

Coenzyme Q10 – A summary of current science and marketing trends supporting remarkable growth in global markets

Chemical Name and Class

Ubiquinone (2,3-dimethoxy-5-methyl-6-decaprenyl-1,4-benzoquinone); quinone

Common Names

CoQ₁₀, coenzyme Q₁₀, coenzyme Q, ubidecarenone

General Description

CoQ₁₀ is a naturally occurring lipid-soluble antioxidant and electron-transporting coenzyme available as a dietary supplement in the form of a yellow to orange crystalline powder. CoQ₁₀ is a component of the respiratory chain and acts as an effective scavenger of oxygen free radicals known to inhibit the oxidation of LDL-cholesterol. It functions as a bioenergetic, being the coenzyme for mitochondrial enzyme complexes that ultimately produce cellular ATP. CoQ₁₀ bears a close relationship with vitamin E which it allows to regenerate in its active, reduced form (α -tocopherol). It also serves in the regeneration of the reduced form of ascorbate.

Applications

The demand for CoQ₁₀ as a dietary supplement in the U.S. may be anticipated to grow substantially in coming years as awareness of its benefits continues to be shown in clinical trials in diverse conditions and deficiencies are discovered in the same and other conditions. Currently, CoQ₁₀ is widely promoted in the U.S. as dietary supplement for maintaining cardiovascular health and as an antioxidant. The majority of clinical studies on CoQ₁₀ have focused on and found positive effects from its application in cardiovascular disease, including heart surgery, ischemic heart disease, congestive heart failure, and hypertensive heart disease.^{1,2} As of 2003, at least 13 double-blind, placebo-controlled trials of CoQ₁₀ supplementation in heart disease involving over 1000 patients in total found statistically significant benefits in all but 3 studies in which the results were neutral. Based on those findings, it was concluded that CoQ₁₀ is a

“promising, safe and effective approach in chronic heart failure” and a multicenter randomized, placebo-controlled trial in 550 patients with NYHA class III to IV heart disease taking CoQ₁₀ (100 mg t.i.d.) along with standard therapy was initiated in Europe in the same year. A follow-up study lasting 2 years is planned to determine whether CoQ₁₀ will reduce the number of unplanned hospitalizations caused by worsening heart failure (cardiovascular morbidity) which will help “to establish the future role of CoQ₁₀ as part of a maintenance therapy in patients with chronic heart failure.”³

Statin-induced CoQ₁₀ Deficiency

At the same time that congestive heart failure in the U.S. has attained epidemic proportions, the prevailing use of statins to treat heart disease and their confirmed depleting effect on CoQ₁₀ levels is prompting many to recommend that patients taking statins supplement their diet with CoQ₁₀. Moreover, increasing potencies of statin drugs has caused a noticeable increase in the prevalence and severity of CoQ₁₀ deficiency.⁴

In 2003 an estimated 36 million Americans were candidates for treatment with statins.⁴ Over the next two years, sales of statins in the U.S. are expected to grow by 9% per annum and could further increase following their current investigation for potential use in other conditions (e.g., cancer, dementia, multiple sclerosis, proteinuria nephropathies, and transplant rejection).⁵ Worldwide, an estimated one billion people are candidates for statin therapy owing to high serum cholesterol levels.⁶

Skin Care

The other major use of CoQ₁₀ is found in cosmetics designed to correct or inhibit fine lines and a growing number of skin care products now contain the coenzyme. Since 1998, Nivea’s Visage product line containing CoQ₁₀ became the best-selling anti-wrinkle cream in the world (e.g., Nivea Visage Coenzyme Q10 Plus Wrinkle Control Eye Cream, Nivea Visage Coenzyme Q10 Wrinkle Control Night cream, Nivea for Men Revitalizing Crème Q10). Others are attempting to follow with their own formulations containing CoQ₁₀ (e.g., DermaQuest, Eucerin, Emergin-C, Juvena, etc).

