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COQ10 A wonder enzyme: A review

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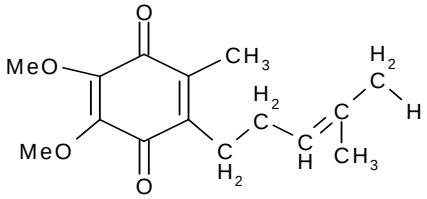
Abstract

The COQ 10 enzyme is oil-soluble vitamin-like substance is present in most eukaryotic cells, primarily in the mitochondria. It is a component of the electron transport chain and participates in aerobic cellular respiration, generating energy in the form of ATP.It has various biochemical roles in our body. The present review addresses the synthetic pathway of COQ 10, its Pharmacokinetics, bioavailability and its occurance in nature. The review also state the variuous interactions of the COQ 10 other drugs and its clinical uses in various diseases.

Keywords: Coenzyme, Quinone, Ubiquinone,Vitamins.

Introduction

Coenzyme Q_{10} (also known as ubiquinone, ubidecarenone, coenzyme Q and abbreviated at times to CoQ_{10} – pronounced like "ko-cue-ten" , CoQ, Q10, or simply Q) is a 1,4-benzoquinone[1], where Q refers to the quinone chemical group and 10 refers to the isoprenyl chemical subunits.This oil-soluble vitamin-like substance is present in most eukaryotic cells, primarily in the mitochondria[2]. It is a component of the electron transport chain and participates in aerobic cellular respiration, generating energy in the form of ATP. Ninety-five percent of the human body's energy is generated this way. Therefore, those organs with the highest energy requirements such as the heart and the liver have the highest CoQ_{10} concentrations [3, 4].

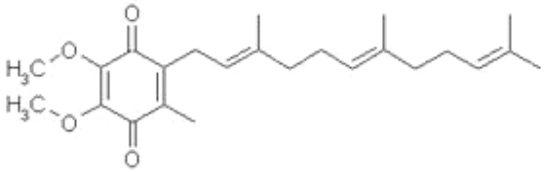


History

Coenzyme Q was first discovered by professor Fredrick L. Crane and colleagues at the University of Wisconsin–Madison Enzyme Institute in 1957. In 1958, its chemical structure was reported by Dr. Karl Folkers and coworkers at Merck; in 1968, Folkers became a Professor in the Chemistry Department at the University of Texas at Austin [5, 6].

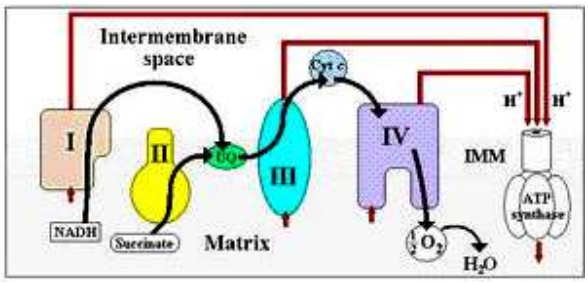
Chemical properties

The oxidized structure of **CoQ10** is shown on the top right. The various kinds of Coenzyme Q can be distinguished by the number of isoprenoid side-chains they have. The most common CoQ in human mitochondria is Q_{10}. The 10 refers to the number of isoprene repeats. The image below has three isoprenoid units and would be called Q_3. [7, 8]



Biochemical role

Figure 1: Biochemical Role of CoQ10



Electron transport chain ("UQ" visible in green near center.)CoQ is found in the membranes of many organelles. Since its primary function in cells is in generating energy, the highest concentration is found on the inner membrane of the mitochondrion. Some other organelles that contain CoQ_{10} include endoplasmic reticulum, peroxisomes, lysosomes and vesicles.[9, 10]

