Coenzyme Q10

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Coenzyme Q10 is a vitamin-like substance used in the treatment of a variety of disorders primarily related to suboptimal cellular energy metabolism and oxidative injury. Studies supporting the efficacy of coenzyme Q10 appear most promising for neurodegenerative disorders such as Parkinson's disease and certain encephalomyopathies for which coenzyme Q10 has gained orphan drug status. Results in other areas of research, including treatment of congestive heart failure and diabetes, appear to be contradictory or need further clarification before proceeding with recommendations. Coenzyme Q10 appears to be a safe supplement with minimal side effects and low drug interaction potential. (Am Fam Physician 2005;72:1065-70. Copyright © 2005 American Academy of Family Physicians.)

Coenzyme Q10 (2,3 dimethoxy-5 methyl-6-decaprenyl benzoquinone) is a fat-soluble, vitamin-like quinone commonly known as ubiquinone, CoQ, and vitamin Q10.[1,2] It is available in more than 100 single-ingredient and combination-ingredient products, and in 2002 it accounted for more than $200 million in sales in the United States.[3] Coenzyme Q10 was first isolated in 1957 in beef mitochondria, and is found in highest concentrations in tissues with high energy turnover such as the heart, brain, liver, and kidney.[2] Coenzyme Q10 is a ubiquitous compound vital to a number of activities related to energy metabolism. Because dysfunctional energy metabolism has been cited as a contributing factor for a number of conditions, coenzyme Q10 has been indicated in the treatment of cardiac, neurologic, oncologic, and immunologic disorders. Although the Dietary Supplement Health and Education Act of 1994 does not allow claims for treatment of specific diseases in the United States, coenzyme Q10 has been cleared for treatment indications in other countries, such as for congestive heart failure (CHF) in Japan since 1974.[2]

Pharmacology

Coenzyme Q10 is vital for the proper transfer of electrons within the mitochondrial oxidative respiratory chain, whose main function is adenosine triphosphate production. Coenzyme Q10 also appears to increase adenosine triphosphate levels by preventing the loss of the adenine nucleotide pool from cardiac cells.[4] Additionally, coenzyme Q10 has demonstrated activity in preventing lipid peroxidation as an antioxidant scavenger and an indirect stabilizer of calcium channels to decrease calcium overload.[5,6]

Much of the basic research in support of coenzyme Q10 supplementation has focused on the CHF model. The myocardium of patients with CHF demonstrates increased oxidative stress[7] as well as decreased concentrations of coenzyme Q10 as confirmed by tissue assays.[8] These levels appear to correlate with CHF severity in the animal and human model, with coenzyme Q10 supplementation protecting against ischemia and reperfusion injury in animal studies.[9,10]

Uses and Efficacy

Coenzyme Q10's wide-ranging cellular properties implicate it for the potential treatment of numerous conditions that may improve with mitochondrial and antioxidant support.

NEUROLOGIC AND METABOLIC INDICATIONS

Parkinson's Disease. A randomized, double-blind, placebo-controlled, multicenter study[11] of 80 patients found that 1,200 mg per day of

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
Coenzyme Q10 may be used for slowing of functional decline in patients with Parkinson's disease.	B	11, 12
The evidence is too inconsistent to recommend use of coenzyme Q10 in symptomatic treatment of congestive heart failure.	B	19-22
Data are insufficient to recommend use of coenzyme Q10 for improved glycemic control in diabetes mellitus.	B	29-31

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 983 or http://www.aafp.org/afpsort.xml.

coenzyme Q10 was associated with up to 44 percent less functional decline in patients with Parkinson's disease, including activities of daily living. A study[12] of 28 patients with Parkinson's disease also demonstrated mild symptom improvement with daily oral dosing of 360 mg of coenzyme Q10. These results are awaiting confirmation.

Mitochondrial Encephalomyopathies. In studies[13-15] with eight to 44 patients, coenzyme Q10 also has demonstrated positive trends in reducing symptoms associated with selected mitochondrial abnormalities including the mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome, Kearns-Sayre syndrome, and the myoclonus epilepsy with ragged-red fibers (MERRF) syndrome. Maximum effect often requires six or more months of therapy.[13-15] One type of coenzyme Q10, UbiQGel, was granted U.S. Food and Drug Administration (FDA) orphan drug status for treatment of mitochondrial cytopathies based on several small trials.[16]

Migraine. A preliminary open label trial[17] of 32 patients taking 150 mg of coenzyme Q10 daily demonstrated efficacy in reducing the frequency of migraine attacks. A recent randomized double-blind, placebo-controlled trial[18] of 42 patients taking coenzyme Q10 at 300 mg a day found similar benefit. The response rate (i.e., decrease in headache frequency by 50 percent or more) was 47.6 percent in the coenzyme Q10 group and 14.4 percent in the placebo group. The number needed to treat was three.

