IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)
e-ISSN:2278-3008, p-ISSN:2319-7676. Volume 11, Issue 3 Ver. I (May.- Jun.2016), PP 14-19
www.iosrjournals.org

Coenzyme Q10 - A Review of Its Promise

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Abstract: *Coenzyme Q10 (CoQ10) is a powerful antioxidant found in the membranes of many organelles. Experimental studies in animal models suggest that CoQ10 may protect against neuronal damage that is caused by ischemia, atherosclerosis and toxic injury. It buffers the potential adverse consequences of free radicals produced during oxidative phosphorylation in the inner mitochondrial membrane. Oxidative stress, resulting in glutathione loss and oxidative DNA and protein damage, has been involved in many neurodegenerative disorders, including Alzheimer's disease, Parkinson's disease, and Huntington's disease. Though most preliminary clinical trials showing that CoQ10 may offer promise in many brain disorders. Available data suggests that oral CoQ10 seems to be relatively safe and tolerated across the range of 300–2,400 mg/day. This, antioxidant has potential for use in prevention and treatment of cardiovascular disease, particularly hypertension, hyperlipidemia, coronary artery disease, heart failure, diabetes and cancer. This article focuses on the action of Coenzyme Q10 and its uses.*

Keywords: *Coenzyme Q10, antioxidant, statins, cardiovascular diseases, neurodegenerative disorders, diabetes, cancer.*

I. Introduction

Coenzyme Q10, is also known as ubiquinone, ubidecarenone, coenzyme Q as it is a coenzyme that is ubiquitous in the bodies of most animals. It is a 1,4-benzoquinone, where Q refers to the quinone chemical group and 10 refers to the number of isoprenyl chemical subunits. It is a fat-soluble substance, which resembles a vitamin and it is present in most eukaryotic cells, primarily in the mitochondria. CoQ_{10} is a 2,3-dimethoxy, 5-methyl, 6-polyisoprene parabenzoquinone and the enzyme found in humans has a polyisoprene chain containing 10 isoprene units (5 carbons each) or a total of 50 carbons. It is a component of the electron transport chain and participates in aerobic cellular respiration, which generates energy in the form of ATP. Ninety-five percent of the human body's energy is generated this way[1-2] Therefore, those organs which has highest energy requirements like the heart, liver and kidney have the highest Co Q10 concentrations[3-5].

Coenzyme Q10 plays a unique role in the electron transport chain (ETC). It functions as an electron carrier from enzyme complex I and enzyme complex II to complex III which is crucial in the process, since no other molecule can perform this function (Note: recent research now establishes that Vitamin K_2 co-performs this role with CoQ10[6]). Thus, CoQ10 functions in every cell of the body to synthesize energy and it acts as a lipid antioxidant regulating membrane fluidity, recycling radical forms of vitamin C and E, and protecting membrane phospholipids against per oxidation. Because of its antioxidant property, high degree of hydrophobicity and universal occurrence in biological system, suggest an important role for ubiquinone and ubiquinol in cellular defense against oxidative damage. Thus, it plays a crucial role in cellular mechanism.

HISTORY:

CoQ10 was first discovered by Professor Fredrick L. Crane and colleagues at the University of Wisconsin–Madison Enzyme Institute in 1957[7,8] and in1958 its chemical structure was reported by Dr. Karl

Folkers and coworkers at Merck. In 1961 Peter Mitchell proposed the electron transport chain (which includes the vital proton motive role of CoQ_{10}) and he received a Nobel prize for the same in 1978. Gian Paolo Littarru and Karl Folkers separately demonstrated a deficiency of CoQ10 in human heart disease in 1972 and in 1980s a steep rise in the number of clinical trials due to the availability of large quantities of pure CoQ10 and methods to measure plasma and blood CoQ10 concentrations took place. The antioxidant role of the molecule as a free radical scavenger was widely studied by Lars Ernster. Numerous scientists around the globe started studies on this molecule since then in relation to various diseases including cardiovascular diseases and cancer. Coenzyme Q10 was first isolated in 1957 in beef mitochondria, and is found in highest concentrations in tissues with high energy turnover such as the heart, brain, liver, and kidney[9].