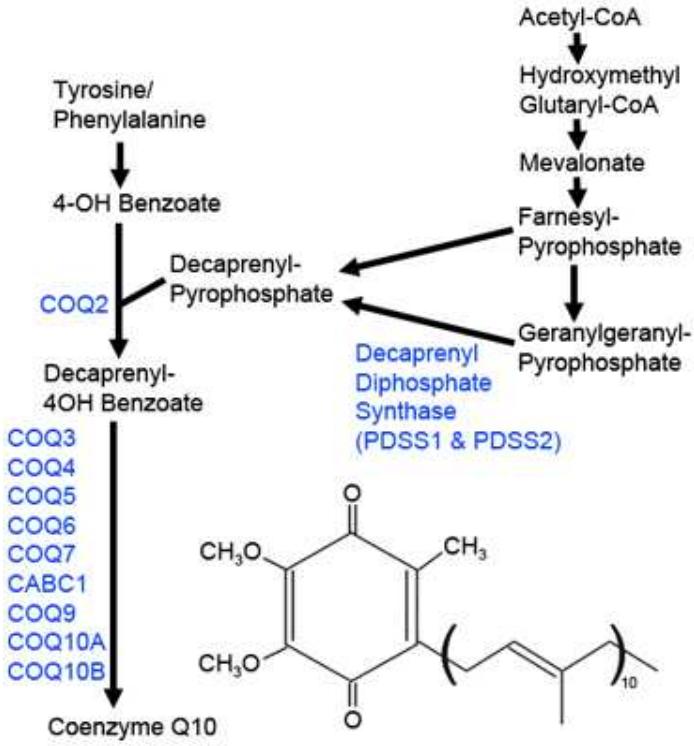
Lifespan

One study demonstrated that low dosages of coenzyme Q_{10} reduce oxidation and DNA double-strand breaks and a combination of a diet rich in polyunsaturated fatty acids and coenzyme Q_{10} supplementation leads to a longer lifespan in rats. Coles and Harris demonstrated an extension in the lifespan of rats when they were given coenzyme Q_{10} supplementation. Another study demonstrated that coenzyme Q_{10} extends the lifespan of c. elegans (nematode). [11, 12]

Biosynthesis

The benzoquinone portion of Coenzyme Q_{10} is synthesized from tyrosine, whereas the isoprene sidechain is synthesized from acetyl-CoA through the mevalonate pathway. The mevalonate pathway is also used for the first steps of cholesterol biosynthesis. [13]

Figure 2: Biosynthesis of CoQ10



Inhibition by statins and beta blockers

Coenzyme Q_{10} shares a common biosynthetic pathway with cholesterol. The synthesis of an intermediary precursor of Coenzyme Q_{10}, mevalonate, is inhibited by some beta blockers, blood pressure-lowering medication and statins, a class of cholesterol-lowering drugs. Statins can reduce serum levels of coenzyme Q_{10} by up to 40%.[14] Some research suggests the logical option of supplementation with coenzyme Q_{10} as a routine adjunct to any treatment that may reduce endogenous production of coenzyme Q_{10}, based on a balance of likely benefit against very small risk. [15, 16]

Absorption and metabolism

CoQ_{10} is a crystalline powder that is insoluble in water due to its low polarity. It has a relatively high molecular weight (863 g/mol) and its solubility in lipids is also limited so it is very poorly absorbed in the gastrointestinal tract.[17] Absorption follows the same process as that of lipids and the uptake mechanism appears to be similar to that of vitamin E, another lipid-soluble nutrient. Emulsification and micelle formation is required for the absorption of fats.[18] For CoQ_{10}, this process is chiefly facilitated by secretions from the pancreas and bile salts in the small intestine. A general rule is that the higher the dose orally administered, the lower the percent of the dose absorbed. Data on the metabolism of CoQ_{10} in animals and humans are limited. A study with ^{14}C-labeled CoQ_{10} in rats showed most of the radioactivity in the liver 2 hours after oral administration when the peak plasma radioactivity was observed, but it should be noted that CoQ_9 is the predominant form of coenzyme Q in rats. It appears that CoQ_{10} is metabolised in all tissues, while a major

route for its elimination is biliary and fecal excretion. After the withdrawal of CoQ_{10} supplementation, the levels return to their normal levels within a few days, irrespective of the type of formulation used.[19, 20]

Pharmacokinetics and bioavailability

Some reports have been published on the pharmacokinetics of CoQ10. The plasma peak can be observed 2–6 hours after oral administration, mainly depending on the design of the study. In some studies, a second plasma peak was also observed at about 24 hours after administration, probably due to both enterohepatic recycling and redistribution from the liver to circulation.Tomono et al. used deuterium-labelled crystalline CoQ10 to investigate pharmacokinetics in human and determined an elimination half-time of 33 hours. [21, 22]

