



## NATURAL HEALTH PRODUCT

### COENZYME Q<sub>10</sub> (UBIQUINONE-10)

This monograph is intended to serve as a guide to industry for the preparation of Product Licence Applications (PLAs) and labels for natural health product market authorization. It is not intended to be a comprehensive review of the medicinal ingredient.

#### Notes

- ▶ Text in parentheses is additional optional information which can be included on the PLA and product labels at the applicant's discretion.
- ▶ The solidus (/) indicates that the terms and/or statements are synonymous. Either term or statement may be selected by the applicant.

#### Date

July 31, 2018

#### Proper name(s), Common name(s), Source material(s)

Table 1. Proper name(s), Common name(s), Source material(s)

Proper name(s)	Common name(s)	Source material(s)			
		Proper name(s)	Common name(s)	Part(s)	Preparation(s)
2,5-Cyclohexadiene-1,4-dione, 2-[(2E,6E,10E,14E,18E,22E,26E,30E,34E)-3,7,11,15,19,23,27,31,35,39-decamethyl-2,6,10,14,18,22,26,30,34,38-tetracontadecaenyl]-5,6-dimethoxy-3-methyl	<ul style="list-style-type: none"> <li>▶ Coenzyme Q<sub>10</sub></li> <li>▶ CoQ<sub>10</sub></li> <li>▶ Ubidecarenone</li> <li>▶ Ubiquinone-10</li> </ul>	<ul style="list-style-type: none"> <li>▶ <i>Agrobacterium rhizogenes</i></li> <li>▶ <i>Agrobacterium tumefaciens</i></li> <li>▶ <i>Aspergillus clavatus</i></li> <li>▶ <i>Escherichia coli</i></li> <li>▶ <i>Escherichia coli</i></li> <li>▶ <i>Gluconobacter suboxydans</i></li> <li>▶ <i>Leucosporidium scotti</i></li> <li>▶ <i>Paracoccus denitrificans</i></li> <li>▶ <i>Rhodobacter sphaeroides</i></li> <li>▶ <i>Rhodospirillum rubrum</i></li> <li>▶ <i>Saccharomyces cerevisiae</i></li> <li>▶ <i>Schizosaccharomyces pombe</i></li> </ul>	N/A	Whole	Biosynthesis
		N/A	Coenzyme Q10	N/A	Synthetic



References: Proper name: USP 30 2007; Common names: Storch et al. 2007, Sweetman 2007, USP 30 2007, Park et al. 2005, O'Neil et al. 2001; Source materials: Lipshutz et al. 2005, Kawamukai 2002, Lipshutz et al. 2002, Szkopinska 2000, Yoshida et al. 1998, Zhao et al.1997.

### **Route of administration**

Oral

### **Dosage form(s)**

This monograph excludes foods or food-like dosage forms as indicated in the Compendium of Monographs Guidance Document.

Acceptable dosage forms for the age category listed in this monograph and specified route of administration are indicated in the Compendium of Monographs Guidance Document.

### **Use(s) or Purpose(s)**

- ▶ Helps to maintain and/or support cardiovascular health (Rosenfeldt et al. 2007; Baggio et al. 1994; Langsjoen et al. 1988).
- ▶ Helps to reduce the frequency of migraine headaches and associated nausea and vomiting when taken as a prophylactic/preventative (Hershey et al. 2007; Sandor et al. 2005; Rozen et al. 2002).
- ▶ (Provides) An antioxidant (Kalpravidh et al. 2005; Rosenfeldt et al. 2005; Crane 2001; Chello et al. 1994).

### **Dose(s)**

#### **Subpopulation(s)**

Adults 18 years and older

#### **Quantity(ies)**

##### *Antioxidant*

Not to exceed 300 milligrams of Coenzyme Q<sub>10</sub>, per day (Bonakdar and Guarneri 2005; Kalpravidh et al. 2005; Rosenfeldt et al. 2005; Chello et al. 1994; Langsjoen 1994; Langsjoen et al. 1988; Tanaka et al. 1982)



### *Cardiovascular health*

30 - 300 milligrams of Coenzyme Q<sub>10</sub>, per day (Bonakdar and Guarneri 2005; Kalpravidh et al. 2005; Rosenfeldt et al. 2005; Chello et al. 1994; Langsjoen 1994; Langsjoen et al. 1988; Tanaka et al. 1982)

### *Migraine prophylaxis*

150 - 300 milligrams of Coenzyme Q<sub>10</sub>, per day (Sandor et al. 2005; Rozen et al. 2002)

### **Direction(s) for use**

No statement required.

### **Duration(s) of use**

#### *Migraine prophylaxis/prevention*

Use for at least 3 months to see beneficial effects (Hershey et al. 2007; Sandor et al. 2005; Rozen et al. 2002).

#### *Other uses*

No statement required.

### **Risk information**

#### **Caution(s) and warning(s)**

##### *All products*

- ▶ Consult a health care practitioner/health care provider/health care professional/doctor/physician prior to use if you are pregnant or breastfeeding.
- ▶ Consult a health care practitioner/health care provider/health care professional/doctor/physician prior to use if you are taking blood pressure medication (Rosenfeldt et al. 2007; Singh et al. 1999).

