

## Coenzyme Q10 (CoQ10)

### TRADE NAMES

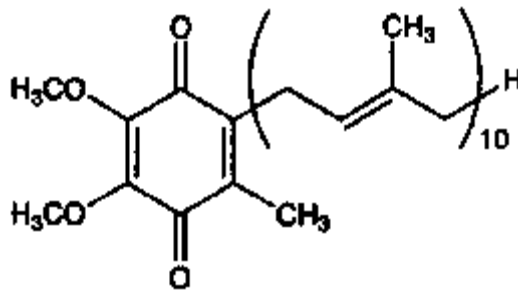
Coenzyme Q10 (CoQ10) is available generically from numerous manufacturers. Branded products include Lynae CoQ10 (Boscogen), Natures Blend Coenzyme Q10 (National Vitamin Company) and Ultra CoQ10 (Twinlab).

### DESCRIPTION

Coenzyme Q<sub>10</sub> or CoQ<sub>10</sub> belongs to a family of substances called ubiquinones. Ubiquinones, also known as coenzymes Q and mitoquinones, are lipophilic, water-insoluble substances involved in electron transport and energy production in mitochondria. The basic structure of ubiquinones consists of a benzoquinone "head" and a terpinoid "tail." The "head" structure participates in the redox activity of the electron transport chain. The major difference among the various coenzymes Q is in the number of isoprenoid units (5-carbon structures) in the "tail." Coenzymes Q contain one to 12 isoprenoid units in the "tail"; 10 isoprenoid units are common in animals.

Coenzymes Q occur in the majority of aerobic organisms, from bacteria to plants and animals. Two numbering systems exist for designation of the number of isoprenoid units in the terpinoid "tail": coenzyme Q<sub>n</sub> and coenzyme Q(x). N refers to the number of isoprenoid side chains, and x refers to the number of carbons in the terpinoid "tail" and can be any multiple of five. Thus, coenzyme Q<sub>10</sub> refers to a coenzyme Q having 10 isoprenoid units in the "tail." Since each isoprenoid unit has five carbons, coenzyme Q<sub>10</sub> can also be designated coenzyme Q(50). The structures of coenzymes Q are analogous to those of vitamin K2.

Coenzyme Q<sub>10</sub> is also known as Coenzyme Q(50), CoQ<sub>10</sub>, CoQ(50), ubiquinone (50), ubiquinol— 10 and ubidecarerone. Chemically, CoQ<sub>10</sub> is known as 2, 3-dimethoxy-5-methyl-6-decaprenyl-1,4-benzoquinone, and its structural formula is:



CoEnzyme Q<sub>10</sub>

It is a solid wax-like substance. CoQ<sub>10</sub> is the predominant form in humans, and CoQ<sub>9</sub> is the predominant form in rats.

Supplemental CoQ<sub>10</sub> is typically derived from tobacco leaf extracts and fermented sugar cane and beets.

## ACTIONS AND PHARMACOLOGY

### ACTIONS

Supplemental CoQ<sub>10</sub> may have cardioprotective, cytoprotective and neuroprotective activities.

### MECHANISM OF ACTION

Since the actions of supplemental CoQ<sub>10</sub> have yet to be clarified, the mechanism of these actions is a matter of speculation. However, much is known about the biochemistry of CoQ<sub>10</sub>. CoQ<sub>10</sub> is an essential cofactor in the mitochondrial electron transport chain, where it accepts electrons from complex I and II, an activity that is vital for the production of ATP.

CoQ<sub>10</sub> has antioxidant activity in mitochondria and cellular membranes, protecting against peroxidation of lipid membranes. It also inhibits the oxidation of LDL-cholesterol. LDL-cholesterol oxidation is believed to play a significant role in the pathogenesis of atherosclerosis.

CoQ<sub>10</sub> is biosynthesized in the body and shares a common synthetic pathway with cholesterol. CoQ<sub>10</sub> levels decrease with aging in humans. Why this occurs is not known but may be due to decreased synthesis and/or increased lipid peroxidation which occurs with aging.

### PHARMACOKINETICS

CoQ<sub>10</sub> is absorbed from the small intestine into the lymphatics; from there it enters the blood. Absorption of CoQ<sub>10</sub> is poor. Well over 60%

of an oral dose is excreted in the feces. Furthermore, absorption of CoQ<sub>10</sub> is highly variable and depends not only on food intake but also on the amount of lipids present in the food. Absorption is lower on an empty stomach and greater when taken with food of high lipid content. In the blood, CoQ<sub>10</sub> is partitioned into the various lipoprotein particles, including VLDL, LDL and HDL.

It takes about three weeks of daily dosing with CoQ<sub>10</sub> to reach maximal serum concentrations, which then plateau with continuous daily dosing. CoQ<sub>10</sub> is distributed to the various tissues of the body and is able to enter the brain. The main elimination of CoQ<sub>10</sub> occurs via bile.