II. Role Of Coenzyme Q10

Coenzyme Q10 (COQ10) is a molecule produced in the body. It aids mitochondria during energy production and it is similar to other Pseudo vitamin compounds because its vital for survival, but does not necessarily need to be supplemented. It is a crucial component in the oxidative phosphorylation process in mitochondria as it converts the energy in carbohydrates and fatty acids into ATP to drive cellular machinery and synthesis. New aspects have been developed from the recognition that coenzyme Q can undergo oxidation/reduction reactions in other cell

membranes such as lysosomes, Golgi or plasma membranes during which it transfers protons across the membrane to form a proton gradient. The presence of high concentrations of quinol in all membranes provides a basis for antioxidant action and by participating in transmembrane electron transport coenzyme Q can carry reducing equivalents to the inside of vesicles or to the outside of cells. There is also evidence for role of CoQ10 in proton gradient formation in endomembranes and at the plasma membrane. In addition to this, there is evidence that coenzyme Q can take part in control of membrane structure and phospholipid status [10-11]. CoQ10 is distributed in all membranes throughout the cell [12] and in mitochondria, there are well defined protein binding sites on the enzymes which involves in coenzyme Q oxidation reduction[13]. Enzymes in other membranes can be expected to have specific coenzyme Q binding sites, but these have not been defined. It is thought that the isoprenoid chain present in CoQ10 may help to stabilize the lipid bilayer[9] in phospholipids membrane. The quinone head group can be either in the oxidized (quinone) or reduced (quinol) form. The percent of quinol form in various membranes and serum ranges from 30% to 90%, depending on the metabolic state of the cell [14].

Coenzyme Q can participate in several aspects of oxidation/ reduction control of signal origin and transmission in cells and it acts as a primary scavenger of free radicals. In many membranes the amount of CoQ is from 3 to 30 times the tocopherol content [15]. Since much of the coenzyme Q in cell membranes is in the quinol form[16], and acts as a very effective antioxidant[17].

III. Benefits Of Coenzyme Q10

Coenzyme Q10 is a naturally occurring enzyme and also can be bought as a dietary supplement. Because of its vital role in the human body, it has become a popular dietary supplement as it helps in converting food into energy. In humans CoQ10 deficiency can cause autosomal recessive condition with a clinical spectrum that encompasses at least five major phenotypes: (1) encephalomyopathy characterized by the triad of recurrent myoglobinuria, brain involvement and ragged red fibers; (2) severe infantile multisystemic disease; (3) cerebellar ataxia; (4) Leigh syndrome with growth retardation, ataxia and deafness; and (5) isolated myopathy.
CoQ10 acts a powerful antioxidant and it helps in treating variety of disorders. The role of antioxidants in our body is to fight with damaging particles in the body known as free radicals which damage cell membranes, tamper with DNA, and even cause cell death. Scientists believe that these free radicals contribute to the aging process, as well as a number of health problems, including heart disease and cancer. So, antioxidants like CoQ10, can neutralize free radicals and may reduce or even help prevent some of the damage they cause. Some researchers believe that CoQ10 may help with heart-related conditions, as it can improve energy production in cells, prevent blood clot formation, and act as an antioxidant.
Doctors believe that coenzyme Q10 gives the following health benefits.

- It helps in treating high blood pressure and heart disease.
- It helps in enhancing the immune system function.
- It provides an energy boost for people dealing with fatigue.
- It reduce high cholesterol levels in the blood and it improves exercise ability in people with angina.
- It helps in stabilizing blood sugar levels of people with diabetes.
- It assists in the treatment of cancer or the protection of organs from toxic chemotherapy drugs.
- It helps in treating gum diseases, slowing down dementia progression and increasing sperm count and motility as well as in preventing migraine headaches.

  It is available in both solid & liquid dosage forms. The recommended dose of CoQ10 supplementation for adults is **30 to 200 mg** daily.