##### *Products providing more than 100 mg of Coenzyme Q<sub>10</sub> per day*

Consult a health care practitioner/health care provider/health care professional/doctor/physician prior to use if you are taking blood thinners (Engelsen et al. 2003; Landbo and Almdal 1998; Spigset 1994).



### *Migraine prophylaxis/prevention*

Consult a health care practitioner/health care provider/health care professional/doctor/physician if migraine frequency increases and associated nausea and vomiting persist or worsen.

#### **Contraindication(s)**

No statement required.

#### **Known adverse reaction(s)**

No statement required

#### **Non-medicinal ingredients**

Must be chosen from the current Natural Health Products Ingredients Database (NHPID) and must meet the limitations outlined in the database.

#### **Storage conditions**

No statement required.

#### **Specifications**

- ▶ The finished product specifications must be established in accordance with the requirements described in the Natural and Non-prescription Health Products Directorate (NNHPD) Quality of Natural Health Products Guide.
- ▶ The medicinal ingredient must comply with the requirements outlined in the NHPID.

#### **References cited**

Baggio E, Gandini R, Plancher AC, Passeri M, Carmosino G. Italian multicenter study on the safety and efficacy of coenzyme Q10 as adjunctive therapy in heart failure. CoQ10 Drug Surveillance Investigators. *Molecular Aspects of Medicine* 1994;15(Supplement 1):S287-S294.

Bonakdar RA, Guarneri E. Coenzyme Q10. *American Family Physician* 2005;72(6):1065-1070.

Chello M, Mastroroberto P, Romano R, Bevacqua E, Pantaleo D, Ascione R, Marchese AR, Spampinato N. Protection by Coenzyme Q10 from myocardial reperfusion injury during coronary artery bypass grafting. *Annals of Thoracic Surgery* 1994;58(5):1427-1432.

Crane FL. Biochemical functions of coenzyme Q10. *Journal of the American College of Nutrition* 2001;20(6):591-598.

Engelsen J, Nielsen JD, Hansen KF. [Effect of coenzyme Q10 and Ginkgo biloba on warfarin dosage in patients on long-term warfarin treatment. A randomized, double-blind, placebo-controlled cross-over trial]. *Ugeskr Laeger* 2003;165(18):1868-1871 (in Danish).

Hershey AD, Powers SW, Vockell AL, Lecates SL, Ellinor PL, Segers A, Burdine D, Manning P, Kabbouche MA. Coenzyme Q10 deficiency and response to supplementation in pediatric and adolescent migraine. *Headache* 2007;47(1):73-80.

Kalpravidh RW, Wichit A, Siritanaratkul N, Fucharoen S. Effect of coenzyme Q10 as an antioxidant in  $\beta$ -thalassemia/Hb E patients. *BioFactors* 2005;25(1-4):225-234.

Kawamukai M. Biosynthesis, bioproduction and novel roles of ubiquinone. *Journal of Bioscience and Bioengineering* 2002;94(6):511-517.

Landbo C, Almdal TP. [Interaction between warfarin and coenzyme Q10]. *Ugeskr Laeger* 1998;160(22):3226-3227 (in Danish).

Langsjoen PH. Introduction to coenzyme Q10. Online in: A Physician's Update on Coenzyme Q10 in U.S. Medicine. University of Washington faculty webpage of John T.A. Ely, Ph.D. Tyler (TX); 1994. [Accessed 2018 June 1]. Available from: <https://www.grc.com/sr6dev/misc/coq10/coenzyme%20q10.pdf>

Langsjoen PH, Folkers K, Lyson K, Muratsu K, Lyson T, Langsjoen P. Effective and safe therapy with coenzyme Q10 for cardiomyopathy. *Klinische Wochenschrift* 1988;66(13):583-590.

Lipshutz BH, Lower A, Berl V, Schein K, Wetterich F. An improved synthesis of the "miracle nutrient" coenzyme Q10. *Organic Letters* 2005;7(19):4095-4097.

Lipshutz BH, Mollard P, Pfeiffer SS, Chrisman W. A short, highly efficient synthesis of coenzyme Q10. *Journal of the American Chemical Society* 2002;124(48):14282-14283.

O'Neil MJ, Smith A, Heckelman PE, Budavari S, editors. *The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals*. 13<sup>th</sup> edition. Whitehouse Station (NJ): Merck & Co., Inc; 2001.

Park YC, Kim SJ, Choi JH, Lee WH, Park KM, Kawamukai M, Ryu YW, Seo JH. Batch and fed-batch production of coenzyme Q10 in recombinant *Escherichia coli* containing the decaprenyl diphosphate synthase gene from *Gluconobacter suboxydans*. *Applied Microbiology and Biotechnology* 2005;67(2):192-196.

Rosenfeldt F, Marasco S, Lyon W, Wowk M, Sheeran F, Bailey M, Esmore D, Davis B, Pick A, Rabinov M, Smith J, Nagley P, Pepe S. Coenzyme Q10 therapy before cardiac surgery improves



mitochondrial function and in vitro contractility of myocardial tissue. *Journal of Thoracic Cardiovascular Surgery* 2005;129(1):25-32.

