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CoQ10: A miraculous and clinically vital coenzyme for normal body functions, prevention and treatment of diseases

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Abstract

Present review is designed to highlight and compile the sources, chemistry, physiology, clinical uses and pharmacological activities of the coenzyme Q10 (CoQ10), which is a very important fat soluble vitamin like substance produced by all biological systems. CoQ10 is also present in vegetables, all meats and dairy products. It is necessarily required for proper functioning of body's organs and each cells. It is a member of the mitochondrial respiratory chain regulating the functions of the cellular metabolism. It is like a rechargeable battery in the transfer of energy in the form of adenosine triphosphate. The concentration of CoQ10 is indirectly proportional to the age and the diseased conditions like cardiac disease, Parkinson's, cancer, diabetes, muscular dystrophies, HIV/AIDs. Thus, it can be concluded that CoQ10 is really a miraculous and clinically vital coenzyme required for normal body functions, prevention and treatment of such diseases and several others.

Keywords: Coenzyme, CoQ10, Ubiquinone, Antioxidant, Disease, Cardioprotective.

1. INTRODUCTION

The coenzyme Q10 (CoQ10) known as ubiquinone also is a lipid soluble benzoquinone molecule. [1, 2] It plays an important role in mitochondrial respiratory chain system for the production of cellular adenosine triphosphate (ATP). It is an intracellular antioxidant enzyme and synthesized endogenously in human body. It preserves mitochondrial proteins, membrane phospholipids and small low density lipoprotein cholesterol protected from free radical-induced oxidative cell destruction. [3] Oxidative stress is directly related to inflammation, and which can be easily induced by other factors. [4] Therefore, antioxidants have protective effects in various diseases due to oxidative stress and inflammation in the body. [5, 6, 7] CoQ10 is active in mammalian organs, such as heart, liver, and kidneys. It also present in the membrane of exactly all mammalian cell types and can reversibly allow or lose 2 electrons to form hydroquinone or benzoquinone, correspondingly, which makes it a essential component in the mitochondrial electron transport chain and essential constituent of membrane oxidoreductase System It has been reported that anti lipogenesis. [8] Antidiabetes [9] antiatherosclerosis [10, 11] And large gene dictatorial properties. studies in animals and cells. [12] The Previous clinical trials have shown that adding CoQ10 to existing antihypertensive treatments added lowered systolic blood pressure (SBP) and diastolic blood pressure (DBP) compared to conduct with habitual antihypertensive agents only. [13] The clinical settlement of CoQ10 supplementation in impediment and cure of heart failure have been observed. [14 , 15] CoQ10 may be suggested to patients at risk of or diagnosed with cardiovascular disease as an accumulation to traditional treatment. [16, 17, 18] And elongated-term therapy with CoQ10 has been revealed to improve heart failure symptoms and diminish key adverse cardiovascular trial as being secure and well-tolerated. [19, 20] At this time, Europe, Russia, the USA, [21] and Japan compose up 85% of the total consumption of CoQ10 supplementation. In Japan, CoQ10 was permitted as treatment for heart failure in 1974. [22, 23] In 1982, it became one of the top five medications used in Japan [24] CoQ10 may comprise a helpful effect in patients with heart failure by three different actions: first, it increases adenosine triphosphate (ATP) generation and cellular energy by mediating electron transfer in the electron transport chain; second, by tumbling oxidative stress, as well recognized marker of humanity in heart failure, and by preventing membrane oxidation and lipid per oxidation; third, by stabilizing calcium dependent ion channels in the myocardium, accordingly enhancing ATP synthesis. [25, 26]

2. REVIEW OF LITERATURE

2.1. DISCOVERY AND HISTORY OF CoQ10

Coenzyme Q10 was primary revealed from beef mitochondria by Prof. Fredrick L.Crane and contemporaries at the University of Wisconsin Madison Enzyme Institute in 1957. [27] In 1958, its element arrangement was reported by Dr. Karl Folkers. In 1961, Peter Mitchel anticipated the electron transport sequence of which Coenzyme Q10 is a module (being a crucial proton intention gathering of CoQ10) he was awarded the Nobel prize in 1978. From the 1980s onward, several scientists something like the humanity ongoing studies on this molecule in relative to different diseases including cardiovascular diseases (due to exhibition of deficiency of CoQ10 in human being heart diseases) and cancer. The antioxidant function of CoQ10 as a free radical scavenger was also extensively studied. [28]

Common Names: Co-Enzyme Q10, Coenzyme Q10, Co-enzyme Q-10, Co Enzyme Q 10, CoQ, CoQ10, Co Q 10, Co-Q-10, CoQ-10, CO Q10, Q10, Vitamin Q10. [29, 30]

Scientific Names: Ubiquinone, Ubidecarenone, Mitoquinone.

2.2. CHEMISTRY OF CoQ10

CoQ10 was firstly isolated in the form of beef mitochondria and highly strong in heart muscle cells due to the high energy requirements of cell type. [31] It is also called ubiquinone as it is ubiquitous or present in all eukaryotic cells. Chemically CoQ10 is 2, 3 dimethoxy 5 methy l,6 decaprenyl benzoquinone (**Figure 1**). The functional group in CoQ10 is the quinone ring. By reduction of the quinone to quinol a carrier of protons and electrons is produced. [32] Coenzyme Q10 is the active ingredient. The term "Coenzyme" denotes it is an organic, non protein molecule. The "Q" refers to the quinine chemical group and the "10" refers to the 10 isoprenyl chemical subunits. [33]