Table 1: Improving the bioavailability of CoQ_{10}

Reduction of particle size	The obvious strategy is reduction of the particle size to as low as the micro- and nano-scale. Nanoparticles have been explored as a delivery system for various drugs and an improvement of the oral bioavailability of drugs with poor absorption characteristics has been reported; the pathways of absorption and the efficiency were affected by reduction of particle size. This protocol has so far not proved to be very successful with CoQ10, although reports have differed widely[23].The use of the aqueous suspension of finely powdered CoQ_{10} in pure water has also only revealed a minor effect. [24]
Soft-gel capsules with CoQ10 in oil suspension	A successful approach was to use the emulsion system to facilitate absorption from the gastrointestinal tract and to improve bioavailability. Emulsions of soybean oil (lipid microspheres) could be stabilised very effectively by lecithin and were utilised in the preparation of soft gelatine capsules. In one of the first such attempts, [25] performed a pharmacokinetic study on beagle dogs in which the emulsion of CoQ_{10} in soybean oil was investigated; about two times higher plasma CoQ_{10} level than that of the control tablet preparation was determined during administration of a lipid microsphere. Although an almost negligible improvement of bioavailability was observed by Kommuru et al. with oil-based soft-gel capsules in a later study on dogs, the significantly increased bioavailability of CoQ10 was confirmed for several oil-based formulations in most other studies. [26]
Novel forms of CoQ10 with increased water-solubility	Facilitating drug absorption by increasing its solubility in water is a common pharmaceutical strategy and has also been shown to be successful for Coenzyme Q10. Various approaches have been developed to achieve this goal, with many of them producing significantly better results over oil-based soft-gel capsules in spite of the many attempts to optimize their composition.[27] Examples of such approaches are use of the aqueous dispersion of solid CoQ10 with tyloxapol polymer, formulations based on various solubilising agents, i.e. hydrogenated lecithin and complexation with cyclodextrins; among the latter, complex with β-cyclodextrin has been found to have highly increased bioavailability. and is also used in pharmaceutical and food industry for CoQ10-fortification. Also some other novel carrier systems like liposomes, nanoparticles, dendrimers etc can be used to increase the bioavailability of Coenzyme Q10.[28]

Occurrence in nature

Fresh tissue samples from both mackerel and herring found the concentration of Coenzyme Q10 to be higher in the heart tissue (105-148 μg/g) compared to concentrations found in the body tissue. The red tissue of mackerel contained a higher concentration (67μg/g) of CoQ10 than the white tissue (15μg/g) whilst in herring tissue the concentration was found to range between 15–24 μg/g. A small seasonal variance in the concentrations of CoQ10 was observed in both fish.Cooking by frying reduces Q10 content by 14-32%.[29,30]

What COQ 10 Does

The body survives on the energy that is created when cells break down sugars, fats and amino acids (proteins). Much of this breakdown happens within tiny enclosures in the cells called mitochondria. COQ 10 is the substance in the mitochondria that carries electrons involved in producing energy from the food that you eat. COQ 10 is believed to be one of the first antioxidants that are depleted when LDL (the good cholesterol) is subjected to oxidation. In other words, it prevents the oxidation of lipoproteins in the blood, reducing the risk of harmful plaques that narrow arteries and contribute to heart disease. COQ 10 also seems to have anti-inflammatory properties, which may account for its reported benefits in treating migraines. There is also research to support its role in bolstering the immune system and helping the body to fight off infection and deal with the many disorders that have been connected to autoimmune system dysfunctions (diabetes, in particular) [31]

Interactions [31-33]

