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Co-enzyme Q10 (Ubiquinone): It's Implication in Improving the Life Style of the Elderly

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Abstract

Coenzyme Q10 (CoQ10) (1) is lipid-soluble and an important mitochondrial redox component, endogenously produced antioxidant in the human organisms. CoQ10 (1) plays an important role in the production of cellular energy, strengthens the immune system and acts as a free radical scavenger. Aging, poor eating habits, infections and stress affect the amounts of CoQ10 (1) in the humans. As human beings age, they begin to lose the ability to synthesize CoQ10 (1) from food resulting in its deficiency. CoQ10 (1) facilitates the production of adenosine triphosphate (ATP) in the mitochondria by participating in redox reactions within the electron transport chain. Cardiovascular disease deaths in elders are 80% in males and 75% in females. The average age of death from cardiovascular diseases in the developing world is 68 years and in developed world it is 80 years. Cardiovascular disease onset is 7-10 years earlier in men as compared to women. A low level of myocardial CoQ10 (1) is related to the severity of heart failure. Long-term CoQ10 (1) treatment of patients with chronic heart failure is safe and reduces major adverse cardiovascular complications.

Keywords: Coenzyme Q10; Prostacyclin; Adenosine triphosphate; Deoxyribonucleic acid; Glycosylated haemoglobin; Reaction oxygen species; Alzheimer's disease; Atherosclerosis; Cardiovascular disease; Cancer; Huntington's disease; Hypertension; Oxidative stress; Parkinson's disease; Periodontal infection; Nutraceuticals; Reindeer heart; Beef heart; Chicken liver; Olive oil; Peanuts; Avocado

Abbreviations:

AD: Alzheimer's Disease; ATP: Adenosine Triphosphate; CoQ; Coenzyme Q; CoQ10: Coenzyme Q10; DNA: Deoxyribonucleic Acid; HbA1C: Glycosylated Haemoglobin; HD: Huntington's Disease; PD: Parkinson's Disease; ROS: Reaction Oxygen Species.

Introduction

A coenzyme is a simple molecule that is essential for the normal function of specific enzyme systems in our cells. Coenzyme Q (CoQ) is a naturally occurring vitamin like molecule formed from the conjugation of benzoquinone ring with a substituted prenyl side chain of varying chain length among different species including bacteria, plants and animals. Coenzyme Q10 (CoQ10) (1) (**Figure 1**) [1] is lipid soluble and a cofactor for three large enzyme systems which are essential for human cellular energy production. CoQ10 is a component of electron transport chain and participates in aerobic respiration for generating energy in the form of adenosine triphosphate (ATP). In humans, CoQ10 (1) is essential for cellular production of ATP, the basic source of energy for the cellular metabolism. Ninety-five present of the human body's energy requirement is met by generating ATP through aerobic glycolysis. Therefore, the organs with utmost energy needs like heart, kidney and liver have the highest concentrations of CoQ10 (1) [2-5]. Nevertheless, CoQ10 (1) is necessary as an antioxidant to neutralize harmful free radicles and protects the endothelium, the inner lining of the blood and lymph vessels. CoQ10 (1) is a potent free radical scavenger in lipid and mitochondrial membranes. It is mostly present in the phospholipid bilayer of the inner membrane of the mitochondria. Besides, it is present in all the biological membranes and plasma lipoproteins. Its omnipresent nature gave the name ubiquinone. CoQ10 (1) supplementation reduced cardiovascular, fibromyalgia, diabetes mellitus, cancer, male infertility, periodontal, mitochondrial and neurodegenerative diseases [6]. Ubiquinol (2) (**Figure 1**), an electron-rich (reduced) form of CoQ10 (1) with an increased polarity showed improvement in its absorption and bioavailability [7].

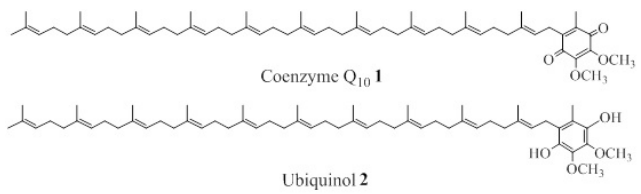

Figure 1: CoQ10 (1) and ubiquinol (2).

CoQ10 (1) levels diminish with advancing age and contribute to some of the symptoms associated with aging. The mitochondria have a close relationship with the aging process. The decrease of CoQ10 (1) levels during aging could be one of the main reasons to develop chronic diseases in the aged. CoQ10 (1) is involved in multiple cellular processes including proper uptake of CoQ10 (1) into cells which is crucial for the improvement of cell activity during aging [6]. The dietary supplementation of CoQ10 (1) can be a key strategy to improve the health in the elderly.