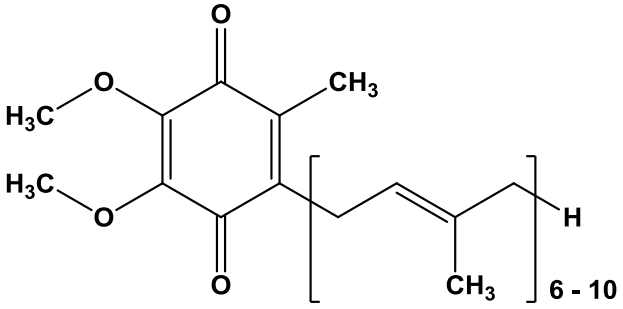

Figure 1. Chemical structure of CoQ10

Coenzyme Q10 is a lipophilic molecule present in cell membranes, but especially abundant in mitochondria. [34] It is comprised of a quinone group and of a polyisoprenoid tail of variable length in different species yeast have six units (CoQ6), mice nine (CoQ9) and humans ten (CoQ10). The ability of this peculiar molecule to sustain continuous oxidation reduction cycles makes it an excellent membrane antioxidant. [35] And an electron carrier in many crucial cellular pathways. [36] In the respiratory chain it transfers electrons from NADH coenzyme Q reductase (complex I) and succinate coenzyme Q reductase (complex II) to coenzyme Q cytochrome c reductase (complex III). The biochemical pathway responsible for CoQ10 biosynthesis is still incompletely characterized. *S.* cerevisiae is able to use either para aminobenzoic acid (PABA) or 4, hydroxybenzoate (4HB) as a precursor of CoQ10. [37, 38] while in mammals the precursor of the quinone ring is which is derived from tyrosine through an uncharacterized set of reactions. The isoprenoid extremity is synthesized through the mevalonate pathway, which also to cholesterol biosynthesis. [39, 40]

2.3. SOURCES OF CoQ10

In the list of supreme premier 50, which would mainly consist of the livers, hearts, and brains of different animals, we have compile the top 10 for both meat and vegetables, and the top 5 for both other category. We consider this is supplementary constructive, given that there are many category of food which people may exclusively steer clear of in a generalized diet; vegans, vegetarians, dairy free, nut free, no red meat, gluten free, and so forth.

Meats: With the exemption of the shoulder, sirloin steak, and thigh of a cow, as you see the others on the list are infrequently devoted (Table 1). While not make the top 10, to give you some perspective of more common meats the following. All contained less than 2mg chicken breasts, chicken wings, pork sirloin, and unspecified beef.

Table 1. Meats Sources

S. No.	Type	% of CoQ10
1.	Reindeer meat unspecified parts	0.015%
2.	Pork heart	0.0118%
3.	Chicken liver	0.0116%
4.	Beef heart	0.0113%
5.	Chicken heart	0.0092%
6.	Pork shoulder	0.0045%
7.	Beef shoulder	0.004%
8.	Beef liver	0.0039%
9.	Beef sirloin	0.0031%
10.	Beef thigh	0.0030%

Vegetables: There are various vegetables sources which have the greatest CoQ10 which is useful for our health problems. Some vegetables have maximum CoQ10 listed below (table 2). There are dozens of vegetables which are devoted daily in the American diet that have been tested and the results are unacceptable. For example, lettuce, pumpkin, okra, and mushrooms don't have a sufficient amount CoQ10 to be demonstrable. Fresh spinach leaves, potatoes, onions, tomatoes, cabbage, and Brussels sprouts all have less than 0.1 mg per 100 grams. Garlic, peas, cauliflower, asparagus, carrots, and mustard spinach do contain it, but the amount isn't enough to crack the top 10.

Table 2. Vegetables sources

S. No	Type	% of Co Q_{10}
1	Soybeans	0.00187%
2	Boiled Soybeans	0.00121%
3	Parsley	0.0075%
4	Dry Soybeans	0.0068%
5	Broomrape (flower cluster)	0.0067%
6	Broccoli	0.0059%
7	Natto (fermented soybeans)	0.0056%
8	Sorrel herb (spinach dock, narrow-leaved dock)	0.0036%
9	Japanese radish leaves	0.0033%
10	Sweet potato	0.0033%

Eggs and dairy product: One would estimate that at smallest amount eggs would have CoQ10 in well-brought-up amounts, but whole eggs don't even be eligible for the top 5. The yolk does, but that has a lower amount than the top 7 vegetables. The richest source of CoQ10 is the butter. (Table 3).

Table 3. Eggs & dairy products

S. No.	Type	% of CoQ10
1.	Butter	0.0071%
2.	Egg yolk	0.0052%
3.	Unpasteurized fresh whole milk (3.6% fat)	0.0019%
4.	Pasteurized whole milk (3.5% fat)	0.0017%
5.	Swiss cheese	0.013%

Fruits and Berries: Others tested which did compose the top spots are oranges (as well as orange juice), lingo berries, clemencies, bananas, persimmon, and kiwi, with the exemption of definitely avocado, fruit is a poor natural source for CoQ10 (Table 4).

Table 4. Fruits and Berries

S. No	Type	% of CoQ10
1.	Avocado	0.0095%
2.	Black currants	0.0034%
3.	Strawberries	0.0014%
4.	Grape fruit	0.0013%
5.	Apples	0.0011%

Fish and seafood: No disclosure at this time in that the hearts of the fish have the highest concentrations. As much as the flesh that people scoff, the amounts are much lower and as good as to other representative forms of meat. Present are many other fish and types of seafood which have been tested, but they hold still lower amounts higher than those include salmon, Pollack, rainbow trout, common mussel, cuttlefish, scallops, pike, octopus, oysters, squid, cod, shrimp, sea bass, and a few others (Table 5).

Table 5. Fish and sea foods

S.NO.	Type	% CoQ10
1	Herring, heart	0.12%
2	Mackerel, heart	0.0105%
3	Mackerel, red flesh	00068%
4	Herring, flesh	0.0015%

Table 6. Cooking oils

S.NO.	Type	% CoQ10
1.	Extra virgin olive oil	0.0114%
2.	Peanut oil	0.0077%
3.	Grapeseed oil	0.0064%
4.	Soybean oil	0.0054%
5.	Sesame oil	0.0032%

Cooking oils: With other foods, when there was more than one source which had measured the CoQ10 content, The top 5 cooking oil (Table 6). Have measurable amount of coq_{10}. While not making the top 5 but still being a source of CoQ10 are sunflower, cottonseed, and safflower oil. Rice bran and coconut oils had none detectable.