Table 2: Interactions of COQ 10

Beta-adrenergic Blockers	Many beta-blockers are antagonistic to CoQ10 enzymes, enzymes which are indispensable for the bioenergetics of the myocardium. Kishi et al found that adrenergic blockers for beta-receptors inhibited mitochrondrial CoQ10-enzymes to varying degrees. Propranolol is frequently used to treat hypertension; in some patients, it depresses myocardial function as an adverse reaction. Timolol showed negligible inhibition of the CoQ10-enzyme, NADH-oxidase and exerted pharmacologically low cardiac depressant effects. Metoprolol was less inhibitory than propranolol. Five alprenolols showed inhibition which approached that of propranolol. The 1-isomer of alprenolol showed weak inhibition of another CoQ10-enzyme, succinoxidase, but the other beta-blockers were essentially non-inhibitory to this enzyme.
Doxorubicin	CoQ10 reduces free radical formation induced by doxorubicin.
Lovastatin	Lovastatin functions by inhibiting the enzyme HMG-CoA, 3-hydroxy-3-methylglutaryl-coenzyme A reductase, which is required for the conversion of 3-hydroxy-3-methylglutaryl-coenzyme A to mevalonic acid. Biosynthesis of both cholesterol and coenzyme Q (CoQ) requires mevalonic acid as a precursor. Consequently, lovastatin therapy could also result in a lowering of cellular levels of Coenzyme Q10.
Pravastatin	Coenzyme Q10 is a component of the LDL + VLDL fractions of cholesterol which plays a key role as an essential mitochondrial redox-component and endogenous antioxidant. Much attention has been given to its role in reducing the

	risk of atherosclerosis based on the theory that the pathological changes result from oxidative processes. Likewise Q10 is often used in the treatment of cardiovascular disease.
Tricyclic Antidepressants	Tricyclic antidepressants are antagonistic to CoQ10 enzymes. Furthermore these drugs are class I antiarrhythmics.
Warfarin	Warfarin exerts its therapeutic effect by interfering with vitamin K metabolism. Coenzyme Q10, also known as Ubiquinone or Ubidecarenone, has a chemical structure similar to the various forms of vitamin K.

Clinical Uses of CoQ10

Table 3: Clinical Uses of CoQ10

Cardiovascular Disease (CD)	Various clinical trials have supported the use of CoQ10 in the prevention and treatment of several disorders related to oxidative stress. It has been demonstrated that antioxidant properties and central role of CoQ10 in mitochondrial oxidative phosphorylation make it useful as adjunctive therapy for cardiovascular diseases leading to CoQ10 deficiency include congestive heart failure, cardiomyopathy, angina pectoris, coronary artery disease, hypertension, mitral valve prolapsed, coronary revascularization, chronic obstructive pulmonary disease (COPD).[34] Heart tissue biopsies in patients with various heart diseases showed a CoQ10 deficiency in 50-75% of cases due to the fact that there is more CoQ10 in the heart tissue than in any other muscle in the body. Most of the investigations have focused on CoQ10 as a treatment for CD. In a clinical study of 424 patients with various forms of CD over an 8-year period, researchers reported that CoQ10 is a safe and effective adjunctive treatment for a broad range of CD. [35]
Congestive Heart Failure (CHF	The presence of increasing symptoms associated with CHF has been correlated to the severity of CoQ10 deficiency. CoQ10 myocardial tissue levels in CHF patients are on average 33% lower than in control patients. The degree of CoQ10 deficiency correlated with the severity of symptoms and presence of dilated cardiomyopathy. [36] The heart muscle may become ischemic and the result of myocardial infarction (MI) or during cardiac surgery. Increased generation of ROS when the heart muscle's oxygen supply is restored is thought to be an important contributor to myocardial damage occurring during ischemia-reperfusion. Pretreatment of animals with CoQ10 has been found to decrease myocardial damage due to ischemia-reperfusion.[37]
Angina	CoQ10 has been shown to be effective in the treatment of angina. In a study, patients with specific types of angina inclined to have more active oxygen forms by leukocytes, higher concentration of malonic dialdehyde in plasma and lower antiperoxide resistance of plasma. [38] By combining CoQ10 with antianginal therapy, the generation of free radicals was suppressed by leukocytes, allowing antiperoxide plasma resistance to increase. In a trial of 12 adults with stable angina on conventional therapy, 150 mg/day of CoQ10 for four weeks showed a decrease in both anginal frequency and use of nitroglycerin ($p>0.05$).[39]