IV. Role Of CoQ10 In Heart Diseases

One clinical study found that people who took daily supplements of CoQ10 within 3 days of a heart attack were less likely to have subsequent heart attacks and chest pain. Anyone who had heart attack should talk with their health care provider before taking any drugs or supplements, including CoQ10. There is a another study which says CoQ10 may help to treat heart failure when combined with conventional medications. People who have CHF(congestive heart failure) where the heart is unable to pump blood as well as it should may also have low levels of CoQ10 can cause blood to pool in parts of the body, such as the lungs and legs and also causes shortness of breath. Several clinical studies suggests that CoQ10 supplements helps in reducing swelling in the legs; reduce fluid in the lungs, making breathing easier; and increase exercise capacity in people with heart failure. But not all studies supports this effect as some found no effect. So, CoQ10 for heart failure remains controversial, and you should ask your provider before taking it for this condition. Several clinical studies suggested that Co enzyme Q10 may help in preventing heart damage caused by certain chemotherapy drugs, adriamycin, or other athracycline medications. Some clinical researches showed that introducing CoQ10 prior to heart surgery, including bypass surgery and heart transplantation, can reduce damage caused by free radicals, strengthen heart function, and lower the incidence of irregular heart beat (arrhythmias) during the recovery phase.

V. Role of CoQ10 in High Blood Pressure

Several clinical studies says that CoQ10 may lower blood pressure. However, it may take 4 to 12 weeks to see any change. In one analysis, after reviewing 12 clinical studies, researchers concluded that CoQ10 has the potential to lower systolic blood pressure by up to 17 mm Hg and diastolic blood pressure by 10 mm Hg, without significant side effects. The evidence for CoQ_{10} use in other cardiovascular settings is promising and requires larger, longer-term trials.

VI. Role of CoQ10 in High Cholesterol

People with high cholesterol tend to have lower levels of CoQ10 so this CoQ10 has been proposed as a treatment for high cholesterol, but scientific studies are lacking. However, there are some evidences that states that it may reduce side effects from conventional treatment with cholesterol-lowering drugs called statins, which reduce natural levels of CoQ10 in the body. By taking these supplements we can bring levels back to normal. Plus, some studies showed that CoQ10 may reduce the muscle pain associated with statin treatment. Ask your provider if you are interested in taking CoQ10 with statins.

VII. Role of CoQ10 in Diabetes

Preliminary studies found that CoQ10 improves blood sugar control. It has been considered for improving glycemic control through various mechanisms, including a decrease in oxidative stress. Many studies shows that diabetes mellitus (type 1 and 2) is associated with increased formation of free radicals and decreased antioxidant potential, leading to oxidative damage of cell components[18]. Two earlier randomized controlled trails[19-20] using 100 to 200 mg of coenzyme Q10 in patients with type 1 or 2 diabetes found no difference in glycemic control and insulin requirement. . But a recent randomized controlled trial (n = 74)[21] using 200 mg per day for 12 weeks found modest improvements in A1C levels (-0.37 ± 0.17 percent, $P = .32$).

VIII. Role of CoQ10 in Gum (Periodontal) Disease

Periodontal diseases are one of the most common problem that causes swelling, bleeding, pain, and redness of the gums. Some clinical researches showed that people with gum disease tend to have low levels of CoQ10 in their gums. A few studies found that these supplements led to faster healing and tissue repair, but more research is needed.

IX. Role Of CoQ10 In Statin-Associated Myopathy

Statins (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors) are currently the most effective medications for reducing low-density lipoprotein cholesterol concentrations. Although they are generally safe, but they have been associated with a variety of myopathic complaints. Some studies says that statins show effect on nonlipoprotein CoQ10 levels in the circulation, although at least 1 study[22] reported 12.5% reductions in platelet CoQ10 levels. But the mechanism and significance of this is it is yet unclear, because platelets do not contain mitochondria. The statins block production of farnesyl pyrophosphate, an intermediate in the production of CoQ10. Plus, the role of CoQ10 in mitochondrial energy production and the importance of mitochondria in muscle function has prompted the hypothesis that statin-induced CoQ10 deficiency participates in statin-associated myopathy. Statins have been well known to reduce circulating CoQ10 levels in animal models[23] and humans[24] since at least 1990. Since, that time studies was started and with rare exceptions at least 9 observational studies[25-35] and 6 randomized controlled trials [36-41] have demonstrated that statins reduce

plasma/serum levels of CoQ10 16% to 54% and a largest trial[38] including 1,049 patients had noted reductions in plasma, CoQ10 levels of 38% and 27% after treatment with atorvastatin 10 mg/day to 20 mg/day or lovastatin 20 mg/day to 40 mg/day, respectively.