Other Neurologic Indications. Coenzyme Q10 at 600 mg or less did not delay progression of decline[19] in functional ability in Huntington's disease, but it also has FDA orphan drug status for this disease.

CARDIOVASCULAR INDICATIONS

CHF. A number of randomized controlled trials,[20-22] including those in a 1997 meta-analysis,[23] found improvement in several clinical parameters related to CHF, including frequency of hospitalization, dyspnea, and edema. These trials were weakened by small numbers (only two of 14 trials had more than 25 participants) and older techniques for calculating ejection fraction. Of the more recent randomized trials using ventriculography and echocardiography, two found coenzyme Q10 at 100 to 200 mg daily no more effective than placebo in improving ejection fraction,

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peak oxygen consumption, exercise duration, or quality of life.[24,25] A more recent trial[26] using coenzyme Q10 in combination with carnitine and taurine did find modest clinical improvement. The recently released Agency for Healthcare Research and Quality (AHRQ) report[27] that examined cardiovascular trials with more than 60 participants followed for at least six months concluded that coenzyme Q10's role is still an open question. The planned SYMptoms, BIomarker status (BNP), and long-term Outcome trial with more than 500 patients with New York Heart Association class III and IV CHF followed over two years, should help answer this question.[28]

Hypertension. A systematic review[29] of eight trials using coenzyme Q10 at various doses for essential hypertension, typically as adjuvant therapy, found a mean decrease in systolic and diastolic blood pressure of 16 and 10 mm Hg, respectively. Several of these trials[30] demonstrated confounding variables or were weakened by low statistical power.

Other Indications. The evidence for coenzyme Q10 use in other cardiovascular settings is promising and requires larger, longer-term trials. In placebo-controlled trials, the coenzyme's use following cardiopulmonary resuscitation demonstrated improvement in three-month survival (n = 49),[31] and its use following cardiac surgery demonstrated improvements in myocardial isoenzyme levels, left ventricular function, and postoperative recovery time (n = 20).[32]

Preliminary data also imply benefit in the setting of atherosclerosis. This includes a randomized, placebo-controlled trial[33] of 73 patients who were randomized to 120 mg a day of coenzyme Q10 following myocardial infarction. At one year, the coenzyme Q10 group demonstrated a significant decrease in total cardiac events including nonfatal myocardial infarctions and cardiac deaths. This improvement has been attributed to possible attenuation of endothelial dysfunction.[34] Research in other conditions, including angina pectoris, cardiomyopathy and physical exercise capacity, demonstrate conflicting results and require additional study.

DIABETES

Coenzyme Q10 has been considered for improving glycemic control through various mechanisms, including a decrease in oxidative stress. Two earlier randomized controlled trails[35,36] using 100 to 200 mg of coenzyme Q10 in patients with type 1 or 2 diabetes found no difference in glycemic control and insulin requirement. A more recent randomized controlled trial (n = 74)[37] using 200 mg per day for 12 weeks found modest improvements in A1C levels (-0.37 ± 0.17 percent, $P = .32$).

OTHER INDICATIONS

Although it is used for the prevention and treatment of cancer, the AHRQ found no evidence to assess the efficacy of coenzyme Q10 for this use.[38] Research continues with several phase II trials underway to clarify its potential contribution in the treatment of conditions, such as Duchenne's muscular dystrophy, breast cancer, human immunodeficiency virus and acquired immunodeficiency syndrome, periodontal disease, and Alzheimer's disease.