Hypertension	CoQ10 is used as a treatment for high blood pressure for 40 years. In the United States, 109 patients with [40] symptomatic essential hypertension were observed after adding CoQ10 to their antihypertensive drug therapy. Researchers studied the antihypertensive effects of 50 mg doses of CoQ10 in twice daily in 26 patients with essential hypertension.[41] After 10 weeks, both diastolic and systolic blood pressure were significantly reduced ($p<0.001$), serum CoQ10 concentrations were increased, serum total cholesterol decreased and serum HDL-cholesterol increased significantly.[42]
Atherosclerosis	Antioxidant therapy with CoQ10 in doses of 3 mg/ kg daily was suggested to be used as an auxiliary to lipid lowering for beneficial effects related to characteristics of atheroma independent of hypolipidemic agents.[43, 44]
Surgery-Induced Stress	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 pretreatment could improve the recovery of the myocardium after stress.[45]
Cardiomyopathy	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. CoQ10 had shown to be deficient in myocardial tissue biopsies taken from dilated cardiomyopathy (DC) hearts. Researchers demonstrated that CoQ10 therapy is potentially useful in the treatment of children with idiopathic DC [46]. Usefulness of CoQ10 as an adjunct to conventional therapy in pediatric Cardiomyopathy also demonstrated. It was studied the long-term efficacy and safety of CoQ10 therapy for idiopathic DC in 126 symptomatic patients received 33.3 mg CoQ10 three times daily over 6 years additional to their traditional therapy. Survival rates at 1, 2, 3, 4 and 5 years were 97%, 84%, 79%, 70% and 57%, respectively.[47]
In Open Heart Surgery / Arrhythmias	CoQ10 is also used in open-heart surgery to obtain myocardial protection. In a study, 40 patients undergoing coronary artery bypass graft received either CoQ10 150 mg daily for 7 days prior to surgery or a placebo. The serum concentrations of post-operative markers of oxidative damage in the treatment group and the incidence of ventricular arrhythmias were significantly lower ($p<0.05$) than in the control group during the recovery period. In a placebo-controlled study, it was showed that the administration of CoQ10 may improve surgical recovery and lessen the magnitude of surgical insult in heart surgery. [48, 49]
Doxorubicin Cardiotoxicity Prophylaxis	Doxorubicin (Adriamycin) which is an anthracycline used in cancer chemotherapy inhibits CoQ10-dependent enzymes. CoQ10 may have a potential role in the prevention of doxorubicin-induced cardio toxicity. Pretreatment with CoQ10 may decrease its cardio toxic effects by inhibiting of doxorubicin-induced lipid per oxidation and scavenging free radicals. The researchers studied the early detection of cardio toxicity in doxorubicin-treated patients with cancer, using 50 mg doses of CoQ10 daily. The mean systolic interval improved or shortened, with increasing cumulative doses of doxorubicin (200–500 mg/m2), resulting in a decreased incidence of cardiac dysfunction. [50]
Immune Modulation	Studies have demonstrated the degree of CoQ10 deficiency is correlated with the severity of immune compromised diseases. [51] In a clinical condition of 8 adult patients treated with 60 mg of CoQ10 daily it was reported significant increases

	in serum IgG levels over 1– 4 months. CoQ10 stimulates immune system, causing augmented resistance to infection, higher antibody levels, greater numbers and/or activities of macrophages and T lymphocytes and. CD4 and CD8 are proteins found on the surface of T cells, CD4 to CD8 T-cell ratios decreased in cancer patients. [52]
Cancer	Research has shown a possible connection between CoQ10 deficiency and both carcinomas and non-malignant lesions. Blood levels of CoQ10 are frequently reduced in cancer patients; supplementation with this compound has been tested in patients undergoing traditional treatment. [53] The supplementation with the antioxidant formula including CoQ10 resulted into a significant decrease in the frequency of apoptotic CD4 and CD8 lymphocytes. They may function as antimetabolites to disrupt normal biochemical reactions required for cell growth and/or survival. [54]
Diabetes mellitus (DM)	DM is a condition of increased oxidative stress and impaired energy metabolism. Plasma levels of CoQH2 have been found to be lower in diabetic patients than healthy subjects when normalized to plasma cholesterol levels. However, 200 mg of CoQ10 daily for 6 months did not improve glycemic control or serum lipid levels in Type-2 diabetics. [55] In a trial with Type-1 diabetic patient's supplementation with 100 mg of CoQ10 daily for 3 months neither increased glycemic control nor decreased insulin requirements. Therefore, supplemented CoQ10 could be used safely as adjunct therapy for CD in diabetic patients. It was reported CoQ10 may be effective in the neuromuscular symptoms associated with mitochondrial dysfunction in DM. Although mitochondrial diabetes accounts for less than 1% of all diabetes, long-term CoQ10 addition in doses of 150 mg daily may enhance insulin secretion and prevent progressive hearing loss in these patients.[56]
Periodontal Disease	Decreased serum and gingiva levels of CoQ10 were recorded in patients with periodontal diseas. In 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. [57]
Migraine Headaches	CoQ10 was shown to prevent migraine. 32 patients with a history of migraine were treated with of CoQ10 in doses of 150 mg daily. 61.3% of the patients had a greater than 50% reduction with migraine headache. The reduction in migraine frequency after 1 month of treatment was 13.1% and this increased to 55.3% by the end of 3 months with no side-effects of CoQ10.[58]
Male Fertility	An excess of ROS weaken sperm cell function and play a negative role in male fertility. CoQ10 may play a positive role in the treatment of asthenozoospermia because of its antioxidant properties. CoQ10 levels increased in seminal plasma and in sperm cells after treatment. Due to its energy supporting properties, CoQ10 is also responsible for sperm production and all energy- dependent processes in the sperm cell. In a research on 17 patients with low fertilization rates were given 60 mg of CoQ10 for 103 days. [59] It was demonstrated the sperm's motility rate nearly doubled. Because of the fact that benefits of CoQ10 to sperm production and that a related molecule, CoQ7, may increase the production of healthy sperm, CoQ10 was studied in infertile men and it was considered as one part of a pregnancy plan. Exposure of to a magnetic field