Rosenfeldt FL, Haas SJ, Krum H, Hadj A, Ng K, Leong JY, Watts GF. Coenzyme Q10 in the treatment of hypertension: a meta-analysis of the clinical trials. *Journal of Human Hypertension* 2007;21(4):297-306.

Rozen TD, Oshinsky ML, Gebeline CA, Bradley KC, Young WB, Shechter AL, Silberstein SD. Open label trial of coenzyme Q10 as a migraine preventative. *Cephalgia* 2002;22(2):137-141.

Sandor PS, Di Clemente L, Coppola G, Saenger U, Fumal A, Magis D, Seidel L, Agosti RM, Schoenen J. Efficacy of coenzyme Q10 in migraine prophylaxis: a randomized controlled trial. *Neurology* 2005;64(4):713-715.

Singh RB, Niaz MA, Rastogi SS, Shukla PK, Thakur AS. Effect of hydrosoluble coenzyme Q10 on blood pressures and insulin resistance in hypertensive patients with coronary artery disease. *Journal of Human Hypertension* 1999;13(3):203-208.

Spigset O. Reduced effect of warfarin caused by ubidecarenone. *Lancet* 1994;344(8933):1372-1373.

Storch A, Jost WH, Vieregge P, Spiegel J, Greulich W, Durner J, Müller T, Kupsch A, Henningsen H, Oertel WH, Fuchs G, Kuhn W, Niklowitz P, Koch R, Herting B, Reichmann H, German Coenzyme Q10 Study Group. Randomized, double-blind, placebo-controlled trial on symptomatic effects of coenzyme Q10 in Parkinson disease. *Archives of Neurology* 2007;64(7):938-944.

Sweetman SC, editor. *Martindale: The Complete Drug Reference*, 35<sup>th</sup> edition. London (UK): Pharmaceutical Press; 2007.

Szkopińska A. Review: Ubiquinone. Biosynthesis of quinone ring and its isoprenoid side chain. Intracellular localization. *Acta Biochimica Polonica* 2000;47(2):469-480.

Tanaka J, Tominaga R, Yoshitoshi M, Matsui K, Komori M, Sese A, Yasui H, Tokunaga K. Coenzyme Q10: the prophylactic effect on low cardiac output following cardiac valve replacement. *Annals of Thoracic Surgery* 1982;33(2):145-151.

USP 30 2007: *United States Pharmacopeia and the National Formulary (USP 30 - NF 25)*. Rockville (MD): United States Pharmacopoeial Convention, Inc.; 2007.

Yoshida H, Kotani Y, Ochiai K, Araki K. Production of ubiquinone-10 using bacteria. *Journal of General and Applied Microbiology* 1998;44(1):19-26.

Zhao J, Wang C, Sun X. [Determination of solanesol in the extracts of tobacco leaves by high performance liquid chromatography (HPLC)]. *Chinese Journal of Chromatography* 1997;15(6):544-545 (in Chinese).



## References reviewed

Actis-Goretta L, Carrasquedo F, Fraga CG. The regular supplementation with an antioxidant mixture decreases oxidative stress in healthy humans. Gender effect. *Clinica Chimica Acta* 2004;349(1-2):97-103.

Aejmelaeus R, Metsa-Ketela T, Laippala P, Solakivi T, Alho H. Ubiquinol-10 and total peroxy radical trapping capacity of LDL lipoproteins during aging: the effects of Q-10 supplementation. *Molecular Aspects of Medicine* 1997;18(Supplement 1):S113-S120.

Badmaev V, Majeed M, Prakash L. Piperine derived from black pepper increases plasma levels of coenzyme Q10 following oral supplementation. *Journal of Nutritional Biochemistry* 2000;11(2):109-113.

Barbiroli B, Frassinetti C, Martinelli P, Iotti S, Lodi R, Cortelli P, Montagna P. Coenzyme Q10 improves mitochondrial respiration in patients with mitochondrial cytopathies. An in vivo study on brain and skeletal muscle by phosphorous magnetic resonance spectroscopy. *Cellular and Molecular Biology* 1997;43(5):741-749.

Bargossi AM, Grossi G, Fiorella PL, Gaddi A, Di Giulio R, Battino M. Exogenous CoQ10 preserves plasma ubiquinone levels in patients treated with 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors. *Internal Journal of Clinical Laboratory Research* 1994;24(3):171-176.

Baumann L. How to prevent photoaging? *The Journal of Investigative Dermatology* 2005;125(4):xii-xiii.

Beal MF, Matthews RT. Coenzyme Q10 in the central nervous system and its potential usefulness in the treatment of neurodegenerative diseases. *Molecular Aspects of Medicine* 1997;18(Supplement 1):S169-S179.

Belardinelli R, Mucaj A, Lacalaprice F, Solenghi M, Principi F, Tiano L, Littarru GP. Coenzyme Q10 improves contractility of dysfunctional myocardium in chronic heart failure. *BioFactors* 2005;25(1-4):137-145.

Bonetti A, Solito F, Carmosino G, Bargossi AM, Fiorella PL. Effect of ubidecarenone oral treatment on aerobic power in middle-aged trained subjects. *Journal of Sports Medicine and Physical Fitness* 2000;40(1):51-57.