Seeds and Nuts: We're not surprised to see peanuts, as they are one of the most underrated nuts for nutritional value. In addition to this phytonutrient, they are one of the most potent natural sources of resveratrol. While none of these amounts are impressive, nuts are more potent than many common forms of meat like chicken breasts and average beef. (Table 7)

Table 7. Seeds and nuts

S.NO.	Type	% of CoQ10
1.	Peanuts roasted	0.00267%
2.	Pistachios roasted	0.002%
3.	Walnuts raw	0.0019%
4.	Sesame seeds roasted	0.00167%
5.	Hazelnuts roasted	0.00167%

Grains: The findings suggest that most of the CoQ10 in these plants is found in their germ (Table 8). When the grains are milled, the germ is removed. As a result, the whole grain corn, wheat, and rice had none detectable. Barley and oats with germ intact were not tested, but the whole grain versions for them had none. [41]

Table 8. Grains

S.NO.	Type	% of CoQ10
1.	Corn germ	0.0007%
2.	Rice bran	0.0049%
3.	Wheat germ	0.0035%
4.	Japan barnyard millet whole grain	0.0014%
5.	Buckwheat whole grain	0.0011%

2.4. PHYSIOLOGY OR FUNCTIONS OF CoQ10

CoQ10 is an obligatory member of the respiratory chain in the mitochondrial cells. CoQ10 is located in the mitochondrial lysosomes, Golgi and provide the inhibition of free radical molecule either by direct reaction or by regeneration of tocopherol and ascorbate from their oxidised form. [42] It competently protects membrane phospholipids from per oxidation and also mitochondrial DNA and membrane proteins from free radical induced oxidative damage. More recently, expression profiling revealed that CoQ10 affects the expression of few hundred genes and use many of its effects via the induction of gene transcription. [43, 44]

It involved in a cellular metabolism and several other metabolic process such as helpful in electron transport in mitochondrial respiratory chain, involved in extra mitochondrial electron transport, synthesized in the body, and lipid-soluble antioxidant, regulate the mitochondrial permeability transition pores, essential for activation of mitochondrial uncoupling proteins, regulation of the physicochemical properties of membranes, modulation of the surface of blood monocytes and enhancement of endothelial function (by increasing nitric oxide release) [45]

The plasma membrane of most cells contains a CoQ dependent NADH oxidase which regulates the cytosolic ratio of NAD+/ NADH ratio and ascorbate reduction and is involved in regulation of cell growth and differentiation. [46] CoQ10 is only lipid soluble antioxidant synthesized endogenously and efficiently prevents oxidation of proteins, lipids and DNA. Effective enzymatic systems strive continuously to maintain this compound in its active reduced form. [47] CoQ10 mediate both oxidation of sulfide in yeast and the introduction of disulfide bonds into bacterial proteins. [48] Opening of the mitochondrial membrane transition pore allows the translocation of molecules as large as 1500 Da in size, which leads to a collapse of mitochondrial functions. CoQ10 is one of the compounds that prevent such pore opening, thereby it is counteracting apoptotic events such as ATP depletion, release of cytochrome c into the cytosol, caspase activation, depolarization, of the mitochondrial membrane potential and DNA fragmentation. [49] By protecting LDL from oxidation, this lipid also has antiatherosclerotic properties. Moreover, it reduces the levels of lipid peroxides associated with lipoproteins in atherosclerotic lesions, as well as the size of such lesions in the aorta. Furthermore, CoQ10 decreases the levels of b2 integrin CD 11b in monocytes, which counteracts monocyte endothelial cell interaction. [50]

2.5. CLINICAL USES

CoQ10 is used in numerous diseases such as cardiovascular or ischemic heart disease, arteriosclerosis, chronic heart failure (for both systolic and diastolic heart failure), cardiomyopathy, hypertension, neuronal disease etc. [51]

Antioxidant therapy with CoQ10 in doses of 3 mg/kg daily was suggested to be used as an auxiliary to lipid lowering for beneficials effects related to characteristics of atheroma (atherosclerosis) independent of hypolipidemic agents. [52]

It was found that CoQ10 can provide rapid protective effects in patients with acute myocardial infarction (sudden heart failure) if administered within three days of the onset of symptoms. [53]

Additional to reducing the effects of oxidative stress CoQ10 has the potential to improve energy production in mitochondria by bypassing defective components in the MRC. CoQ10 treatment may possibly improve the recovery of the myocardium after surgery induced stress. [54]

It was stated given CoQ10 in doses 300 to 400 mg daily to patients with CHF and cardiomyopathy. By boosting the energy output of heart cells, CoQ10 makes damaged heart muscles stronger and better able to pump blood. [55]

Decreased serum and gingival levels of CoQ10 were recorded in patients with periodontal disease. A trial it was found CoQ10 50 mg/day for 21 days to significantly improve clinical aspects of periodontal disease such as inflammation, pocket depth and tooth mobility. [56]

CoQ10 was shown to prevent migraine headaches. A history of migraine were treated with of CoQ10 in doses of 150 mg daily. 61.3% of the patients have a greater than 50% reduction with migraine headache. Decrease in migraine frequency after 1 month of treatment was 13.1% and increased to 55.3% by the end of 3 months with no side effects of CoQ10. [57]

Over 50% of the obese patients studied in a clinical study were deficient in CoQ10. After 3 months given 100 mg of CoQ10 daily have lost an average of 38 pound. [58]

2.6. PHARMACOLOGICAL ACTIVITIES OF CoQ10

Antioxidant activity

CoQ10 as an potent antioxidant which protects the body from damage caused by harmful molecules known as free radicals. The antioxidant role of CoQ10 as a free radical scavenger or neutralize free radicals and may reduce or prevent some of cause like damage to cell membranes, tamper with DNA, and cell death. the CoQ10 molecule is constantly going throughout as oxidation reduction. [59]

Anti-atherosclerosis

Preliminary data imply benefit in the setting of atherosclerosis. As mentioned earlier, oxidation of the circulating LDL is thought to play a key role in the pathogenesis of atherosclerosis, which is the underlying disorder leading to heart attack, ischaemic strokes, and CHD. [60, 61]