CoQ10 (1) levels are particularly high in organ meats such as kidney, liver, heart, beef, soy oil, sardines, mackerel and peanuts. Nevertheless, meat and fish are the richest sources of dietary CoQ10 (1) [8]. The CoQ10 (1) levels present in some of the foods are shown in **Table 1**.

Table 1: CoQ10 (1) contents in various foods.

Meats & Fishes		Fruits & Vegetables		Oils & Nuts	
Reindeer	157.9	Avocado	9.5	Olive Oil (E.V.)	114-160
Beef Heart	113.3	Rape (Flowers)	6.7-7.4	Peanut Oil	77
Pork Heart	118.1-282	Broccoli	5.9-8.6	Rapeseed Oil	63.5-73.4
Chicken Liver	116.2-132.2	Sweet Potato	3.0-3.6	Peanuts (Roasted)	26.7
Herring Heart	120.0-148.4	Sorrel	3.6	Pistachio Nuts (Roasted)	20.1
Mackerel Heart	105.5-109.8	Sweet Pepper	3.3	Walnuts (Raw)	19.0

Disease Treatments by CoQ10 and Relates

CoQ10 deficiency diseases

After the age of 35 years, the organisms begin to lose the capacity to synthesize CoQ10 (1) which results in its deficiency. In such circumstances, CoQ10 (1) supplementation alone or in combination with other nutritional supplements may help maintain health and treat some of the health problems. Therefore, CoQ10 (1) finds its usage in food, cosmetic and pharmaceutical industries. The accumulation of indiscriminate damage to genetic material and other critical cellular structures results in many neoplastic alterations. For this and other reasons, cardiovascular and other pathological states such as cancer and neurodegenerative diseases are considered as “diseases of aging”. Several compartments of immune system are affected by the cellular breakdown throughout the aging process. The CoQ10 (1) supplementation improved deoxyribonucleic acid (DNA) repair enzymes and reduced the age related complications and mortality [9].

Cardiovascular diseases

Oxidative stress plays an important role in pathogenesis of cardiovascular diseases including heart failure and hypertension in the elderly. The heart muscle uses more energy than any other tissue, normally has the highest concentration of CoQ10 (1) and is very sensitive to CoQ10 (1) deficiency. The weakening of heart muscle causes swelling in the liver, lungs, the lining of intestine, the lower legs and feet. Heart failure is characterized by a loss of contractile function due to energy depletion in mitochondria associated with low CoQ10 (1) levels. Many studies have searched the benefit of CoQ10 (1) supplementation for improving cardiovascular function through increased energy production, contractility of cardiac muscles, antioxidant activity and prevention of low-density lipoproteins oxidation. Two important studies reported significant benefits of CoQ10 (1) on heart failure of various causes [10,11]. Dilated cardiomyopathy is a form of cardiac muscle disease characterized by ventricular dilation, contractile dysfunction and eventual congestive heart failure. The CoQ10 (1) oral supplementation ameliorated cardiac contractility and endothelial dysfunction [12]. CoQ10 (1) is found to be highly concentrated in the heart muscle cells because of the high energy requirements of this cell type. The congestive heart failure has been strongly linked to low blood and tissue levels of CoQ10 (1). The treatment with CoQ10 significantly improved the heart muscle function while producing no adverse effects or drug interactions [13-15].

Hypertension

Various antihypertensive drugs display adverse side effects such as depression, renal as well as cardiac dysfunction and cough [16]. CoQ10 (1) supplementation reduced the need to take multiple antihypertensive drugs [11]. Nitric oxide relaxed peripheral arteries thereby lowering blood pressure. In some types of hypertension, superoxide radicles which inactivate nitric oxide are over produced. CoQ10 (1) with its antioxidant property prevented the inactivation of nitric oxide by these free radicles. Simultaneously, CoQ10 (1) either boosted the production of prostacyclin (3) (**Figure 2**), a potent vasodilator and inhibitor of platelet aggregation or increased the sensitivity of arterial smooth muscles to prostacyclin (3) [17].

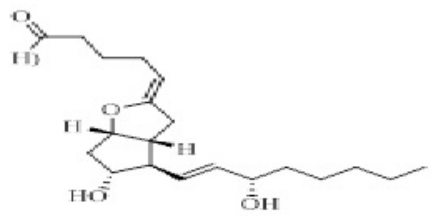

Figure 2: Prostacyclin (3).