Boon H, Jurgens T. Drug interactions with natural health products: a discussion paper. In "Perspectives on Natural Health Products - A Collection of Executive Summaries from Stakeholder Consultation Reports, 2001-2002. Quality and Safety". Ottawa (ON): Natural Health Products Directorate, Health Canada; 2001. [Accessed 2007October 23]. Available from: [http://www.hc-sc.gc.ca/dhp-mps/pubs/complement/hp-ps\\_perspectives/hp-ps\\_perspectives\\_2\\_e.html#1](http://www.hc-sc.gc.ca/dhp-mps/pubs/complement/hp-ps_perspectives/hp-ps_perspectives_2_e.html#1)



Braun B, Clarkson PM, Freedson PS, Kohl RL. Effects of coenzyme Q10 supplementation on exercise performance, VO<sub>2</sub>max, and lipid peroxidation in trained cyclists. *International Journal of Sport Nutrition* 1991;1(4):353-365.

Bresolin N, Doriguzzi C, Ponzetto C, Angelini C, Moroni I, Castelli E, Cossutta E, Binda A, Gallanti A, Gabellini S. Ubidecarenone in the treatment of mitochondrial myopathies: a multi-center double-blind trial. *Journal of Neurological Sciences* 1990;100(1-2):70-78.

Burke BE, Neuenschwander R, Olson RD. Randomized, double-blind, placebo-controlled trial of coenzyme Q10 in isolated systolic hypertension. *Southern Medical Journal* 2001;94(11):1112-1117.

Caso G, Kelly P, McNurlan MA, Lawson WE. Effect of coenzyme q10 on myopathic symptoms in patients treated with statins. *American Journal of Cardiology* 2007;99(10):1409-1412.

Chen RS, Huang CC, Chu NS. Coenzyme Q10 treatment in mitochondrial encephalomyopathies. Short-term double-blind, crossover study. *European Neurology* 1997;37(4):212-218.

Choi JH, Ryu YW, Seo JH. Biotechnological production and applications of coenzyme Q10. *Applied Microbiology and Biotechnology* 2005;68(1):9-15.

Cohen BH, Gold DR. Mitochondrial cytopathy in adults: what we know so far. *Cleveland Clinical Journal of Medicine* 2001;68(7):625-642.

De Pinieux G, Chariot P, Ammi-Saïd M, Louarn F, Lejonc JL, Astier A, Jacotot B, Gherardi R. Lipid-lowering drugs and mitochondrial function: effects of HMG-CoA reductase inhibitors on serum ubiquinone and blood lactate/pyruvate ratio. *British Journal of Clinical Pharmacology* 1996;42(3):333-337.

Digiesi V, Cantini F, Oradei A, Bisi G, Guarino GC, Brocchi A, Bellandi F, Mancini M, Littarru GP. Treatment of essential hypertension with coenzyme Q10. *Molecular Aspects of Medicine* 1994;15(Supplement 1):S257-S263.

Di Giovanni S, Mirabella M, Spinazzola A, Crociani P, Silvestri G, Broccolini A, Tonali P, Di Mauro S, Servidei S. Coenzyme Q10 reverses pathological phenotype and reduces apoptosis in familial CoQ10 deficiency. *Neurology* 2001;57(3):515-518.

Engelsen J, Nielsen JD, Winther K. Effect of coenzyme Q10 and Ginkgo biloba on warfarin dosage in stable, long-term warfarin treated outpatients. A randomised, double blind, placebo-crossover trial. *Thrombosis and Haemostasis* 2002;87(6):1075-1076.

Eriksson JG, Forsen TJ, Mortensen SA, Rohde M. The effect of coenzyme Q10 administration on metabolic control in patients with type 2 diabetes mellitus. *BioFactors* 1999;9(2-4):315-318.





Eshginia S, Gapparov MM. [The influence of phospholipids food and antioxidant at patients with hypertension]. *Voprosy Pitaniia* 2006;75(2):37-39 (in Russian).

Fang LC, Huang XF, Du ZH, Yuan J, Wei H, Cheng HH, Liu Y. [Isolation and identification of a photosynthetic bacteria producing coenzyme Q10]. *Wei Sheng Wu Xue Bao* 2005;45:772-775 (in Chinese).

Ferrante KL, Shefner J, Zhang H, Betensky R, O'Brien M, Yu H, Fantasia M, Taft J, Beal MF, Traynor B, Newhall K, Donofrio P, Caress J, Ashburn C, Freiberg B, O'Neill C, Paladenech C, Walker T, Pestronk A, Abrams B, Florence J, Renna R, Schierbecker J, Malkus B, Cudkowicz M. Tolerance of high-dose (3,000 mg/day) coenzyme Q10 in ALS. *Neurology* 2005;65(11):1834-1836.

Folkers K, Simonsen R. Two successful double-blind trial with coenzyme Q10 (vitamin Q10) on muscular dystrophies and neurogenic atrophies. *Biochimica et Biophysica Acta* 1995;1271(1):281-286.

Folkers K, Wolaniuk J, Simonsen R, Morishita M, Vadhanavikit S. Biochemical rationale and the cardiac response of patients with muscle disease to therapy with coenzyme Q10. *Proceedings of the National Academy of Science* 1985;82(13):4513-4516.

