

PQQ Supplementation and SARS-CoV-2 Spike Protein-Induced Heart Inflammation

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Abstract

SARS-CoV-2 spike protein-induced heart inflammation may originate from either COVID-19 infection or the administration of COVID-19 mRNA vaccines. As pyrroloquinoline quinone (PQQ) is a scavenger of free radicals, redox cofactor, and antioxidant which supports cognitive and mitochondrial functions, supplementation with PQQ could have a positive effect to reduce heart inflammation after COVID-19 mRNA vaccines. However, there is no evidence yet for this opportunity in the literature. Cellular and animal model results are missing. Similarly, no clinical trials have been conducted. While it is recommended to measure the levels of the cardiac biomarkers before and after COVID-19 vaccination, no recommendation can be made about supplementation with PQQ, which, however, we note has no contraindication.

Keywords

pyrroloquinoline quinone, pyrroloquinoline quinone supplementation, mRNA vaccines

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To the Editor

The present study aimed to understand if supplementation with pyrroloquinoline quinone (PQQ)¹ may have positive effects to reduce the heart inflammation associated with the administration of COVID-19 mRNA vaccines, which have been claimed to produce COVID-19-like symptoms in some patients, at different degrees of severity. SARS-CoV-2 spike protein-induced inflammations have been shown in many works²⁻¹⁵ with attribution in some cases to the spike protein produced by the vaccines by itself rather than the virus.^{6-9,11-15}

There is no doubt that oxidative and inflammatory conditions may originate from the administration of the COVID-19 vaccines. Generally speaking, potential risks include local and systemic inflammatory responses and toxic effects of synthetic nucleosides and components for vaccine delivery.¹⁶ These risks are generally low but can be more relevant in risk categories such as immune-depressed or immune-compromised patients. Mostly unexplored in the literature is the specific opportunity to develop COVID-19-like symptoms following vaccinations which create the SARS-CoV-2 spike protein, which starts to be covered consistently in the literature.^{6-9,11-15}

mRNA vaccine works by providing the body with genetic information as a form of mRNA to produce viral proteins.¹⁷⁻¹⁹ These viral proteins are the spike proteins found on the surface of SARS-CoV-2. These proteins trigger an immune response producing specific antibodies. The vaccine prepares the body to fight off the infection in the case it will come into contact with the pathogen. COVID-19-like symptoms following vaccinations may be the result of the spike protein. This work aims to understand if PQQ supplementation may reduce some of the

side effects of COVID-19 mRNA vaccines, more specifically heart inflammatory processes.

PQQ is a pyrroloquinoline having oxo groups at the 4- and 5-positions and carboxy groups at positions 2-, 7-, and 9.²⁰ It is the conjugate acid of PQQ (3-) of chemical formula $C_{14}H_6N_2O_8$. PQQ is contained in fruits such as papaya or kiwi fruit, vegetables such as spinach, green pepper, parsley or celery, human breast milk, dark chocolate, and green tea.¹

PQQ is a supplement for the support of cognitive and mitochondrial functions, also working as a free radicals' scavenger. PQQ is a redox cofactor and antioxidant.²¹ It works as a water-soluble vitamin. It is a plant growth factor, a bacterial cofactor, and a pyrroloquinoline cofactor.

PQQ has nutritional importance²² and is physiologically relevant.²³ It was proposed as a new redox cofactor vitamin for mammals.²⁴ However, Felton and Anthony²⁵ argued against PQQ being considered a vitamin. Recently,²⁶ PQQ has been described as a longevity vitamin that is not indispensable for survival, but needed for long-term health. PQQ stimulates the growth of microorganisms.²⁷ There are many examples of growth stimulation of microorganisms by PQQ,⁴¹ such as the microbial production of PQQ of,⁴² or the report of PQQ as an essential growth factor of a poly (vinyl alcohol)-degrading bacteria of.⁴³

PQQ disodium salt helps with cognitive function and may protect from UVA irradiation-induced aging.^{28,29} PQQ supports the health of mitochondria, the membrane-bound cell organelles producing most of the chemical energy needed, stored in adenosine triphosphate (ATP), then used to power the biochemical reactions across cells. PQQ protects the



mitochondria from oxidative damage, and is the only nutrient capable of helping the growth of new mitochondria.³⁰

Elevated levels of oxidative stress are relevant to many conditions, for example, bone fracture healing.³¹ By inhibiting oxidative stress PQQ promoted osteoblastic bone formation, and inhibited osteoclastic bone resorption in a mice model.³¹ Also, in a mice model,³² PQQ protected against exercise-induced fatigue. In chicks, PQQ helped with fatty liver disease.³³ PQQ supplementation helped with reproductive aging in mice,³⁴ and helped with mitochondrial biogenesis in a rotenone-induced Parkinson's disease model.³⁵

Especially, heart and brain are dense with mitochondria. PQQ protects the mitochondria from free radicals and promotes the production of new mitochondria within cells. PQQ may thus support heart health and preserve cognitive function.