	caused a significant reduction in amount, motility and daily production of sperm and LDH-X activity which was more articulated than that of acute dose. CoQ10 was demonstrated to provide protection from magnetic field exposure. Supplemented CoQ10 before exposure to high magnetic field caused an important recovery. Treated mice that were harmed by the effects of the magnetic field recovered more quickly than those that had not been pretreated with CoQ10.[60, 61]
Neurodegenerative Diseases	A strong correlation is found between human myotonic dystrophic conditions and deficiencies in mitochondrial functions and energy metabolism and also a marked biochemical deficiency of CoQ10 in the cardiac and skeletal muscles of animals and humans with hereditary muscular dystrophy. In patients suffering from progressive muscular dystrophy or neurogenic atrophic disease, supplemented CoQ10 in doses of 100 mg daily for 3 months was demonstrated improvements in exercise tolerance, leg pain, fatigue, stroke volume and cardiac output. [62] The CoQ10 deficiency appears to initiate problem causing the brain damage, particularly in the cerebellum which is responsible for balance and coordination. It was reported in a patient with an encephalomyopathy, there was a muscle deficiency of CoQ10 because both brain and muscle tissues share a common step in the synthesis of this substance. [63]
Parkinson's Disease (PD)	PD is a degenerative neurological disorder for which no treatment has been shown to slow the progression. There is considerable evidence indicating oxidative damage and mitochondrial dysfunction may play a role in the pathogenesis of PD.[64] Patients with PD have low levels of CoQ10 in their mitochondria, which are a major source of free radicals within the cell. Therefore, the specificity of mitochondrial impairment was demonstrated to play a role in the degeneration of nigrostriatal dopaminergic neurons. In addition, MPTP generating 1-methyl-4-phenylpyridine (MPP (+)) destroyed dopaminergic neurons in the SN. CoQ10 was able to attenuate the MPTP-induced loss of striatal dopaminergic neurons because of the fact that the serum levels of CoQ10 are normal in patients with PD. On the other hand, there was no relation found between the normality of serum CoQ10 and CoQ10 /cholesterol ratio with the risk for PD.[65]
Huntington's disease (HD)	HD is a neurodegenerative disorder characterized by selective degeneration of striatal spiny neurons. Symptoms, such as movement disorders and impaired cognitive function, typically develop in the fourth decade of life and progressively deteriorate over time. Impaired mitochondrial function and glutamate-mediated neurotoxicity was found to play roles in the pathology of HD. Additional CoQ10 was demonstrated to decrease brain lesion size in animal models of HD and to decrease brain lactate levels in HD patients. On the other hand, a combination of CoQ10 and remacemide, N-methyl-D-aspartate receptor antagonist, resulted in temporarily improved motor performance and did not prolong survival in mice with HD.[66] The potential beneficial effects of CoQ10 in animal models of PD, amyotrophic later a sclerosis (ALS) and HD were investigated. CoQ10 protected against striatal lesions produced by the mitochondrial toxins malonate and 3-nitropropionic acid which was utilized to model the striatal pathology occurs in HD and also protected against MPTP