## INDICATIONS AND USAGE

Coenzyme Q<sub>10</sub> may be indicated in cardiovascular disease, particularly in congestive heart failure. It may also be indicated to correct reduced blood levels of CoQ<sub>10</sub> that result from the use of HMG-CoA reductase inhibitors used to treat elevated cholesterol levels. It also appears to have usefulness in the management of periodontal disease in some. There is far less evidence to support claims that it has positive effects in cancer, muscular dystrophy and immune dysfunction. Similarly, there is as yet no reliable evidence that it can inhibit obesity or enhance athletic performance.

## RESEARCH SUMMARY

There are many studies, spanning more than two decades, reporting positive results from the use of CoQ<sub>10</sub> as adjunctive therapy in the treatment of congestive heart failure. CoQ<sub>10</sub> has been an approved drug in Japan for use in congestive heart failure since 1974. It has also been approved for this use in some other countries. Several studies have demonstrated a strong correlation between severity of heart disease and severity of CoQ<sub>10</sub> deficiency. Some have suggested that this deficiency is the primary cause of some variations of heart muscle dysfunction, while others believe it plays a secondary role in the etiology of heart failure.

Early studies of congestive heart failure focused on idiopathic dilated cardiomyopathy, testing CoQ<sub>10</sub> against placebo using echocardiography to assess heart function. Echocardiographic improvement seen in these studies was generally slow but sustained and was accompanied by diminished fatigue, chest pain, dyspnea and palpitations. Normal heart size and function were restored in some patients using only CoQ<sub>10</sub>; this occurred primarily in patients with recent onset of congestive heart failure.

Subsequently, nearly all of the several placebo-controlled studies investigating CoQ<sub>10</sub>'s effects on heart muscle function have reported significant positive results. One multi-center Italian study included 2,664 patients with congestive heart failure. No notable adverse

effects on drug interactions have been reported in these studies except for one report that noted a slight diminution in coumadin activity.

Many studies to date have examined CoQ<sub>10</sub> as an addition to standard medical treatments. In several studies involving hypertension and other manifestations of cardiovascular disease, there was a significant reduction in the use of concomitant drug therapies when CoQ<sub>10</sub> was added to the treatment regimen.

It is now known that the HMG-CoA reductase inhibitors, while very effective in lowering cholesterol levels, also significantly lower levels of CoQ<sub>10</sub>. This may be particularly hazardous for patients with heart failure, suggesting a possible indication for CoQ<sub>10</sub> in many, if not all, individuals using these cholesterol-lowering drugs. There has been some suggestion that CoQ<sub>10</sub>, especially if it could be more readily absorbed, might be a cholesterol-lowering agent itself. There is, however, no evidence for this.

Significant CoQ<sub>10</sub> deficiencies have been noted in diseased gingiva. CoQ<sub>10</sub>'s efficacy in reducing gingival inflammation and periodontal pocket-depth has been demonstrated in placebo-controlled trials. Claims that CoQ<sub>10</sub> might be an effective anti-cancer agent are based upon a few suggestive case histories that will require far more rigorous clinical investigation before these claims can be properly evaluated. Similarly, claims that CoQ<sub>10</sub> might be useful in AIDS and some other immune dysfunctions are premature.

It is not unreasonable to hypothesize that CoQ<sub>10</sub> might be helpful in muscular dystrophy—and there is some very preliminary animal and clinical data suggesting that it might be. Muscular dystrophy is usually associated with cardiac disease. Research is ongoing but, to date, is inconclusive.

There is also some evidence that CoQ<sub>10</sub> might boost energy and speed recovery of exercise-related muscle exhaustion and damage. This work, too, needs more rigorous followup.

There is no evidence that CoQ<sub>10</sub> can inhibit obesity.

## **CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS**

### **CONTRAINDICATIONS**

None known.

### **WARNINGS AND PRECAUTIONS**

There is one report of CoQ<sub>10</sub> decreasing the effectiveness of warfarin. Those taking warfarin should be aware of this possibility.

Because of lack of long-term safety studies, pregnant women and nursing mothers should avoid CoQ<sub>10</sub> supplements.

Clinical reports from Japan suggest that supplemental CoQ<sub>10</sub> may improve beta-cell function and glycemic control in type II diabetics. CoQ<sub>10</sub> does not appear to improve glycemic control in type I diabetics. Diabetics should be made aware of this possibility, and those diabetics who do use supplemental CoQ<sub>10</sub> should determine by appropriate monitoring if they need to make any adjustments in their diabetic medications.

## ADVERSE REACTIONS

Mild gastrointestinal symptoms such as nausea, diarrhea and epigastric distress have been reported, particularly with higher doses (200 milligrams or more daily).