Cardiovascular protective activity

The etiology of several cardiovascular disorders is thought to involve impaired mitochondrial function and oxidative stress. Coenzyme Q10 (CoQ10) acts as both an antioxidant and as an electron acceptor at the level of the mitochondria. also in cardiac patients, plasma CoQ10 has found to be an free predictor of mortality. Based on the fundamental role of CoQ10 in mitochondrial bioenergetics and its well acknowledged antioxidant properties, CoQ10 deficiency has been observed in patients with congestive heart failure, angina pectoris, coronary artery disease, cardiomyopathy, and hypertension. The clinical benefits of CoQ10 supplementation in prevention and treatment of cardiovascular diseases have been observed CoQ10 may be recommended to patients at risk for or diagnosed with cardiovascular disease. with either preserved or reduced ejection fraction is associated with increased morbidity and mortality. Coenzyme Q10 (CoQ10) may represent a safe therapeutic option for patients with Heart failure. [62,63]

Hypertrophic cardiomyopathy

CoQ10 given orally to decrease the thickness of heart wall and decrease symptoms of shortness of breath and fatigue. Some trials have found CoQ10 may be helpful in certain types of cardiomyopathy. [64]

Anti-inflammatory activity

CoQ10 is able to suppress the IL1 induced inflammatory response in dermal fibroblasts CoQ10 enhanced suppression of inflammation. CoQ10 in topical skin care products may provide enhanced protection from inflammation and premature aging caused by sun exposure. [65]

Meniere syndrome

CoQ10 has been found to be helpful in vertigo and Meniere like syndrome by improving the immune system. [66]

Mitochondrial Dysfunction

Coenzyme Q10 is an important factor in mitochondrial respiration. Several primary deficiency states of coenzyme Q10 exist that encephalopathy, severe infantile multisystem disease, Leigh syndrome, myopathies, and cerebellar ataxia. Some drugs have been associated with a reduction in serum and muscle tissue coenzyme Q10 levels and may play a role in statin-induced myopathy. Given the low risk of toxicity and the potential benefit in treating statin induced myopathy. [67]

Periodontal diseases

Periodontal disease is an inflammatory disease interaction of a bacterial attack and host inflammatory response. CoQ10 is an endogenous antioxidant which increases the concentration of CoQ10 in the disease gingival and suppresses the periodontal inflammation. CoQ10 is use for treatment of periodontitis. [68]

Anticancer activity

Coenzyme Q10 (CoQ10) or ubiquinone is a well known inborn antioxidant with different biologic activities like immune boosting, demonstrated the potential benefits of CoQ10 as an anticancer agent against solid tumors including BC However most of such studies demonstrated an acceptable efficacy for CoQ10 supplements in combination products, none of them were able to stratify the effect of sole CoQ10 on breast malignancies. [69]

Antiparkinson activity

Reactive oxygen species (ROS) are well known to contribute to the pathophysiology of Parkinson's disease (PD). Clinical trials of antioxidant (CoQ10) are currently underway in PD patients, however, antioxidant research has been hindered by a lack of peripheral biomarkers. [70]

Hepatoprotective activity

CoQ10 reduced the levels of serum aminotransferases, and suppressed lipid per oxidation, and reduced glutathione and catalase activity, It was concluded that CoQ10 protects rat liver against acute acetaminophen hepatotoxicity. [71]

Hepatocellular carcinoma

The therapeutic potential of coenzyme Q10 was investigated in rats with hepatocellular carcinoma induced Coenzyme Q10 treatment (0.4 mg/kg/day, i.p.) was given for four weeks Coenzyme Q10 significantly suppressed lipid peroxidation, prevented the depletion of reduced glutathione and superoxide dismutase activity, and decreased the elevations of tumor necrosis factor α and nitric oxide in liver tissue of rats with hepatocellular carcinoma. Q10 significantly decreased the expression of alpha fetoprotein, inducible nitric oxide synthase, cyclooxygenase 2 and nuclear factor K_B in liver tissue of rats with hepatocellular carcinoma. It was concluded that coenzyme Q10 may represent a potential therapeutic option for liver carcinogenesis. [72]

Nephroprotective activity

Coenzyme Q10 significantly reduced blood urea nitrogen and serum creatinine levels which were increased by cisplatin. Coenzyme Q10 significantly compensated deficits in the antioxidant defense mechanisms (reduced glutathione level and superoxide dismutase activity), suppressed lipid per oxidation, decreased the elevations of tumor necrosis factor α nitric oxide and platinum ion concentration, it also significantly decreased the cisplatin induced over expression of inducible nitric oxide synthesis, nuclear factor $K_B$caspase-3 and p53 in renal tissue. It was concluded that coenzyme Q10 represents a potential therapeutic option to protect against acute cisplatin nephrotoxicity. [73]

Neuronal cell effect

CoQ10 deficiency causes the autosomal disorder. Rare presenting features include both muscle and neurological dysfunction. Muscle abnormalities can improve, both clinically given by CoQ10 supplementation. [74]

Antidepressant activity

Depression is accompanied by an induction of oxidative nitrosative stress (O&NS). CoQ10 is an essential cofactor in the mitochondrial electron transport pathway and has a powerful antioxidant CoQ10 showed a significant antidepressant effect CoQ10 possesses antidepressant activity and can protect against CRS induced hippocampal DNA damage which could be mediated in part by maintaining mitochondrial function and its well documented antioxidant properties. Therefore, CoQ10 have a potential therapeutic value for the management of depressive disorders. [75]

Anti-ageing activity

Decrease of CoQ10 levels during aging could be one of the main factors in the development of chronic diseases in old people. Furthermore since CoQ10 is not only an antioxidant but also is involved in a plethora of cellular processes, appropriate uptake of CoQ10 into cellular is crucial for improvement of cell activity

during aging. CoQ10 Maintenance the cell membranes either by dietary supplementation or enhance health during aging. [76]

Anti-angiogenic activity

CoQ10 possessed the antiangiogenic, anti-inflammatory and antinociceptive activity, down regulating the level of nitric oxide, it is use as dietary supplement and in combination therapy. CoQ10 possessed strong antiangiogenic activity in the chick chorioallantoic membrane assay. CoQ10 was shown to have in vivo anti-inflammatory activity using the acetic acid induced vascular permeability and air pouch models, and show the antinociceptive activity by using the acetic acid induced abdominal response. [77]