Periodontal infection

Periodontal infection is an inflammatory illness resulting from the interaction of a bacterial attack and host inflammatory response. Periodontal pathogens induced reaction oxygen species (ROS) production and caused collagen as well as periodontal cell breakdown. The scavenging activity of antioxidants against ROS resulted in the reduction of collagen degradation. Ubiquinol10 (2), a reduced form of CoQ10 (1), acted as an endogenous antioxidant which increased the concentration of CoQ10 (1) in the disease gingiva and efficiently suppressed periodontal inflammation [18].

Atherosclerosis

Atherosclerosis is a specific form of arteriosclerosis where an artery wall thickens as a result of invasion and accumulation of white blood cells and proliferation of intimal-smooth- muscle cells creating fibro-fatty plaque. The wall stiffening increased pulse pressure causing dysfunction in the major arteries [19,20]. Oxidation of low density lipids (LDL) is linked to atherogenesis and selective antioxidants curb atherosclerosis. Ubiquinol10 (2) inhibited LDL peroxidation *in vitro*. CoQ10 (1) displayed a direct anti-atherogenic effect in apolipoprotein E deficient mice fed with a high fat diet [21]. CoQ10 (1) supplementation increased the concentrations of ubiquinol10 (2) in plasma and in all of its lipoproteins. A single dose of 100-200 mg of CoQ10 (1) raised the total plasma coenzyme by 80-150%. Long term supplementation resulted in four fold increase of ubiquinol10 (2) in plasma and LDL. However, the rate of lipid oxidation increased noticeably with the disappearance of 80 to 90% of ubiquinol10 (2). Therefore, oral supplementation with CoQ10 (1) increased ubiquinol10 (2) in the plasma and lipoproteins thereby improving the resistance of LDL to radical oxidation [22]. CoQ10 (1) supplementation reduced the oxidative stress and inflammatory marker IL-6 while increasing antioxidant enzyme activity in atherosclerosis patients [23,24].

Diabetes

Diabetes is a chronic metabolic disorder responsible for major health problems worldwide. It is characterized by absolute or relative deficiencies in insulin secretion or action. Diabetes is associated with chronic hyperglycemia and disturbances of carbohydrate, lipid and protein metabolisms. The oxidative stress was a major cause in the pathogenesis of this complex metabolic disorder which encouraged the use of antioxidants as a complementary therapeutic approach [25]. Serum CoQ10 (1) levels in diabetic patients often decreased and associated with subclinical diabetic cardio-myopathy which was reversed by CoQ10 (1) supplementation [26]. CoQ10 (1) therapy raised plasma CoQ10 (1) levels, improved endothelial function in the brachial artery, and markedly decreased both systolic/diastolic blood pressures as well as glycosylated hemoglobin (HbA1C). CoQ10 (1) intake in combination with fenofibrate markedly improved both endothelial and non-endothelial vasodilation. CoQ10 (1) improved nerve conduction parameters of diabetic polyneuropathy and reduced oxidative stress without any adverse effects [27]. CoQ10 (1) improved beta cell function and increased insulin sensitivity which reduced insulin requirements for diabetic patients [28].

Hypercholestemia

Hypercholesterolemia is an important component affecting a significant part of the aging population [7]. Statins treatment reduced CoQ10 (1) biosynthesis in hypercholesterolemia patients. The depletion of CoQ10 (1) accounted for statin-induced myopathies and rhabdomyolysis [29]. Furthermore, statins showed side effect of energy depletion with exceptional fatigue. However, CoQ10 (1) treatment prevented the myopathic side effects of statin drugs [30].

Neurodegenerative diseases

Parkinson's disease is a long-term degenerative disorder of the central nervous system that mainly affects the motor system. The symptoms in generally develops over time. The most obvious early symptoms are shaking, slowness of movement, rigidity and default with walking. Sometimes they are associated with thinking and behavioral problems. In the advanced stage of the disease dementia, depression and anxiety becomes very common. CoQ10 (1) levels were remarkably low in the blood, platelet-mitochondria and plasma of Parkinson's disease (PD) patients [31,32]. Recently, CoQ10 (1) therapy reduced the cellular pathophysiological alterations associated with mitochondrial dysfunction in PD patients [33]. In addition, CoQ10 (1) played a major role in the cellular dysfunction in PD patients [31].

Huntington's disease (HD) is a neurodegenerative genetic disorder caused by an expansion of CAG repeats in the HD gene encoding for Huntington. This results in progressive death of striatal neurons with symptoms of chorea, dementia and dramatic weight loss as a result of metabolic and mitochondrial dysfunction [34]. CoQ10 (1) treatment reduced markers of oxidative stress responsible for HD in the patients [35].