Gazdikova K, Gvozdjakova A, Kucharska J, Spustova V, Braunova Z, Dzurik R. [Effect of coenzyme Q10 in patients with kidney diseases]. *Casopis Lekarska Ceskych* 2001;140(10):307-310 (in Slovak).

Ghirlanda G, Oradei A, Manto A, Lippa S, Uccioli L, Caputo S, Greco AV, Littarru GP. Evidence of plasma CoQ10-lowering effect by HMG-CoA reductase inhibitors: a double-blind, placebo-controlled study. *Journal of Clinical Pharmacology* 1993;33(3):226-229.

Giovannini L, Bertelli AA, Scalori V, Dell'Osso L, Alessandri MG, Mian M. Skin penetration of CoQ10 in the rat. *International Journal of Tissue Reactions* 1988;10(2):103-105.

Hanioka T, Tonaka M, Ojima M, Shizukuishi S, Folkers K. Effect of topical application of coenzyme Q10 on adult periodontitis. *Molecular Aspects of Medicine* 1994;15(Supplement 1):S241-S248.

Hathcock JN, Shao A. Risk assessment for coenzyme Q10 (ubiquinone). *Regulatory Toxicology and Pharmacology* 2006;45(3):282-288.

HC 2007: Health Canada. MedEffect Canada: Adverse Reaction Reporting. Ottawa (ON): Health Canada; 2007. [Accessed 2007October 23]. Available from: [http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index\\_e.html](http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index_e.html)

Hendler SS, Rorvik D, editors. *PDR for Nutritional Supplements*, 1<sup>st</sup> edition. Montvale (NJ): Thomson PDR; 2001.



Henriksen JE, Andersen CB, Hother-Nielsen O, Vaag A, Mortensen SA, Beck-Nielsen H. Impact of ubiquinone (coenzyme Q10) treatment on glycaemic control, insulin requirement and well-being in patients with Type 1 diabetes mellitus. *Diabetic Medicine* 1999;16(4):312-318.

Hodgson JM, Watts GF, Playford DA, Burke V, Croft KD. Coenzyme Q10 improves blood pressure and glycaemic control: a controlled trial in subjects with type 2 diabetes. *European Journal of Clinical Nutrition* 2002;56(11):1137-1142.

Hoppe U, Bergemann J, Diembeck W, Ennen J, Gohla S, Harris I, Jacob J, Kielholz J, Mei W, Pollet D, Schachtschabel D, Sauermann G, Schreiner V, Stab F, Steckel F. Coenzyme Q10, acutaneous antioxidant and energizer. *BioFactors* 1999;9(2-4):371-378.

Huertas JR, Palomino N, Carrasco R, Quiles J, Ramirez-Tortosa MC, Ochoa J, Cassinello M, Battino M, Robles R, Mataix J. Lipid peroxidation and antioxidants in newborns. *Molecular Aspects of Medicine* 1997;18(Supplement 1):S229-S232.

Iarussi D, Auricchio U, Agretto A, Murano A, Giuliano M, Casale F, Indolfi P, Iacono A. Protective effect of coenzyme Q10 on anthracyclines cardiotoxicity: control study in children with acute lymphoblastic leukemia and non-Hodgkin lymphoma. *Molecular Aspects of Medicine* 1994;15(Supplement 1):S207-S212.

Isobe C, Murata T, Sato C, Terayama Y. Increase of oxidized/total coenzyme Q-10 ratio in cerebrospinal fluid in patients with Parkinson's disease. *Journal of Clinical Neuroscience* 2007;14(4):340-343.

Jellin JM. *Natural Medicines Comprehensive Database: Coenzyme Q-10*. Stockton (CA): Therapeutic Research Faculty; 1995-2007. [Accessed 2007 October 23]. Available from: [http://www.naturaldatabase.com/\(S\(hhjwxb453fs5kk55sxqrp255\)\)/nd/Search.aspx?cs=&s=ND&pt=100&id=938&ds=&name=CoQ10+\(COENZYME+Q-10\)](http://www.naturaldatabase.com/(S(hhjwxb453fs5kk55sxqrp255))/nd/Search.aspx?cs=&s=ND&pt=100&id=938&ds=&name=CoQ10+(COENZYME+Q-10))

Kaikkonen J, Kosonen L, Nyysönen K, Porkkala-Sarataho E, Salonen R, Korpela H, Salonen JT. Effect of combined coenzyme Q10 and d-alpha-tocopheryl acetate supplementation on exercise-induced lipid peroxidation and muscular damage: a placebo-controlled double-blind study in marathon runners. *Free Radical Research* 1998;29(1):85-92.

Kaikkonen J, Nyysönen K, Porkkala-Sarataho E, Poulsen HE, Metsa-Ketela T, Hayn M, Salonen R, Salonen JT. Effect of oral coenzyme Q10 supplementation on the oxidation resistance of human VLDL+LDL fraction: absorption and antioxidative properties of oil and granule-based preparations. *Free Radical Biology and Medicine* 1997;22(7):1195-1202.

Kaikkonen J, Tuomainen TP, Nyysönen K, Salonen JT. Coenzyme Q10: absorption, antioxidative properties, determinants, and plasma levels. *Free Radical Research* 2002;36(4):389-397.