3. Pharmacokinetics And Pharmacodynamics Of CoQ10

Despite being a lipophilic compound, CoQ10 preparations often have low bioavailability. Lower bioavailability of CoQ10 could be associated with its hydrophobicity, large molecular weight (863 Da), and thermo ability. [78] CoQ10 has two forms ubiquinol and ubiquinone, with ubiquinol having higher bioavailability. [79] Different CoQ10 bioavailability is provided using various pharmaceutical forms (powder, suspension, oil solution, or solubilized form). Solubilized CoQ10 is preferred because of better absorption and higher plasma concentration, resulting in improved bioavailability. (3,6 times higher compared to powder) which translate into its high cardioprotective effect (an increase in plasma and myocardium CoQ10 concentration) [80, 81] The hydrophobicity of CoQ10 can be decreased using various methods of emulsification with modified food starch lecithin, gum arabic, polysorbate 80, or including g cyclodextrin. However, soft gelatin capsules containing soya bean oil suspension of CoQ10 have the highest bioavailability compared to those having polysorbate or lecithin as additives. Greater bioavailability of CoQ10 can be obtained if it is taken with meals, because of the action of secreted bile acids. [82, 83] Several human studies reported that it was necessary to use very high daily doses (300–3000 mg/day) of CoQ10 for long periods of time (even months) to observe any significant pharmacological or therapeutic effect. As a result, the amounts needed to provide protection from ROS (Reactive Oxygen Species) were very high. [84, 85]

Normal blood and tissue levels of CoQ10 have been well established by the investigators around in the world. Significantly reduce level of CoQ10 have been noted in a variety of diseases in animal and human studies. Deficient dietary of CoQ10, causes CoQ10 deficiency. decrease dietary ingestion is presumed in chronic malnutrition and cachexia. [86] CoQ10 have been shown to be effective in cases of mitochondrial myopathies, which were sometimes associated with low CoQ10 muscle levels. The progress in molecular biology technique, major CoQ10 deficiencies, and they are associated with four major clinical phenotypes some of these syndromes have shown excellent responses to oral CoQ10 treatment. It has been ascertain that respiratory chain dysfunction and oxidative stress correlate with the severity of primary CoQ10 deficiency. [87, 88] Not all conditions respond to CoQ10 administration, perhaps also on the basis of the time when CoQ10 therapy was started some of the responsive cases also showed an improvement of a nephropathy. [89, 90]

4. Conclusion

CoQ10 is fairly safe and well tolerated. It is a considerable member of the electron transport chain which is required for mitochondrial ATP synthesis and also an important antioxidant effective within mitochondria. This review will be the only way to put CoQ10 on the map with current pharmaceutical options for treatment of conditions like hypercholesterolemia, hypertension, Parkinson's disease, migraines, periodontitis, cancer, diabetes, muscular dystrophies, HIV/AIDs, etc. and many others. Researchers are working hard to uncover the scientific data to support proper dosages for each of the conditions studied. The pairing up of CoQ10 with other beneficial and synergistic nutrients could be another key to unlocking its full potential in standard nutritional medicine.

Conflict Of Interests

The authors declare no conflict of interests related with this manuscript.

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References

[1] L. Ernster, G. Dallner, Biochemical, physiological and medical aspects of ubiquinone function, Biochim. Biophys. Acta 1271 (1995) 195–204.

[2] H.N. Bhagavan, R.K. Chopra, Coenzyme Q10: absorption, tissue uptake, metabolism and pharmacokinetics, Free Radic. Res. 40 (2006) 445–453.

[3] Singh, U., Devaraj, S., & Jialal, I. (2007). Coenzyme Q10 supplementation and heart failure. Nutrition Reviews, 65(6), 286-293.

[4] Linnane AW, Kios M, Vitetta L. Coenzyme Q(10)–its role as a prooxidant in the formation of superoxide anion/hydrogen peroxide and the regulation of the metabolome. Mitochondrion. 2007;7 Suppl:S51–S61.

[5] Bessler, H., Bergman, M., Blumberger, N., Djaldetti, M., & Salman, H. (2010). Coenzyme Q10 decreases TNF-alpha and IL-2 secretion by human peripheral blood mononuclear cells. Journal of Nutritional Science and Vitaminology (Japan).

[6] J.L. Tarry-Adkins, D.S. Fernandez-Twinn, I.P. Hargreaves, V. Neergheen, C.E. Aiken, M.S. Martin-Gronert, J.M. McConnell, S.E. Ozanne, Coenzyme Q10 prevents hepatic fibrosis, inflammation, and oxidative stress in a male rat model of poor maternal nutrition and accelerated postnatal growth, Am. J. Clin. Nutr. 103 (2016) 579–588.

[7] Wang, X. L., Rainwater, D. L., Mahaney, M. C., & Stocker, R. (2004). Cosupplementation with vitamin E and coenzyme Q10 reduces circulating markers of inflammation in baboons. The American journal of clinical nutrition, 80(3), 649-655.

[8] Linnane AW, Kios M, Vitetta L. Coenzyme Q(10)–its role as a prooxidant in the formation of superoxide anion/hydrogen peroxide and the regulation of the metabolome. Mitochondrion. 2007;7 Suppl:S51–S61.

[9] Lee SK, Lee JO, Kim JH, et al. Coenzyme Q10 increases the fatty acid oxidation through AMPK-mediated PPARa induction in 3T3-L1 preadipocytes. Cell Signal. 2012;24(12):2329–2336.

[10] Ahmadvand H, Ghasemi-Dehnoo M. Antiatherogenic, hepatoprotective, and hypolipidemic effects of coenzyme Q10 in alloxan-induced type 1 diabetic rats. ARYA Atheroscler. 2014;10(4):192–198.

[11] Thomas SR, Leichtweis SB, Pettersson K, et al. Dietary cosupplementation with vitamin E and coenzyme Q(10) inhibits atherosclerosis in apolipoprotein E gene knockout mice. Arterioscler Thromb Vasc Biol. 2001;21(4):585–593.

[12] Wang D, Yan X, Xia M, et al. Coenzyme Q10 promotes macrophage cholesterol efflux by regulation of the activator protein-1/miR-378/ATP-binding cassette transporter G1-signaling pathway. Arterioscler Thromb Vasc Biol. 2014;34(9):1860–1870.