Contraindications, Adverse Effects, and Interactions

No absolute contraindications are known for coenzyme Q10, although reliable information about its use in pregnant or breastfeeding mothers or in young children is not available. Adverse effects with coenzyme Q10 are rare. On average, mild gastrointestinal discomfort is reported in less than 1 percent of patients in clinical trials.[39] Potential interactions with warfarin (Coumadin) causing decreased international normalized ratio (INR) have been reported in case studies.[40] However, a prospective placebo-controlled trial of 24 stable patients taking warfarin and 100 mg of coenzyme Q10 over four weeks found no significant change in prothrombin time and INR levels.[41] Because of coenzyme Q10's potential hypoglycemic and hypotensive effects, monitoring is advised, especially when using adjunctively with prescription medications.

Several trials demonstrate coenzyme Q10 depletion subsequent to statin initiation.[42,43] There is conjecture about this depletion as the cause of statin–associated adverse effects

TABLE 1
Selected Coenzyme Q10 Brands*

Product name	*Dosage*	*Formulation*
Biosan	60 to 120 mg	Capsule
Carlson	50 mg	Softgel
CVS pharmacy	100 mg	Softgel
Enzymatic therapy/ Vitaline	100 to 200 mg	Chewable
Nature Made	100 mg	Softgel
Nature's Bounty	75 to 150 mg	Softgel
Nutrilite	30 to 90 mg	Softgel
Olay vitamins	150 mg	Softgel
Origin	100 mg	Softgel
Puritan's Pride	75 to 200 mg	Softgel
Spring Valley	150 mg	Softgel
Sundown	50 to 150 mg	Softgel
Vitamin World	90 to 200 mg	Softgel

*—Passing independent content verification.

Complete product information available online at http://www.consumerlab.com/results/CoQ10.asp.

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(e.g., myopathy) with exogenous coenzyme Q10 supplementation as a possible mediating treatment. This assertion is refuted by a more recent crossover trial[44] that found no significant coenzyme Q10 drop after initiation of selected statins. Several doxorubicin (Adriamycin) trials, mostly in animal models, have noted a reduction in cardiac coenzyme Q10 depletion and cardiotoxicity associated with coadministration of coenzyme Q10. The clinical implications on disease state and adverse reaction profile with coenzyme Q10 supplementation in depleted states requires further evaluation.

Dosage and Standardization

The majority of coenzyme Q10 products are synthesized in Japan through proprietary fermentation of yeast strains.[45] It is available in various formulations, with research demonstrating variation in bioavail-

TABLE 2
Key Points About Coenzyme Q10

Efficacy	Parkinson's disease and mitochondrial cytopathies: preliminary evidence for benefit Congestive heart failure, hypertension, and ischemic heart disease: conflicting or preliminary evidence Diabetes: conflicting evidence for improvement in glycemic control
Adverse effects	Rare: gastrointestinal upset reported in less than 1 percent of study participants
Interactions	Warfarin (Coumadin): potential interaction in case report only, with no interaction noted in prospective trial Hypoglycemia: potential synergistic effects; monitor patients Antihypertensive agents: potential synergistic effects; monitor patients
Dosages	Mitochondrial cytopathies: 150 mg per day or 2 mg per kg per day with titration up to 3,000 mg per day in some patients Parkinson's disease: 300 to 1,200 mg per day in four divided doses Cardiovascular: typically 50 to 200 mg per day Diabetes: 100 to 200 mg per day Available in various oral formulations
Cost*	Varies with dosage and brand; monthly cost for 100 mg per day is approximately $30 and for 1,200 mg per day is approximately $300
Bottom line	Safe but expensive supplement with preliminary benefit in neurology, including Parkinson's disease, and inconsistent results in cardiovascular disease requiring further long-term research

*—Average wholesale cost, based on Red Book, Montvale, N.J., Medical Economics Data, 2005.

ability and dosage consistency.[46,47] Selected brands that have passed independent testing for product purity and consistency are listed in *Table 1*.[47] Brands used in positive randomized controlled trials include Vitaline for Parkinson's disease and UbiQGel for mitochondrial cytopathies. The efficacy, adverse effects, interactions, dosages, cost, and bottom line are summarized in *Table 2*.

Update

The American College of Cardiology recently published an expert consensus document on integrating complementary medicine into cardiovascular medicine. Their conclusions regarding the use of coenzyme Q10 are consistent with those discussed above. The value of coenzyme Q10 in cardiovascular disease and with statin use has not been clearly established. *(Vogel JH, Bolling SF, Costello RB, Guarneri EM, Krucoff MW, Longhurst JC, et al. Integrating complementary medicine into cardiovascular medicine. J Am Coll Cardiol 2005;46:184-221.)*

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