	toxicity. [67] CoQ10 significantly extended survival in a transgenic mouse model of ALS. In addition, it also extended survival, delay motor deficits and weight loss and attenuate the development of striatal atrophy in a transgenic mouse model of HD. In this model, when combined with the remacemide, CoQ10 was able to work synergistically with it.[68]
HIV/AIDS	There is limited evidence that natural levels of CoQ10 in the body may be reduced in people with HIV/AIDS. [69] There is no reliable scientific research showing that CoQ10 supplements have any effect on this disease.[70]
Mitochondrial diseases and Kearns-Sayre syndrome:	COQ10 is often recommended for patients with mitochondrial diseases, including myopathies, encephalomyopathy and Kearns-Sayre syndrome. Several early studies report improvements in metabolism and physical endurance in patients with these conditions after treatment with CoQ10, although most available research is not high quality or definitive.[70]
Aging & Life Extension	Coenzyme Q10 may retard various aspects of the Aging Process (including the Aging Process within the Brain). The Heart's Coenzyme Q10 levels decline with the progression of the Aging Process. Coenzyme Q10 may possess Life Extension potential: Coenzyme Q10 may reverse accelerated Apoptosis of Cells involved in the Aging Process (this means that Coenzyme Q10 may have potential as a Life Extension agent by retarding the accelerated death of Cells involved in the Aging Process). [71]

Coenzyme Q10 may enhance the Function of these Substances [72, 73]

Table 4: CoQ10 Enhance the Function of These Substances

Carbohydrates	Coenzyme Q10 (applied topically) may increase the synthesis of Hyaluronic Acid by the Skin's Fibroblasts.
Electron Transport System	Coenzyme Q10 may enhance the function of Complex I.
Hormones	Coenzyme Q10 may facilitate the production of Insulin by the Pancreas
Immune System Chemicals	Coenzyme Q10 may increase the body's production of IgG.
Krebs Cycle Chemicals	Coenzyme Q10 may facilitate the production of Adenosine Triphosphate (ATP) in the Mitochondria.
Neurotransmitters	Coenzyme Q10 (especially when administered concurrently with NADH) may prevent the depletion of Dopamine caused by the Neurotoxin, MPTP: Coenzyme Q10 alone may slightly blocks the depletion of Dopamine caused by MPTP and when Coenzyme Q10 is administered concurrently with NADH it totally blocks Dopamine depletion.
Nucleic Compounds	Coenzyme Q10 may protect Deoxyribonucleic Acid (DNA) from oxidative damage from Free Radicals (via its Antioxidant properties): Coenzyme Q10 may inhibit the Free Radicals damage caused by Doxorubicin to Mitochondrial DNA.

Pharmaceutical Drugs	Coenzyme Q10 may improve the effectiveness of Beta-Blockers. Coenzyme Q10 may reduce the severity of the toxic side effects associated with Doxorubicin and may also increase the potency of Doxorubicin in its ability to kill Cancer cells by 200%. Coenzyme Q10 may prevent the damage to Liver Cells caused by Fluorouracil. Coenzyme Q10 may prevent the damage to Liver Cells caused by Mitomycin-C.
Proteins	Coenzyme Q10 enhance the function of (and in some cases can substitute for) Cytochrome C.
Vitamins	Biotin is synergistic with Coenzyme Q10. Coenzyme Q10 may help to "regenerate" Vitamin E.