[13] Inane AW, Kopsidas G, Zhang C, et al. Cellular redox activity of coenzyme Q10: effect of CoQ10 supplementation on human skeletal muscle. Free Radic Res. 2002;36(4):445–453.

[14] Langsjoen P, Langsjoen P, Willis R, Folkers K. Treatment of essential hypertension with coenzyme Q10. Mol Aspects Med. 1994;15 Suppl: S265–S272.

[15] Langsjoen PH, Langsjoen PH, Folkers K. A six-year clinical study of therapy of cardiomyopathy with coenzyme Q10. Int J Tissue React. 1990;12(3):169–171.

[16] Langsjoen PH. Alleviating congestive heart failure with coenzyme Q10. LE Mag. 2008.
[17] Folkers K, Vadhanavikit S, Mortensen SA. Biochemical rationale and myocardial tissue data on the effective therapy of cardiomyopathy with coenzyme Q10. Proc Natl Acad Sci U S A. 1985;82(3):901–904.
[18] Yang YK, Wang LP, Chen L, Yao XP, Yang KQ, Gao LG, et al. Coenzyme Q10 treatment of cardiovascular disorders of ageing including heart failure, hypertension and endothelial dysfunction. Clin Chim Acta: Int J Clin Chem. 2015;450:83–89.
[19] Coenzyme Sarter B. Q10 and cardiovascular disease: a review. J Cardiovasc Nurs. 2002;16(4):9–20.
[20] DiNicolantonio JJ, Bhutani J, McCarty MF, O'Keefe JH. Coenzyme Q10 for the treatment of heart failure: a review of the literature. Open Heart. 2015;2(1): e000326.
[21] Kuimov AD, Murzina TA. Coenzyme q10 in complex therapy of patients with ischemic heart disease. Kardiologiia. 2013;53(8):40–43.
[22] Crane FL, Hatefi Y, Lester RL, Widmer C. Isolation of a quinone from beef heart mitochondria. Biochim Biophys Acta. 1957;25(1):220–221. 22.
[23] Khatta M, Alexander BS, Krichten CM, Fisher ML, Freudenberger R, Robinson SW, et al. The effect of coenzyme Q10 in patients with congestive heart failure. Ann Intern Med. 2000;132(8):636–640.
[24] Tanaka J, Tominaga R, Yoshitoshi M, Matsui K, Komori M, Sese A, et al. Coenzyme Q10: the prophylactic effect on low cardiac output following cardiac valve replacement. Ann Thor Surg. 1982;33(2):145–151.
[25] Oleck S, Ventura HO. Coenzyme Q10 and utility in heart failure: just another supplement? Curr Heart Fail Rep. 2016;13(4):190–195.
[26] Madmani ME, Tamr Agha A, Madmani K, Shahrour Y, Essali Y, et al. Coenzyme Q10 for heart failure. Cochrane Database Syst Rev. 2014;(6):Cd008684.
[27] Tsutsui T, Tsutamoto T, Wada A, Maeda K, Mabuchi N, Hayashi M, et al. Plasma oxidized low-density lipoprotein as a prognostic predictor in patients with chronic congestive heart failure. J Am Coll Cardiol. 2002;39(6):957–962.
[28] Crane F, Hatefi Y, Lester R et al. Isolation of a quinone from beef heart mitochondria. Biochimica et Biophysica Acta 1957; 25(1): 220- 21.
[29] Natural Medicines comprehensive database. COENZYMES Q10 monograph. Available at: http://www.naturaldatabase.com. Accessed January 22, 2003
[30] National Center for Complementary and Alternative Medicine. Available at: http://nccam.nih.gov/. Accessed March 10, 2003.
[31] Crane, F. L., Hatefi, Y., Lester, R. I., & Widmer, C. (1957). Isolation of a quinone from beef heart mitochondria. Biochim Biophys Acta 25, 220–221.(chemiatry)
[32] Tran MT, Mitchell TM, Kennedy DT et al. Role of Coenzyme Q10 in chronic heart failure, angina, and hypertension. Pharmacotherapy 2001; 21: 797-808.
[33] Abe K, Matsuo Y, Kadekawa J, Inoue S, Yanagihara T. Effect of coenzyme Q10 in patients with mitochondrial myopathy, Encephalopathy, lactic acidosis, and stroke-like episodes (MELAS): evaluation by noninvasive tissue oximetry. Journal of the Neurological Sciences 1999 Jan 1;162(1):65-8.
[34] Tsai, K.L Y.H. Huang, C.L. Kao, D.M. Yang, H.C. Lee, H.Y. Chou, Y.C. Chen, G.Y. Chiou,L.H. Chen, Y.P. Yang, et al., A novel mechanism of coenzyme Q10 protects against human endothelial cells from oxidative stress-induced injury by modulating NO-related pathways, J. Nutr. Biochem. 23 (2012) 458–468.
[35] Döring, F., Schmelzer, C., Lindner, I., Vock, C., & Fujii, K. (2007). Functional connections and pathways of coenzyme Q10-inducible genes: An in-silico study. IUBMB life, 59(10), 628-633.
[36] Mikael Turunena,b, Jerker Olssonc, Gustav Dallnera,*Metabolism and function of coenzyme Q. Biochimica et Biophysica Acta 1660 (2004) 171– 199.
[37] Gómez-Díaz, C., Rodriguez-Aguilera, J. C., Barroso, M. P., Villalba, J. M., Navarro, F., Crane, F. L., & Navas, P. (1997). Antioxidant ascorbate is stabilized by NADH-coenzyme Q 10 reductase in the plasma membrane. Journal of bioenergetics and biomembranes, 29(3), 251-257.