The decrease in blood CoQ10 levels with statin treatment is probably due to reductions in lower-density lipoproteins. Although, statins are the most effective medications for reducing LDL cholesterol concentrations, but they have been proven to decrease the incidence of adverse cardiac events in diverse patient populations. The primary adverse effect limiting their use is myopathy, ranging from benign myalgias to rare cases of fatal rhabdomyolysis. Statins interference with the production of CoQ10 prompted the hypothesis that CoQ10 deficiency may play a role in statin-associated myopathy. However, statins reduce circulating levels of CoQ10, this effect is nullified by normalizing CoQ10 concentrations for the reduction in LDL cholesterol or total cholesterol. Low-dose statin treatment does not appear to reduce intramuscular levels of CoQ10 in humans. By the statin therapy mitochondrial function may be impaired, and this effect may be exacerbated by exercise, but confirmatory data are needed. Animal models of statin myopathy demonstrate similar results in that decreases in skeletal muscle ubiquinone levels and mitochondrial function are not consistent and skeletal muscle injury can occur without decreases in muscle CoQ10 concentrations. Supplementation can raise the circulating levels of CoQ10, but whether or not this relieves myopathic symptoms is not clear.

X. Role Of CoQ10 As Neuroprotectant

Co Q10 is a powerful antioxidant that buffers the potential adverse consequences of free radicals produced during oxidative phosphorylation in the inner mitochondrial membrane. Many neurodegenerative disorders including Alzheimer's disease, Parkinson's disease, and Huntington's disease, has been implicated with glutathione loss and oxidative DNA and protein damage, because of oxidative stress. In animal models the experimental studies suggest that CoQ10 may protect against neuronal damage that is produced by ischemia, atherosclerosis and toxic injury. Though most have tended to be pilot studies, there are published preliminary clinical trials showing that CoQ10 may offer promise in many brain disorders. For example, a 16-month randomized, placebo-controlled pilot trial in 80 subjects with mild Parkinson's disease found significant benefits for oral CoQ10 1,200 mg/day to slow functional deterioration. However there are no published clinical trials of CoQ10 in Alzheimer's disease. Available data suggests that oral CoQ10 seems to be relatively safe and tolerated across the range of 300–2,400 mg/day. Randomized controlled trials are warranted to confirm CoQ10's safety and promise as a clinically effective neuroprotectant.

Parkinson's Disease

A randomized, double-blind, placebo-controlled, multicenter study[42] of 80 patients found that 1,200 mg per day of coenzyme Q10 was associated with up to 44 percent less functional decline in patients with Parkinson's disease, including activities of daily living. Another study of 28 patients with Parkinson's disease also demonstrated mild symptom improvement with daily oral dosing of 360 mg of coenzyme Q10. These results are awaiting confirmation.

XI. Efficacy Of Coenzyme Q10 In Cancer Treatments

A study shows that Coenzyme Q10 is effective in cancer treatment, six studies were included in the review, including three randomized clinical trials and three nonrandomized clinical trials. Patients in five of six studies received anthracyclines and observed. The results suggested that CoQ10 provides some protection against cardio toxicity or liver toxicity during cancer treatment. However, because of inadequate reporting and analysis, as well as questionable validity of outcome measures, the results are not conclusive further investigations are needed to determine the efficacy of Coenzyme Q10.

AVAILABLE FORMS

Levels of CoQ10 naturally decline with age in our body and is often naturally lower for those living with cancer, diabetes, heart conditions, HIV/AIDS, muscular dystrophies, and Parkinson's disease. We can replenish these levels by taking supplemental CoQ10. It is available as a supplement in several forms, including soft gel capsules, oral spray, hard shell capsules, tablets and in liquid form. CoQ10 is also added to various cosmetics.

