrane from oxidative stress and reduces membrane depolarization. In a similar study, supplementation with PQQ significantly reduced lipid peroxidation and supported ventricular function in rats.^{(12)*}

Neuroprotective effects of PQQ

A substantial repertoire of nutritional interventions is available to support the health of the nervous system. While many nutrients are precursors, cofactors or raw materials directed toward neurotransmitter synthesis and membrane function, PQQ is a novel biofactor that modulates unique molecular targets and intracellular signaling events. Among these targets is nerve growth factor (NGF), which plays an important role in maintaining the health of the brain and peripheral nerves. Several studies have shown that PQQ promotes the production of NGF.^(13,14) Although the relevance of NGF in the overall bioactivity of PQQ remains to be established, PQQ has been shown to stimulate regeneration of nerves in vitro.^{(15,16)*}

As a redox cycling agent, PQQ is capable of functionally modulating redox-dependent enzymes and receptors. A noteworthy example is the n-methyl-d-aspartic acid (NMDA) receptor, which binds glutamate,

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an excitatory neurotransmitter. Excessive stimulation of NMDA receptors can be neurotoxic. In vitro evidence indicates that PQQ may protect neurons from excessive glutamate stimulation by oxidizing a critical regulatory site of the NMDA receptor.^{(17)*}

PQQ and cognitive function

Several studies also suggest PQQ may support cognitive function. In one study, rats supplemented with PQQ and subjected to a water maze test demonstrated improvements in learning ability and partial resistance to memory deficit caused by oxidative stress.⁽¹⁸⁾ In a randomized, double-blind study of 71 middle aged individuals, PQQ supplementation over 12 weeks significantly improved short term memory. In the same study, a combination of PQQ and CoQ₁₀ was more effective than either agent alone in preventing memory loss.^{(19)*}

While additional clinical investigations are necessary to study the benefits of PQQ in healthy individuals, existing evidence suggests PQQ is a multifaceted cardioprotectant and neuroprotectant with a broad range of potential therapeutic and more importantly, preventative applications.*

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