[38] Ernster, L. (1993). Lipid peroxidation in biological membranes: mechanisms and implications. Active oxygens, lipid peroxides, and antioxidants.
[39] Hamilton, S. J., Chew, G. T., & Watts, G. F. (2007). Therapeutic regulation of endothelial dysfunction in type 2 diabetes mellitus. Diabetes and Vascular Disease Research, 4(2), 89-102.
[40] Witztum, J. L. (1994). The oxidation hypothesis of atherosclerosis. The Lancet, 344(8925), 793-795.
[41] https://www.livestrong.com/article/85773-natural-sources-coenzyme-q10/
[42] Papucci, L., Schiavone, N., Witort, E., Donnini, M., Lapucci, A., Tempestini, A., ... & Brancato, R. (2003). Coenzyme q10 prevents apoptosis by inhibiting mitochondrial depolarization independently of its free radical scavenging property. Journal of Biological Chemistry, 278(30), 28220-28228.
[43] Ernster, L., & Dallner, G. (1995). Biochemical, physiological and medical aspects of ubiquinone function. Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease, 1271(1), 195-204.
[44] Yang, Y. K., Wang, L. P., Chen, L., Yao, X. P., Yang, K. Q., Gao, L. G., & Zhou, X. L. (2015). Coenzyme Q10 treatment of cardiovascular disorders of ageing including heart failure, hypertension and endothelial dysfunction. Clinica Chimica Acta, 450, 83-89.
[45] M. Turunen, J. Olsson, G. Dallner, Metabolism and function of coenzyme Q, Biochim. Biophys. Acta 1660 (2004) 171-99.
[46] Gómez-Díaz, C., Rodriguez-Aguilera, J. C., Barroso, M. P., Villalba, J. M., Navarro, F., Crane, F. L., & Navas, P. (1997). Antioxidant ascorbate is stabilized by NADH-coenzyme Q 10 reductase in the plasma membrane. Journal of bioenergetics and biomembranes, 29(3), 251-257.
[47] Ernster, L. (1993). Lipid peroxidation in biological membranes: mechanisms and implications. Active oxygens, lipid peroxides, and antioxidants.
[48] Hamilton, S. J., Chew, G. T., & Watts, G. F. (2007). Therapeutic regulation of endothelial dysfunction in type 2 diabetes mellitus. Diabetes and Vascular Disease Research, 4(2), 89-102.
[49] Papucci, L., Schiavone, N., Witort, E., Donnini, M., Lapucci, A., Tempestini, A., ... & Brancato, R. (2003). Coenzyme q10 prevents apoptosis by inhibiting mitochondrial depolarization independently of its free radical scavenging property. Journal of Biological Chemistry, 278(30), 28220-28228.
[50] Ernster, L., & Dallner, G. (1995). Biochemical, physiological and medical aspects of ubiquinone function. Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease, 1271(1), 195-204.
[51] Yang, Y. K., Wang, L. P., Chen, L., Yao, X. P., Yang, K. Q., Gao, L. G., & Zhou, X. L. (2015). Coenzyme Q10 treatment of cardiovascular disorders of ageing including heart failure, hypertension and endothelial dysfunction. Clinica Chimica Acta, 450, 83-89.
[52] Singh, R.B., Shinde, S.N., Chopra, R.K., Niaz, M.A., Thakur, A.S., Onouchi, Z. "Effect of coenzyme Q10 on experimental atherosclerosis and chemical composition and quality of atheroma in rabbits." Atherosclerosis, 148, 275-282 (2000).
[53] Singh, R.B., Wander, G.S., Rastogi, A., Shukla, P.K., Mittal, A., Sharma, J.P., Mehrotra, S.K., Kapoor, R., Chopra, R.K. "Randomized, double-blind, placebo-controlled trial of coenzyme Q10 in patients with acute myocardial infarction." Cardiovasc. Drugs Ther., 12(4), 347-353 (1998).
[54] Rosenfeldt, F.L., Pepe, S., Linnane, A., Nagley, P., Rowland, M., Ou, R., Marasco, S., Lyon, W., Esmore, D. "Coenzyme Q10 protects the aging heart against stress: studies in rats, human tissues, and patients." Annals of the New York Academy of Science, 959, 355-359; discussion 463-465 (2002).
[55] Langsjoen, P.H., Langsjoen, A.M. "Overview of the use of CoQ10 in cardiovascular disease." Biofactors, 9(2-4), 273-284 (1999).
[56] Littarru, G.P., Nakamura, R., Lester, H., Folkers, K., Kuzell, W.C. "Deficiency of coenzyme Q10 in gingival tissue from patients with periodontal disease." Proc. Natl. Acad. Sci., 68, 2332-2335 (1971).
[57] Rozen, T.D., Oshinsky, M.L., Gebeline, C.A., Bradley, K.C., Young, W.B., Shechter, A.L., Silberstein, S.D. "Open label trial of coenzyme Q10 as a migraine preventive." Cephalalgia, 22(2), 137-41 (2002).
[58] Van Gaal, L., "Exploratory study of Coenzyme Q10 in obesity." In: Folkers K, Yamamura Y, eds: Biomedical and Clinical Aspects of Coenzyme Q10, Elservier Science Publ, Amsterdam 4, 369-73 (1984).
[59] Sugiyama S, Kitazawa M, Ozawa T et al. Antioxidative effect of Coenzyme Q10. Experentia 1980; 36: 1002-03.