Kamikawa T, Kobayashi A, Yamashita T, Hayashi H, Yamazaki N. Effects of coenzyme Q10 on exercise tolerance in chronic stable angina pectoris. *American Journal of Cardiology* 1985;56(4):247-251.

Khatta M, Alexander BS, Krichten CM, Fisher ML, Freudenberger R, Robinson SW, Gottlieb SS. The effect of coenzyme Q10 in patients with congestive heart failure. *Annals of Internal Medicine* 2000;132(8):636-640.

Kuklinski B, Weissenbacher E, Fahrnich A. Coenzyme Q10 and antioxidants in acute myocardial infarction. *Molecular Aspects of Medicine* 1994;15(Supplement 1):S143-S147.

Kurowska EM, Dresser G, Deutsch L, Bassoo E, Freeman DJ. Relative bioavailability and antioxidant potential of two coenzyme Q10 preparations. *Annals of Nutrition and Metabolism* 2003;47(1):16-21.

Langsjoen H, Langsjoen P, Langsjoen P, Willis R, Folkers K. Usefulness of coenzyme Q10 in clinical cardiology: a long-term study. *Molecular Aspects of Medicine* 1994;15(Supplement 1):S165-S175.

Langsjoen PH. The clinical use of HMG CoA-reductase inhibitors (statins) and the associated depletion of the essential cofactor coenzyme Q10; a review of pertinent human and animal data. Tyler (TX); 2002. [Accessed 2007 October 23]. Available from: [http://www.fda.gov/ohrms/dockets/dailys/02/May02/052902/02p-0244-cp00001-02-Exhibit\\_A-vol1.pdf](http://www.fda.gov/ohrms/dockets/dailys/02/May02/052902/02p-0244-cp00001-02-Exhibit_A-vol1.pdf)

Langsjoen PH, Langsjoen A, Willis R, Folkers K. Treatment of hypertrophic cardiomyopathy with coenzyme Q10. *Molecular Aspects of Medicine* 1997;18(Supplement 1):S145-S151.

Langsjoen PH, Vadhanavikit S, Folkers K. Response of patients in classes III and IV of cardiomyopathy to therapy in a blind and crossover trial with coenzyme Q10. *Proceedings of the National Academy of Science* 1985;82(12):4240-4244.

Langsjoen P, Langsjoen P, Willis R, Folkers K. Treatment of essential hypertension with coenzyme Q10. *Molecular Aspects of Medicine* 1994;15(Supplement 1):S265-S272.

Levy HB, Kohlhaas HK. Considerations for supplementing with coenzyme Q10 during statin therapy. *The Annals of Pharmacotherapy* 2006;40(2):290-294.

Lockwood K, Moesgaard S, Folkers K. Partial and complete regression of breast cancer in patients in relation to dosage of coenzyme Q10. *Biochemical and Biophysical Research Communications* 1994;199(3):1504-1508.

Lockwood K, Moesgaard S, Hanioka T, Folkers K. Apparent remission of breast cancer in high risk patients supplemented with nutritional antioxidants, essential fatty acids and coenzyme Q10. *Molecular Aspects of Medicine* 1994;15(Supplement 1):S231-S240.



Meletis CD, Jacobs T. Interactions between drugs and natural medicines. Sandy (OR): Eclectic Medical Publications; 1999.

Miles MV, Patterson BJ, Schapiro MB, Hickey FJ, Chalfonte-Evans M, Horn PS, Hotze SL. Coenzyme Q10 absorption and tolerance in children with Down syndrome: a dose-ranging trial. *Pediatric Neurology* 2006;35(1):30-37.

Morisco C, Nappi A, Argenziano L, Sarno D, Fonatana D, Imbriaco M, Nicolai E, Romano M, Rosiello G, Cuocolo A. Noninvasive evaluation of cardiac hemodynamics during exercise in patients with chronic heart failure: effects of short-term coenzyme Q10 treatment. *Molecular Aspects of Medicine* 1994;15(Supplement 1):S155-S163.

Morisco C, Trimarco B, Condorelli M. Effect of coenzyme Q10 therapy in patients with congestive heart failure: a long-term multicenter randomized study. *The Clinical Investigator* 1993;71(Supplement 8):S134-S136.

Mortensen SA. Overview on coenzyme Q10 as adjunctive therapy in chronic heart failure. Rationale, design and end-points of "Q-symbio"--a multinational trial. *BioFactors* 2003;18(1-4):79-89.

Mortensen SA, Leth A, Agner E, Rohde M. Dose-related decrease of serum coenzyme Q10 during treatment with HMG-CoA reductase inhibitors. *Molecular Aspects of Medicine* 1997;18(Supplement 1):S137-S144.

Muller T, Buttner T, Gholipour AF, Kuhn W. Coenzyme Q10 supplementation provides mild symptomatic benefit in patients with Parkinson's disease. *Neuroscience Letters* 2003;341(3):201-204.

Nakamura R, Littarru GP, Folkers K, Wilkinson EG. Study of CoQ10-enzymes in gingiva from patients with periodontal disease and evidence for a deficiency of Coenzyme Q10. *Proceedings of the National Academy of Science* 1974;71(4):1456-1460.

