Pyrroloquinoline Quinone
A newly discovered vitamin-like compound

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INTRODUCTION

Pyrroloquinoline quinone (PQQ) is a polyphenolic compound found in plant foods that may represent a major advancement in natural medicine. This important cofactor produces a wide range of physiological benefits based upon preclinical studies and limited clinical evaluation.[1] Although PQQ is not currently viewed as a vitamin, future data may result it in being reclassified. This brief review will highlight how the health benefits of PQQ may translate in the clinical setting.

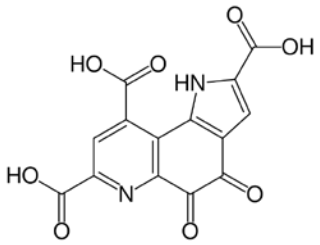

*Figure 1** **Chemical Structure of Pyrroloquinoline Quinone**

WHEN WAS PQQ DISCOVERED?

Though PQQ was first recognized as a bacterial cofactor in 1964, it was not until the mid-1990s that researchers really began exploring its chemical and biological properties. PQQ has been found in all plant foods analyzed to date.[1] PQQ-rich foods include parsley, green peppers, kiwi fruit, papaya and tofu.[2] These foods contain about 2-3 mcg per 100 grams. Green tea provides about the same amount per 120 mL serving.

WHAT ARE SOME OF ITS BASIC FUNCTIONS?

It is interesting to note that PQQ is a component of interstellar dust (or cometary grains) and raises the question of PQQ's evolutionary importance to simpler life forms.[1] In bacteria, PQQ stimulates growth and serves as a cofactor for a special class of dehydrogenases/oxidoreductases. As such, PQQ is a key regulator of cellular function and is involved in signal transduction processes involved in cellular growth, development, differentiation and survival.[1]

It is also as an extremely powerful antioxidant capable of catalyzing continuous redox cycling (the ability to catalyze repeated oxidation and reduction reactions) to a much greater degree compared to other antioxidants. For example, PQQ is able to carry out 20,000 catalytic conversions compared to only 4 for vitamin C.[1,3]

IS PQQ AN ESSENTIAL NUTRIENT?

Based upon the current research there is no question that it plays a critical role in mammalian nutrition.[1,4] When PQQ is omitted from chemically defined diets it leads to growth impairment, compromised immune status, and abnormal reproductive function.[5] The nutritional requirements of PQQ are probably in line with folic acid and biotin in terms of micrograms per day versus milligrams per day. Like essential nutrients, the immune system seems particularly sensitive to low levels of PQQ. With PQQ deprivation there are multiple defects in immune function and loss of B- and T-cell sensitivity.[1]

PQQ AND MITOCHONDRIA

Another key action of PQQ involves a direct action on peroxisome proliferator-activated receptor-gamma coactivator-1 alpha (PGC-1α) and nuclear respiratory factors within mitochondria to improve energy production.[1,6] In addition to PQQ's powerful antioxidant effect protecting against mitochondrial damage, PGC-1α also protects mitochondria against various causes of damage. PQQ not only protects mitochondria from oxidative stress—it promotes the spontaneous generation of new mitochondria within aging cells, a process known as mitochondrial biogenesis or mitochondriogenesis.[1,7,8]

CLINICAL IMPLICATIONS

Given the nutritional importance and tremendous span of physiological effects of PQQ, there are considerable clinical applications particularly those that revolve around low mitochondrial function. Given the growing research documenting mitochondrial dysfunction in aging, many neurological disease (e.g., Alzheimer's disease), and many other chronic degenerative disease there are tremendous possibilities for PQQ. Current research has primarily focused on its neuroprotective action and ability to protect memory and cognition in both aging animals and humans.

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Here are some of the effects noted in the animal studies:

- PQQ reverses cognitive impairment caused by chronic oxidative stress and improves performance on memory tests in animal models.[1,9]
- PQQ supplementation stimulates the production and release of nerve growth factor.[1,10]
- PQQ protects against the self-oxidation of the DJ-1 gene, an early step in the onset of Parkinson's disease.[1,11]
- PQQ protects brain cells against oxidative damage following ischemia-reperfusion injury.[1,12]
- PQQ blocks the formation of inducible nitric oxide synthase (iNOS), a major source of reactive nitrogen species (RNS) that are so damaging to neurons.[1,13]
- PQQ protects against the likelihood of severe stroke in an experimental animal model for stroke and brain hypoxia.[1,14]
- PQQ protects the brain against neurotoxicity induced by other powerful toxins, including mercury, glutamate and oxidopamine (a potent neurotoxin used by scientists to induce Parkinsonism in laboratory animals by destroying dopaminergic and noradrenergic neurons).[1,15,16]
- PQQ prevents development of alpha-synuclein, a protein associated with Parkinson's disease.[1,17]
- PQQ also protects nerve cells from the oxidizing ravages of the beta-amyloid-protein linked with Alzheimer's disease.[1,18]

If PQQ would offer these same sorts of benefits in human studies it would be a serious medical advance. Preliminary clinical studies are extremely encouraging and several larger clinical trials are currently either completed and waiting publication or are in process. In regards to improving cerebral function, while PQQ is somewhat effective on its own, when it is combined with another biological quinone (ubiquinone or coenzyme Q10) even better results may be noted. This synergistic effect was first seen in animal studies and further demonstrated in a human double-blind, placebo-controlled clinical trial conducted in Japan in 2007.[19] In this study of 71 middle-aged and elderly people aged between 40 to 70, supplementation with 20 mg per day of PQQ resulted in improvements on tests of higher cognitive function compared to the placebo group, but in the group receiving 20 mg of PQQ along with 300 mg of CoQ10 the results were even more dramatic. PQQ and CoQ10 are both involved in mitochondrial energy production, so these results are not that surprising.

DOSAGE CONSIDERATIONS

One question that many health care professionals may have regarding PQQ is what is an effective dosage? Specifically, if the nutritional requirement of PQQ is likely less than 500 mcg daily why is the recommended dosage 10 to 20 mg? In order to get a measured response in mitochondrial function in adult animals there is the need to feed higher amounts of PQQ much like why only 8 to 15 mg of vitamin C might protect against the overt signs of scurvy, the recommended dietary allowance currently stands at 75 to 90 milligram per day (for adults, excluding pregnant and lactating women) for optimal function, and even higher amounts are required for clinical applications. The current recommendation of 10 to 20 mg of PQQ daily is based upon the equivalent dose in animals has consistently improved various mitochondrial function. There are also some clinical and observational studies that justify the dosage, especially the 20 mg dosage for enhancing memory.[20]

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