## INTERACTIONS

### DRUGS

*Warfarin:* There is one report of CoQ<sub>10</sub> decreasing the effectiveness of warfarin.

*Statins:* CoQ<sub>10</sub> and cholesterol share the same metabolic pathways. Inhibition of the enzyme 3-hydroxy-3-methylglutonyl coenzyme A (HMG-CoA) reductase would be expected to decrease CoQ<sub>10</sub> levels. The statin drugs lovastatin, simvastatin and pravastatin are known to decrease CoQ<sub>10</sub> levels in humans. It is likely that all statins have this effect.

*Doxorubicin:* CoQ<sub>10</sub> may help ameliorate the cardiotoxicity of doxorubicin.

*Antidiabetic medications:* CoQ<sub>10</sub> may improve glycemic control in some type II diabetics. If this were to occur, antidiabetic medications might need appropriate adjusting.

*Beta Blockers:* Some beta blockers, in particular propanolol, have been reported to inhibit some CoQ<sub>10</sub>-dependent enzymes

*Piperine:* Piperine, found in black pepper, may increase plasma levels of CoQ<sub>10</sub>.

## DOSAGE AND ADMINISTRATION

CoQ<sub>10</sub> is available in different formulations: oil-based capsules, powder-filled capsules, and tablets and solubilized softgels (microemulsions and others). The solubilized softgels are claimed to give higher absorption.

Daily doses of CoQ<sub>10</sub> range from 5 to 300 milligrams. Those who use CoQ<sub>10</sub> for periodontal health take 100 to 150 milligrams daily. Effectiveness, if any, is thought to be obtained with doses of 50 to 200 milligrams daily. The same dose range applies to those who take statin drugs for treatment of hypercholesterolemia.

CoQ<sub>10</sub> is best taken with food. About three weeks of daily dosing are necessary to reach maximal serum concentrations of CoQ<sub>10</sub>.

CoQ<sub>10</sub> is also available topically in some toothpastes and skin creams.

## HOW SUPPLIED

*Capsules* — 10 mg, 30 mg, 50 mg, 75 mg, 100 mg, 150 mg

*Chewable Tablets* — 100 mg, 200 mg

*Liquid* — 30 mg/5 mL

*Powder*

*Tablets* — 25 mg, 50 mg, 60 mg, 200 mg

*Wafers* — 60 mg, 200 mg

## LITERATURE

Atar D, Mortensen SA, Flachs H, Herzog WR. Coenzyme Q<sub>10</sub> protects ischemic myocardium in an open-chart swine model. *Clin Investig.* 1993; 71(Suppl):S103-S111.

Baggio E, Gandini R, Plancher AC, et al. Italian multicenter study on the safety and efficacy of coenzyme Q<sub>10</sub> as adjunctive therapy in heart failure. *Mol Aspects Med.* 1994; 15(Suppl):287-294.

Bergossi AM, Grossi G, Fioletta PL, et al. Exogenous CoQ<sub>10</sub> supplementation prevents plasma ubiquone reduction induced by HMG-CoA reductase inhibitors. *Mol Aspects Med.* 1994; 15(Suppl):187-193.

Bliznakov EM, Wilkins DJ. Biochemical and clinical consequences of inhibiting coenzyme Q<sub>10</sub> biosynthesis by lipid-lowering HMG-CoA reductase inhibitors (statins). *Advanc Therap.* 1998; 15:218-228.

Chopra RK, Goldman R, Sinatra ST, Bhagavan HN. Relative bioavailability of coenzyme Q<sub>10</sub> formulations in human subjects. *Int J Vitam Nutr Res.* 1998; 68:109-113.

Crane FL, Sun IL, Sun EE. The essential functions of coenzyme Q. *Clin Investig.* 1993; 71(Suppl):S55-S59.

Folkers K, Mortensen SA, Littarru GP, Yamagami T, Lenaz G, eds. The biochemical and clinical aspects of coenzyme Q. *Clin Investig.* 1993; 71(Suppl):S51-S178.

Folkers K. Critique of 30 years of research on hematopoietic and immunological activities of coenzyme Q<sub>10</sub> and potentiality for therapy of AIDS and cancer. *Med Chem Res.* 1992; 2:48-60.

Folkers K, Hanioka T, Xia L-J, et al. Coenzyme Q<sub>10</sub> increase T4/T8 ratios of lymphocytes in ordinary subjects and relevance to patients having the AIDS related complex. *Biochem Biophys Res Comm.* 1991; 176:786-791.

Folkers K, Langsjoen P, Willis R, et al. Lovastatin decreases coenzyme Q levels in humans. *Proc Natl Acad Sci USA.* 1990; 87:8931-8934.