NCI 2006: National Cancer Institute. Coenzyme Q10 (PDQ(R)) Health Professional Version. Bethesda (MD): National Cancer Institute, U.S. National Institutes of Health; 2006. [Accessed 2007 October 23]. Available from: <http://www.cancer.gov/cancertopics/pdq/cam/coenzymeQ10/healthprofessional/allpages/print>

NCI 2006: National Cancer Institute. Coenzyme Q10 (PDQ®) Patient Version. Bethesda (MD): National Cancer Institute, U.S. National Institutes of Health; 2006. [Accessed 2007 October 23]. Available from: <http://www.cancer.gov/cancerinfo/pdq/cam/coenzymeQ10>

Overvad K, Diamant B, Holm L, Hølmer G, Mortensen SA, Stender S. Review: coenzyme Q10 in health and disease. *European Journal of Clinical Nutrition* 1999;53(10):764-770.

Peterson PL. The treatment of mitochondrial myopathies and encephalomyopathies. *Biochimica et Biophysica Acta* 1995;1271(1):275-280.



Playford DA, Watts GF, Croft KD, Burke V. Combined effect of coenzyme Q10 and fenofibrate on forearm microcirculatory function in type 2 diabetes. *Atherosclerosis* 2003;168(1):169-179.

Premkumar VG, Yuvaraj S, Vijayasathy K, Gangadaran SGD, Sachdanandam P. Effect of coenzyme Q10, riboflavin and niacin on serum CEA and CA 15-3 levels in breast cancer patients undergoing tamoxifen therapy. *Biological and Pharmaceutical Bulletin* 2007;30(2):367-370.

Ravaglia G, Forti P, Maioli F, Bastagli L, Facchini A, Mariani E, Savarino L, Sassi S, Cucinotta D, Lenaz G. Effect of micronutrient status on natural killer cell immune function in healthy free-living subjects aged  $\geq 90$  y1-3. *The American Journal of Clinical Nutrition* 2000;71(2):590-598.

Reichenbach J, Schubert R, Schwan C, Muller K, Bohles HJ, Zielen S. Antioxidative capacity in patients with common variable immunodeficiency. *Journal of Clinical Immunology* 2000;20(3):221-226.

Roffe L, Schmidt K, Ernst E. Efficacy of Coenzyme Q10 for improved tolerability of cancer treatments: a systemic review. *Journal of Clinical Oncology* 2004;22(21):4418-4424.

Rosenfeldt F, Hilton D, Pepe S, Krum H. Systematic review of effect of coenzyme Q10 in physical exercise, hypertension and heart failure. *BioFactors* 2003;18(1-4):91-100.

Sacher HL, Sacher ML, Landau SW, Kersten R, Dooley F, Sacher A, Sacher M, Dietrick K, Ichkhan K. The clinical and hemodynamic effects of coenzyme Q10 in congestive cardiomyopathy. *American Journal of Therapeutics* 1997;4(2-3):66-72.

Sander S, Coleman CI, Patel AA, Kluger J, White CM. The impact of coenzyme Q10 on systolic function in patients with chronic heart failure. *Journal of Cardiac Failure* 2006;12(6):464-472.

Sasaki K, Watanabe M, Suda Y, Ishizuka A, Nopartnaraporn N. Applications of photosynthetic bacteria for medical fields. *Journal of Bioscience and Bioengineering* 2005;100(5):481-488.

Savidge GS. Candidate foods in the Asia-Pacific region for cardiovascular protection: fish, fruit and vegetables. *Asia Pacific Journal of Clinical Nutrition* 2001;10(2):134-137.

Shults CW. Therapeutic role of coenzyme Q(10) in Parkinson's disease. *Pharmacology and Therapeutics* 2005;107(1):120-130.

Shults CW, Beal MF, Song D, Fontaine D. Pilot trial of high dosages of coenzyme Q10 in patients with Parkinson's disease. *Experimental Neurology* 2004;188(2):491-494.

Shults CW, Oakes D, Kieburtz K, Beal MF, Haas R, Plumb S, Juncos JL, Nutt J, Shoulson I, Carter J, Kompoliti K, Perlmutter JS, Reich S, Stern M, Watts RL, Kurlan R, Molho E, Harrison M, Lew M, Parkinson Study Group. Effects of coenzyme Q10 in early Parkinson disease: evidence of slowing of the functional decline. *Archives of Neurology* 2002;59(10):1541-1550.



Soja AM, Mortensen SA. Treatment of congestive heart failure with coenzyme Q10 illuminated by meta-analyses of clinical trials. *Molecular Aspects of Medicine* 1997;18(Supplement 1):S159-S168.

Strazisar M, Fir M, Golc-Wondra A, Milivojevic L, Prosek M, Abram V. Quantitative determination of coenzyme Q10 by liquid chromatography and liquid chromatography/mass spectrometry in dairy products. *Journal of AOAC International* 2005;88(4):1020-1027.

Strijks E, Kremer HP, Horstink MW. Q10 therapy in patients with idiopathic Parkinson's disease. *Molecular Aspects of Medicine* 1997;18(Supplement 1):S237-S240.