[60] Witztum JL. The oxidation hypothesis of atherosclerosis. Lancet 1994; 344(8925): 793-95
[61] Parthasarathy S, Steinberg D, Witztum JL, The role of oxidized lowdensity lipoproteins in the pathogenesis of atherosclerosis. Annual Review of Medicine 1992; 43: 219-25.
[62] Yang, Y. K., Wang, L. P., Chen, L., Yao, X. P., Yang, K. Q., Gao, L. G., & Zhou, X. L. (2015). Coenzyme Q10 treatment of cardiovascular disorders of ageing including heart failure, hypertension and endothelial dysfunction. Clinica Chimica Acta, 450, 83-89.
[63] Sharma, A., Fonarow, G. C., Butler, J., Ezekowitz, J. A., & Felker, G. M. (2016). Coenzyme Q10 and heart failure: a state-of-the-art review. Circulation: Heart Failure, 9(4), e002639.
[64] Parthasarathy S, Steinberg D, Witztum JL, The role of oxidized lowdensity lipoproteins in the pathogenesis of atherosclerosis. Annual Review of Medicine 1992; 43: 219-25.
[65] Fuller, B., Smith, D., Howerton, A., & Kern, D. (2006). Anti-inflammatory effects of CoQ10 and colorless carotenoids. Journal of cosmetic dermatology, 5(1), 30-38.
[66] Kumar, A., Kaur, H., Devi, P., & Mohan, V. (2009). Role of coenzyme Q10 (CoQ10) in cardiac disease, hypertension and Meniere-like syndrome. Pharmacology & therapeutics, 124(3), 259-268.
[67] Deichmann, R., Lavie, C., & Andrews, S. (2010). Coenzyme q10 and statin-induced mitochondrial dysfunction. The ochsner journal, 10(1), 16-21.
[68] Prakash, S., Sunitha, J., & Hans, M. (2010). Role of coenzyme Q10 as an antioxidant and bioenergizer in periodontal diseases. Indian journal of pharmacology, 42(6), 334.
[69] Tafazoli, A. (2017). Coenzyme Q10 in breast cancer care. Future Oncology, 13(11), 1035- 1041.
[70] Mischley, L. K., Allen, J., & Bradley, R. (2012). Coenzyme Q10 deficiency in patients with Parkinson's disease. Journal of the neurological sciences, 318(1), 72-75.
[71] Fouad, A. A., & Jresat, I. (2012). Hepatoprotective effect of coenzyme Q10 in rats with acetaminophen toxicity. Environmental toxicology and pharmacology, 33(2), 158-167.
[72] Fouad, A. A., Al-Mulhim, A. S., & Jresat, I. (2013). Therapeutic effect of coenzyme Q10 against experimentally-induced hepatocellular carcinoma in rats. Environmental toxicology and pharmacology, 35(1), 100-108.
[73] Fouad, A. A., Al-Sultan, A. I., Refaie, S. M., & Yacoubi, M. T. (2010). Coenzyme Q10 treatment ameliorates acute cisplatin nephrotoxicity in mice. Toxicology, 274(1-3), 49-56.
[74] Duberley, K. E., Heales, S. J. R., Abramov, A. Y., Chalasani, A., Land, J. M., Rahman, S., & Hargreaves, I. P. (2014). Effect of Coenzyme Q10 supplementation on mitochondrial electron transport chain activity and mitochondrial oxidative stress in Coenzyme Q10 deficient human neuronal cells. The international journal of biochemistry & cell biology, 50, 60-63.
[75] Aboul-Fotouh, S. (2013). Coenzyme Q10 displays antidepressant-like activity with reduction of hippocampal oxidative/nitrosative DNA damage in chronically stressed rats. Pharmacology Biochemistry and Behavior, 104, 105-112.
[76] López-Lluch, G., Rodríguez-Aguilera, J. C., Santos-Ocana, C., & Navas, P. (2010). Is coenzyme Q a key factor in aging?. Mechanisms of ageing and development, 131(4), 225-235.
[77] Jung, H. J., Park, E. H., & Lim, C. J. (2009). Evaluation of antiangiogenic, anti-inflammatory and antinociceptive activity of coenzyme Q10 in experimental animals. Journal of Pharmacy and Pharmacology, 61(10), 1391-1395.
[78] Zaki NM. Strategies for oral delivery and mitochondrial targeting of CoQ10. Drug Deliv 2014;(December)1–14 [Epub ahead of print].
[79] Hosoe K, Kitano M, Kishida H, Kubo H, Fujii K, Kitahara M. Study on safety and bioavailability of ubiquinol (Kaneka QHTM) after single and 4-week multiple oral administration to healthy volunteers. Regul Toxicol Pharmacol 2007;47:19–28.
[80] Sun J, Wang F, Sui Y, She Z, Zhai W, Wang C, et al. Effect of particle size on solubility, dissolution rate, and oral bioavailability: evaluation using coenzyme Q10 as naked nanocrystals. Int J Nanomedicine 2012;7:5733–44.
[81] Prakash S, Sunitha J, Hans M. Role of coenzyme Q(10) as an antioxidant and bioenergizer in periodontal diseases. Indian J Pharmacol 2010;42(6):334–7.
[82] Ozaki A, Muromachi A, Sumi M, Sakai Y, Morishita K, Okamoto T. Emulsification of coenzyme Q10 using gum arabic increases bioavailability in rats and human and improves food-processing suitability. J Nutr Sci Vitaminol 2010;56(1):41–7.
[83] Schulz C, Obermüller-Jevic UC, Hasselwander O, Bernhardt J, Biesalski HK. Comparison of the relative bioavailability of different coenzyme Q10formulationswith a novel solubilizate (Solu Q10). Int J Food Sci Nutr 2006;57:546–55.
[84] Swarnakar NK, Jain AK, Singh RP, Godugu C, Das M, Jain S. Oral bioavailability, therapeutic efficacy and reactive oxygen species scavenging properties of coenzyme Q10-loaded polymeric nanoparticles. Biomaterials 2011;32:6860– 74.
[85] Miles, M. V. (2007). The uptake and distribution of coenzyme Q (10). Mitochondrion, 7, S72-S77.
[86] Littarru GP, Lippa S, Oradei A. Metabolic and diagnostic implications of blood CoQ10 levels. In: Biomedical and Clinical Aspects of Coenzyme Q, vol. 6 (1991) Folkers K., Yamagami T., and Littarru G. P. (eds) Elsevier, Amsterdam, pp 167-178.
[87] Quinzii CM, López LC, Naini A, DiMauro S, Hirano M. Human CoQ10 defi ciencies. Biofactors. 2008a;32(1–4):113–8. PubMed PMID: 19096106; PubMed Central PMCID: PMC3625975.
[88] Roberts, J. M., Mascalzoni, D., Ness, R. B., & Poston, L. (2016). Collaboration to understand complex diseases: preeclampsia and adverse pregnancy outcomes. Hypertension, 67(4), 681-687.
[89] Khatta M, Alexander BS, Krichten CM, Fisher ML, Freudenberger R, Robinson SW, et al. The effect of coenzyme Q10 in patients with congestive heart failure. Ann Intern Med. 2000;132(8):636–640.
[90] G.T. Chew, S.J. Hamilton, G.F. Watts, Therapeutic regulation of endothelial dysfunction in type 2 diabetes mellitus, Diab. Vasc. Res. 4 (2007) 89–102.