Thus, the literature supports the use of PQQ as an anti-inflammatory substance, as an antioxidant, and a detox substance.

Regarding COVID-19 therapeutic agents, an analysis of the efficacy of different early treatments for COVID-19 was presented³⁶ (database built on 783 studies as per August 5, 2021). While these treatments do not replace vaccinations or restrictions, they are the only practical, effective, and safe means that can help to reduce the fatality associated with COVID-19 infection. While no treatment is available and effective for all the current and future variants of COVID-19, some treatments can reduce the risk of COVID-19 becoming endemic and reduce mortality and collateral damage.

The literature reports benefit from many different compounds in different stages of COVID-19 infection following different mechanisms of action. Some substances (such as Ivermectin) work as antivirals and their administration may be coupled to vitamins, minerals, and antibiotics. Other substances (such as Fluvoxamine) work as anti-inflammatory agents. Other substances contribute to alleviating the severity of the infection following other pathways. Some of the other compounds mentioned as adjuvants are vitamins, such as vitamin C and D, or minerals, such as zinc.³⁶ Best opportunities are generally offered for treatments in the early stages of infection, rather than in later, more advanced states. Some compounds with antioxidant properties, such as quercetin, a plant flavonol, and curcumin, the principal curcuminoid of turmeric, have been used against COVID-19 infection.³⁶ No study has been performed so far for the use of PQQ against COVID-19 as either an antiviral or anti-inflammatory agent.

The literature is therefore supportive of the use of PQQ as an anti-inflammatory substance, but there is no support for its use as an anti-inflammatory agent against COVID-19 infection or the inflammatory side effects of COVID-19 vaccines.

As PQQ may help lower inflammation while also improving mitochondrial health, and also work as a detox, PQQ has the potential for an agent mitigating the damage from novel COVID-19 vaccines. The topic of how to fight the side effect of the COVID-19 vaccine is undoubtedly noteworthy.

However, there is not enough information for this specific use of PQQ.

As the COVID-19 vaccines work causing an immune response, by using excessive PQQ or other similar anti-inflammatory products, there is in principle also a risk of diminishing the effectiveness of the vaccine by downregulating the immune response. However, this is an extremely remote possibility.

It has been recently discovered that PQQ can prevent chronic heart failure by regulating mitochondrial function.³⁷ As COVID-19 infection (and to some extent vaccination against COVID-19) has associated cardiovascular complications such as arrhythmias, thrombosis, heart failure, cardiomyopathy, myocardial damage, and acute coronary syndromes,^{38,39} through inflammatory processes linked to the SARS-CoV-2 spike protein, PQQ could likely help against these specific complications of COVID-19 infection, as well as against the side effects of COVID-19 vaccinations.

No contraindication is known for ingesting PQQ from food, despite no recommended dosage information existing for supplementing with PQQ. Excessive doses may certainly have adverse effects, especially on kidneys, but the risks of moderate supplementation are very low. In 2017, the EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA) concluded that PQQ is perfectly safe under the intended conditions of use as food pursuant.⁴⁰ The use of moderate PQQ supplementation appears therefore free of major downfall.

In conclusion, while the measure of the levels of cardiac biomarkers before and after COVID-19 mRNA vaccination is certainly recommended, supplementation with PQQ to avoid side effects of COVID-19 mRNA vaccines is not supported by evidence. Despite there being no proof that PQQ may limit the heart inflammation which may be experienced following COVID-19 mRNA vaccination, as supplementation with PQQ has no contraindication, there is no reason to prevent the uptake of PQQ after COVID-19 mRNA vaccinations. Definitely PQQ is one of the substances to test in cellular and animal models, and during appropriate clinical trials, to discover potential uses against COVID-19 infection and side effects of COVID-19 mRNA vaccines.

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Not applicable, because this article does not contain any clinical trials.

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Not applicable, because this article does not contain any studies with human or animal subjects.

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