Alzheimer's, a degenerative disease, is the most common form of dementia, a general term for memory loss and intellectual abilities serious enough to interfere with daily life. Amyloid β peptides were the main components of the amyloid plaques, a crucial cause of Alzheimer's disease. The amyloid plaques were responsible for the degeneration of nerve cells

resulting in Alzheimer's. Alzheimer's disease (AD) was associated with oxidative damage caused by mitochondrial dysfunction [36]. CoQ10 (1) was neuroprotective with the protection of oxidative damage and attenuation of mitochondrial dysfunction [37].

Carcinogenesis

There were no differences in serum CoQ10 (1) levels between hyperlipidemic and normolipidemic elderly women [7]. However, decreased levels of CoQ10 (1) were found in plasma of women's cancerous breast tissue correlated with a worse prognosis [38]. CoQ10 (1) treatment resulted in tumor regression and disappearance of diagnosed metastases and approximately 1-3 years later metastases did not reappear [39,40]. In melanoma patients with and without metastasis, plasma CoQ10 (1) levels were significantly low associated with primary tumor thickness. Cancerous cells mainly depended on anaerobic glycolysis (Warburg effect) for the ATP production. The mitochondrial dysfunction could be attributed to low concentrations of CoQ10 (1) in cancerous tissues [40,41]. The patients of cervical intra-epithelial neoplasia and cervical cancer displayed low plasma levels of CoQ10 (1) [42]. Supplementation of CoQ10 (1) prevented cardiac damage, liver toxicity, diarrhoea and stomatitis without decreasing the therapy effectiveness during chemotherapy with doxorubicin (4) (**Figure 3**) [43,44]. Chemotherapeutic drugs such as doxorubicin (4), camptothecin (5), etoposide (6), and methotrexate (7) (**Figure 3**) induced an increase in CoQ10 (1) levels in cancer lines by up regulation of CoQ7, CoQ4 and CoQ8 gene expression to protect from free radical damage [45]. Hence, foods and beverages containing CoQ10 (1) had been proposed for preventing cancer and mitigating the adverse reactions of cancer [46].

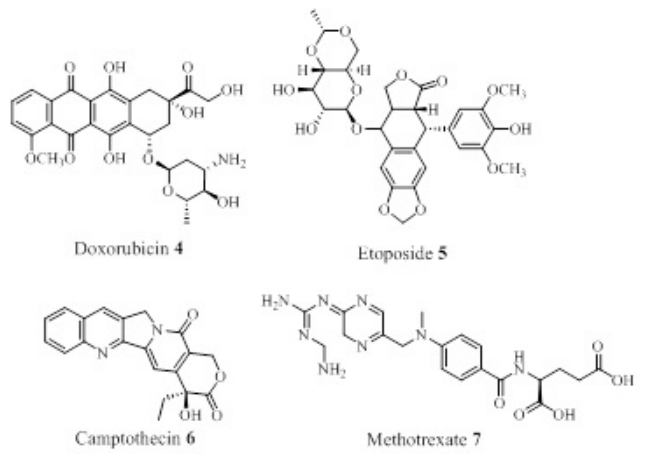

Figure 3: Doxorubicin (4), camptothecin (5), etoposide (6), and methotrexate (7).

Generally, no toxicity was observed with high doses of CoQ10 (1). A daily dosage of 36 g was tolerated by both healthy as well as unhealthy subjects. Long-term trails of CoQ10 supplementation in doses up to 600mg per day with eight years follow-up reported no toxic effects in patients with cardiovascular disease. However, some adverse effects of CoQ10 (1), largely gastrointestinal were observed with very high intake [47-49].

Conclusion

Coenzyme Q10 (CoQ10) (1) is a nutritional supplement available over the counter easily. CoQ10 (1) is an important antioxidant used by the body to delay the progression of diseases. CoQ10 (1) improves endothelial dysfunction and increases the cardiac ATP production. CoQ10 (1) ability to improve the energy production and antioxidant defence in every cell of the body has brought about many remarkable and unexpected improvements in all aspects of human health. Intestinal absorption of dietary CoQ10 (1) is very limited. However, ubiquinol10 (2), a reduced form of CoQ10 (1) has a better intestinal absorption for bioavailability. The injection of relatively large doses of CoQ10 (1) increased CoQ10 (1) concentrations in heart and brain mitochondria in rodent models [50]. Therefore, less hydrophobic derivatives and formulations of CoQ10 (1) with better pharmacokinetics are emerging as promising drugs for mitochondrial dysfunction. Idebenone and MitoQ were evaluated for safety, efficacy and toxicity [46].

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