Folkers K, Vadhanavikit S, Mortensen SA. Biochemical rationale and myocardial tissue data on the protective therapy of cardiomyopathy with coenzyme Q<sub>10</sub>. *Proc Natl Acad Sci USA.* 1985; 82:901-904.

Ghirlanda G, Oradei A, Manto A, et al. Evidence of plasma CoQ<sub>10</sub> - lowering effect by HMG-CoA reductase inhibitors: a double-blind, placebo-controlled study. *J Clin Pharmacol.* 1993; 33:226-229.

Hanioka T, Tanaka M, Oijima M, et al. Effect of topical application of coenzyme Q<sub>10</sub> on adult periodontitis. *Molec Aspects Med.* 1994; 15 (suppl):S241-S248.

Hanaki Y, Sugiyama S, Ozawa T, Ohno M. Coenzyme Q<sub>10</sub> and coronary artery disease. *Clin Investig.* 1993; 71 (suppl):S112-S115.

Henriksen JE, Andersen CB, Hother-Nielsen O, et al. Impact of ubiquinone (coenzyme Q<sub>10</sub>) treatment on glycaemic control, insulin requirement and well-being in patients with type 1 diabetes mellitus. *Diabet Med.* 1999; 16:312-318.

Hofman-Bang C, Rehnqvist N, Swedberg K, et al. Coenzyme Q<sub>10</sub> as an adjunctive in the treatment of chronic congestive heart failure. The Q<sub>10</sub> study group. *J Card Fail.* 1995; 1: 101-107.

Kishi H, Kishi T, Folkers K. Bioenergetics in clinical medicine. III. Inhibition of coenzyme Q<sub>10</sub>-enzymes by clinically used anti-hypertensive drugs. *Res Commun Chem Pathol Pharmacol.* 1975; 12:533-540.

Kishi T, Watanabe T, Folkers K. Bioenergetics in clinical medicine XV. Inhibition of coenzyme Q<sub>10</sub>-enzymes by clinically used adrenergic blockers of beta-receptors. *Rev Commun Chem Pathol Pharmacol.* 1977; 17:157-164.

Lampertico M, Comis S. Italian multicenter study on the efficacy and safety of coenzyme Q<sub>10</sub> as adjuvant therapy in heart failure. *Clin Investig.* 1993; 71 (Suppl):S129-S133.

Lass A, Sohal RS. Effect of coenzyme Q<sub>10</sub> and alpha-tocopherol content of mitochondria on the production of superoxide anion radicals. *FASEB J.* 2000; 14:87-94.

Lucker PW, Werzelberger N, Hennings G, Rehn D. Pharmacokinetics of coenzyme ubiquinone in healthy volunteers. In: Folkers K, Yamamura Y, eds. *Biomedical and clinical aspects of coenzyme Q.* Vol 4. Amsterdam: Elsevier Sci. Publ. BV. 1984; 143-148.

Matthews RT, Yang L, Browne S, et al. Coenzyme Q<sub>10</sub> administration increases mitochondrial concentrations and exerts neuroprotective effects. *Proc Natl Acad Sci USA.* 1998; 95:8892-8897.

Morisco C, Trimarco B, Condorelli M. Effect of coenzyme Q<sub>10</sub> therapy in patients with congestive heart failure: a long-term multi-center randomized study. *Clinic Investig.* 1993; 71(Suppl):S134-S136.

Pozzi F, Longo A, Lazzarini C, Careni A. Formulations of ubiquinone with improved bioavailability. *Eur J Pharm Biopharm.* 1991; 37:243-246.

Spigset O. Reduced effect of warfarin caused by ubiquinone. *Lancet.* 1994; 344:1372-1373..

Stocker R, Bowry VW, Frei B. Ubiquinol-<sub>10</sub> protects human low-density lipoprotein more efficiently against lipid peroxidation than does alpha-tocopherol. *Proc Natl Acad Sci USA.* 1991; 88:1646-50.

Tomasetti M, Littaru GP, Stocker R, Alleva R. Coenzyme Q<sub>10</sub> enrichment decreases oxidative DNA damage in human lymphocytes. *Free Rad Biol Med.* 1999; 27:1027-1032.

Tomono Y, Hasegawa J, Seki T, et al. Pharmacokinetic study of deuterium-labeled coenzyme Q<sub>10</sub> in man. *Int J Clin Pharmacol Ther Toxicol.* 1986; 24:536-541.

Watts GF, Castelluccio CLA, Riceevans CLA, et al. Plasma coenzyme Q (ubiquinone) concentration in patients treated with simvastatin. *J Clin Pathol.* 1995; 46:1055-1057.

Watts TLP. Coenzyme Q<sub>10</sub> and periodontal treatment: is there any beneficial effect? *Br Dent J.* 1995; 178:209-213.