These Substances Enhance the Function of Coenzyme Q10 [74-75]

Table 5: Substances which Enhance the Function if CoQ10

Amino Acids	Carnitine enhances the function of Coenzyme Q10. Methionine activates Coenzyme Q10. Tyrosine is required for the endogenous production of Coenzyme Q10
Coenzymes	NADH increases the effectiveness of supplemental Coenzyme Q10.
Enzymes	HMG-CoA Reductase is an essential catalyst for the endogenous production of Coenzyme Q10.
Lipids	Cardiolipin facilitates the transportation of Coenzyme Q10 into the Mitochondria of Cells.
Minerals	Selenium enhances the body's production of Coenzyme Q10.
Quinones	Healthy humans can convert Coenzymes Q1 - Q9 into Coenzyme Q10 (e.g. 2 x CoQ1 + 4 x CoQ7 = 3 x CoQ10).
Vitamins	Biotin is synergistic with Coenzyme Q10. Folic Acid is an essential cofactor for the endogenous synthesis of Coenzyme Q10. Lipoic Acid regenerates Coenzyme Q10. Vitamin B2 is an essential cofactor for the endogenous synthesis of Coenzyme Q10. The Niacinamide form of Vitamin B3 is an essential cofactor for the endogenous synthesis of Coenzyme Q10. Vitamin B5 is synergistic with Coenzyme Q10 and is involved in the endogenous synthesis of Coenzyme Q10. Vitamin B6 is an essential cofactor for the endogenous synthesis of Coenzyme Q10. Vitamin B12 is an essential cofactor for the endogenous synthesis of Coenzyme Q10.

Coenzyme Q10 may reduce the Toxicity of these Substances [76-78]

Table 6: CoQ10 reduces the Toxicity of these Substances

Aldehydes	Coenzyme Q10 may lower Malondialdehyde levels
Amino Acids	Coenzyme Q10 may counteract the toxicity of Glutamic Acid.
Carbohydrates	Coenzyme Q10 may counteract the toxic effects of Lipopolysaccharides (it counteracts Endotoxemia).
Enzymes	Coenzyme Q10 (applied topically) may inhibit the activity of Collagenase in the Fibroblasts of the Dermis of the Skin.
ImmuneSystem Chemicals (Cytokines):	Coenzyme Q10 may retard the ability of Tumor Necrosis Factor (TNF) to inhibit the maturation of Oligodendroglia.
Neurotoxins	Coenzyme Q10 may inhibit the ability of many Neurotoxins to destroy Neurons in the Brain: Coenzyme Q10 may inhibit the ability of MPP+ to damage Neurons. Coenzyme Q10 (especially when administered concurrently with NADH) may prevent the depletion of Dopamine caused by the Neurotoxin, MPTP.
Pharmaceutical Drugs	Coenzyme Q10 may counteract the Muscle Pain caused by HMG-CoA Reductase Inhibitors (Statins). Coenzyme Q10 may prevent the damage to Liver Cells caused by Mitomycin C. Phenothiazines inhibit various endogenous Enzymes that are dependent upon Coenzyme Q10 (this inhibition may be reversed with the concurrent use of supplemental Coenzyme Q10). Tricyclic Antidepressants (TCAs) inhibit various endogenous Enzymes that are dependent upon Coenzyme Q10 (this inhibition may be reversed with the concurrent use of supplemental Coenzyme Q10).

Adverse Effects

CoQ10 is well-tolerated and no serious adverse effects of CoQ10 in humans have been associated with its use and include epigastric discomfort (0.39%), appetite suppression (0.23%), nausea (0.16%) and diarrhea (0.12%). These dose-related complaints are minimized with dose reduction and/or dose division as mentioned above. Higher than 300 mg daily was reported to increase serum LDH and SGOT levels, but no hepatotoxicity was observed. Late night administration was stated to cause insomnia. It a trial with 2664 patient's minor adverse effects was reported in 1.5% of the patients. The daily dosage of CoQ10 was 50-150 mg orally. After test treatment of 3 months, improved clinical signs and symptoms as follows: sweating 79.8%, oedema 78.6%, cyanosis 78.1%, pulmonary rales 77.8%, palpitations 75.4%, vertigo 73.1%, jugular reflux 71.81%, subjective arrhythmia 63.4%, insomnia 62.8%, nocturia 53.6%, dyspnoea 52.7% and enlargement of liver area 49.3%.[79]

Future trends

The importance of how drugs are formulated for bioavailability is well known. In order to find a principle to boost the bioavailability of CoQ_{10} after oral administration, several new approaches have been taken and different formulations and forms have been developed and tested on animals or humans.[79]

Conclusion

CoQ10 oil soluble synthetic vitamin like substance used in prevention and cure of most life threatening diseases. It also works as immuno modulator and hence proved as a gift for one suffering from immuno deficiency disorders. It also helps in management of pain and depression.

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