DIETARY SOURCE:

Primary dietary sources includes oily fish (such as salmon and tuna), organ meats (such as liver), and whole grains. Most people get enough CoQ10 through a balanced diet, but supplements may help people with particular health conditions.

CoQ10 Dose:

Daily dose recommended for best results are as follows:

- General Health: 30-100 mg
- Family History of Heart Problems: 60-160 mg
- Heavy Exercisers: 90-160 mg
- Mild Heart Problems: 100-120 mg
- If Taking Statin Drugs: 200-300 mg
- Congestive Heart Problems: 300-360 mg
- Those with Parkinson's Disease: 1,200 mg
-

XII. Interactions With Other Drugs

CoQ10 may increase the risk of bleeding, care should be taken while taking blood thinners. Some examples include aspirin, anti-platelet drugs such as clopidogrel (Plavix®), anticoagulants ("blood thinners") such as warfarin (Coumadin®) or heparin, and non-steroidal anti-inflammatory drugs such as ibuprofen (Motrin®, Advil®) or naproxen (Naprosyn®, Aleve®). CoQ10 may also reduce the effectiveness of warfarin, which will increase risk of blood clot. It may also affect blood sugar levels. So, caution should be taken while using medications that may also affect blood sugar. People taking medicines for diabetes by mouth or insulin should be monitored closely by a qualified healthcare professional, including a pharmacist. Medication adjustments may be necessary whenever needed. Patients who take antihypertensive drugs should also have to care when using CoQ10 as it lowers the blood pressure.CoQ10 may also interact with acetylsalicylic acid, agents that may affect the immune system, agents that may enhance exercise performance, agents that may promote urination, agents that may affect the nervous system, agents that may treat asthma, agents that may treat mental illnesses, Alzheimer's agents, agents that may treat HIV, amiodarone, amitriptyline, anabolic androgenic steroids, angiotensin-converting enzyme inhibitors, anticancer agents, antidepressants, antifungal agents, anti-inflammatories, beta-blockers, cholesterol-lowering agents, clonidine, corticosteroids, cyclosporin A, dopamine agonists/antagonists, doxorubicin, eye agents, ezetimibe, fenofibrate, fertility agents, heart agents, hormonal agents, hydralazine, immunoglobulins, iridium, lung agents, mercury, methyldopa, nicotine, nitroglycerin, orlistat, P-glycoprotein-regulated agents, skin agents, statins, steroids, thyroid hormones, timolol, and weight loss agents, heart rate-regulating agents. It may also interacts with some of the herbs and dietary agents.

XIII. Conclusion

Coenzyme Q10 is a endogenous lipid-soluble antioxidant found in all organisms. Many disorders and diseases like Neurodegenerative disorders, cancer, cardiovascular diseases and diabetes mellitus and especially aging and Alzheimer's disease exhibit altered levels of ubiquinone or ubiquinol, indicating their likely crucial role in the pathogenesis and cellular mechanisms of these ailments. This review is geared to discuss the importance of coenzyme Q10 and its biological effect with an emphasis on its impact in initiation, progression, treatment and prevention of neurodegenerative, cardiovascular carcinogenic and many other diseases. Most of the people get enough CoQ10 through a balanced diet, but supplements may help the people with to maintain the correct level. COQ_{10} can also enhance blood flow and protect the blood vessels. It can reduce the damage oxidized Low-density Lipoprotein (LDL) in the blood vessels, as well as reduce plaque buildup in the arteries. Deficiency of coenzyme Q10 occurs based on failure of biosynthesis caused by gene mutation, inhibition of biosynthesis by HMG coA reductase inhibitors (statins) or for unknown reasons in ageing and cancer. Presently, insufficient informattion and evidence exists to implicate CoQ10 deficiency as the cause statin-associated myopathy. But some randomized controlled trials are warranted to confirm CoQ10's safety and promise as a clinically effective antioxidant and a neuroprotectant.

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