Swiezewska E, Dallner G, Andersson B, Ernster L. Biosynthesis of ubiquinone and plastoquinone in the endoplasmic reticulum-Golgi membranes of spinach leaves. *The Journal of Biological Chemistry* 1993;268(2):1494-1499.

The Huntington Study Group. A randomized, placebo-controlled trial of coenzyme Q10 and remacemide in Huntington's disease. *Neurology* 2001;57(3):397-404.

The NINDS NET-PD Investigators. A randomized clinical trial of coenzyme Q10 and GPI-1485 in early Parkinson disease. *Neurology* 2007;68(1):20-28.

Tournas JA, Lin FH, Burch JA, Selim MA, Monteiro-Riviere NA, Zielinski JE, Pinnell SR. Ubiquinone, Idebenone, and kinetin provide ineffective photoprotection to skin when compared to a topical antioxidant combination of vitamins C and E with Ferulic acid. *Journal of Investigative Dermatology* 2006;126(5):1185-1187.

Tran MT, Mitchell TM, Kennedy DT, Giles JT. Role of coenzyme Q10 in chronic heart failure, angina, and hypertension. *Pharmacotherapy* 2001;21(7):797-806.

Tsuneki H, Sekizaki N, Suzuki T, Kobayashi S, Wada T, Okamoto T, Kimura I, Sasaoka T. Coenzyme Q(10) prevents high glucose-induced oxidative stress in human umbilical vein endothelial cells. *European Journal of Pharmacology* 2007;566(1-3):1-10.

Turunen M, Wehlin L, Sjoberg M, Lundahl J, Dallner G, Brismar K, Sindelar PJ.  $\beta$ 2-Integrin and lipid modifications indicate a non-antioxidant mechanism for the anti-atherogenic effect of dietary coenzyme Q10. *Biochemical and Biophysical Research Communications* 2002;296(2):255-260.

Watson JP, Jones DE, James OF, Cann PA, Bramble MG. Case report: oral antioxidant therapy for the treatment of primary biliary cirrhosis: a pilot study. *Journal of Gastroenterology and Hepatology* 1999;14(10):1034-1040.

Watson PS, Scalia GM, Galbraith A, Burstow DJ, Bett N, Aroney CN. Lack of effect of coenzyme Q on left ventricular function in patients with congestive heart failure. *Journal of the American College of Cardiology* 1999;33(6):1549-1552.

Watts GF, Playford DA, Croft KD, Ward NC, Mori TA, Burke V. Coenzyme Q10 improves endothelial dysfunction of the brachial artery in Type II diabetes mellitus. *Diabetologia* 2002;45(3):420-426.

Watts TL. Coenzyme Q10 and periodontal treatment: is there any beneficial effect? *British Dental Journal* 1995;178(6):209-213.

Weant KA, Smith KM. The role of coenzyme Q10 in heart failure. *Annals of Pharmacotherapy* 2005;39(9):1522-1526.

Weber C, Jakobsen TS, Mortensen SA, Paulsen G, Hølmer G. Antioxidative effect of dietary coenzyme Q10 in human blood plasma. *International Journal for Vitamin and Nutrition Research* 1994;64(4):311-315.

Weber C, Jakobsen TS, Mortensen SA, Paulsen G, Hølmer G. Effect of dietary coenzyme Q10 as an antioxidant in human plasma. *Molecular Aspects of Medicine* 1994;15(Supplement 1):S97-S102.

Weston SB, Zhou S, Weatherby RP, Robson SJ. Does exogenous coenzyme Q10 affect aerobic capacity in endurance athletes? *International Journal of Sport and Nutrition* 1997;7(3):197-206.

Wilkinson EG, Arnold RM, Folkers K. Bioenergetics in clinical medicine. VI. adjunctive treatment of periodontal disease with coenzyme Q10. *Research Communications in Chemical Pathology and Pharmacology* 1976;14(4):715-719.

Yamagami T, Shibata N, Folkers K. Study of coenzyme Q10 in essential hypertension. In: Folkers K, Yamamura, editors. *Biomedical and Clinical Aspects of Coenzyme Q*. Amsterdam (NL): Elsevier/North-Holland Biomedical Press; 1977.

Yuvaraj S, Premkumar VG, Vijayasathy K, Gangadaran SG, Sachdanandam P. Ameliorating effect of coenzyme Q(10), riboflavin and niacin in tamoxifen-treated postmenopausal breast cancer patients with special reference to lipids and lipoproteins. *Clinical Biochemistry* 2007;40(9-10):623-628.

Züllli F, Belser E, Schmid D, Liechti C, Suter F. Preparation and properties of coenzyme Q10 nanoemulsions. Hertfordshire (UK): Cosmetic Science Technology; 2006. [Accessed 2007 October 24]. Available from: [http://www.mibellebiochemistry.com/pdfs/Preparation\\_and\\_Properties\\_of\\_Coenzyme\\_Q10\\_Nanoemulsions\\_Cosm\\_Sci\\_Technol\\_2006.pdf](http://www.mibellebiochemistry.com/pdfs/Preparation_and_Properties_of_Coenzyme_Q10_Nanoemulsions_Cosm_Sci_Technol_2006.pdf)