Market Demand

In 2003 it was estimated that world market demand for CoQ₁₀ was 150 tons.⁷ A market research study published forecasting demand for anti-aging products in the U.S. to 2007 and 2012 concluded that the demand for “age-defying appearance products” is anticipated to increase by 8% per annum. The study forecasted “stellar growth” for CoQ₁₀.⁸ Another industry study with projections through to 2008 and 2013 concluded that “smaller-volume antioxidants, such as coenzyme Q₁₀, are expected to record the fastest growth through 2008”.⁹ Since CoQ₁₀ was deregulated in Japan in March 2001, sales have grown by 150% per year. In 2004 the market reached US\$150 million and is expected to reach US\$200 million by 2005.¹⁰

Pharmacology

Antioxidant (against in vivo protein oxidative damage¹¹ and lipid peroxidation)¹²⁻¹⁶ Sparing/regenerative to vitamin E stores¹⁷

Apoptotic cell death-inhibiting¹⁸

Antihypertensive^{19,20}

Anti-atherogenic²¹⁻²⁸

Neuroprotective²⁹⁻³¹

CoQ10 Deficiency-associated Conditions:

Normal aging^{32,33}

Skin surface lipid levels after age 42 (men and women)³⁴

Epidermal levels after age 30.³⁵

Exposure of skin surface lipids to ultraviolet radiation³⁴

Heart disease (ischemic)³⁶⁻³⁸

High cholesterol levels³⁹

Bronchial asthma⁴⁰

Smoking/smokers³⁹

Periodontal disease⁴¹

Type 2 diabetes⁴²

Impaired natural killer cell function³³

Lewy body disease⁴³

Cerebellar ataxia⁴⁴

Varicocele⁴⁵

Low sperm vitality⁴⁶

Preeclampsia⁴⁷

Sickle cell anemia⁴⁸

Prader-Willi syndrome³⁸

Myotonic dystrophy⁴⁹

Quinone-responsive respiratory chain enzyme deficiency⁵⁰

Cervical intraepithelial neoplasia⁵¹

AIDS⁵²

β -thalassemia⁵³

Patients taking certain cholesterol-lowering drugs (i.e. atorvastatin, lovastatin, pravastatin, simvastatin)^{42,54-59}

Positive Effects in Clinical Studies

Antioxidant (against lipid peroxidation caused by organic solvent exposure⁶⁰; in coronary artery disease⁶¹; in coronary heart disease patients treated with pravastatin⁶²

Adjuvant (in addition to standard treatments) in chronic heart failure,^{63,64} hypertension (in patients on blood pressure medication,^{65,66} patients not taking BP medications,⁶⁷ and patients with type 2 diabetes^{68,69}

Cardioprotection (after recent heart attack in patients taking lovastatin,⁷⁰ or other interventions⁷¹)

Moderately raised serum lipoprotein(a) in acute coronary disease patients receiving conventional treatments⁶¹

Prevention of complications in patients chronic congestive heart failure (adjuvant to standard medications)⁷²

Potentiating the beneficial effects of aerobic exercise training on brachial artery health in chronic heart failure patients⁷³

Vision recovery in Leber hereditary optic neuropathy⁷⁴

Neurogenic atrophies and muscular dystrophies (myotonic dystrophy, Becker, Duchenne, and limb-

girdle dystrophies, Welander disease, and Charcot-Marie-Tooth disease)⁷⁵ Familial CoQ₁₀ deficiency⁷⁶⁻⁷⁸

Symptom severity⁷⁹ and progressive deterioration of function in Parkinson's disease (CoQ₁₀ combined with equal doses of vitamin E)⁸⁰

Mitochondrial encephalopathy⁵⁰

Progressive hearing loss in diabetes with mitochondrial DNA 3243 (A-G) mutation⁸¹

Improving endothelial function of peripheral circulation (brachial artery) in type 2 diabetes patients with dyslipidemia⁸²

Restoration of CoQ₁₀ levels in type 2 diabetes patients receiving HMG-CoA reductase inhibitors (e.g., pravastatin, simvastatin)⁴²

Sperm motility-increasing in infertile men with idiopathic athenozoospermia.⁸³

Topical Application Studies

Improving the resistance of the skin against oxidation caused by ultra violet radiation; reducing wrinkles around the eyes (“crow’s feet”)^{35,84}

Adult periodontitis⁸⁵

Regulatory Status

Sold freely in the U.S. Regulated as dietary supplement

Safety

No signs of toxicity or adverse events were found in rats of either sex orally administered CoQ₁₀ at dosages of 100-1,200 mg/kg per day for 12 months.⁸⁶ Hypersensitivity reactions to CoQ₁₀ are rare.⁸⁷

Restrictions

Not to be taken concurrently with high-intensity exercise⁸⁸; may accelerate the metabolism of the chemotherapy drug doxorubicin (adriamycin)^{89,90}; may decrease the dosage requirement of antihypertensive medications⁶⁵; effects during pregnancy unknown.

References

1. Langsjoen PH, Langsjoen AM. Review of coenzyme Q₁₀ in cardiovascular disease with emphasis on heart failure and ischemia reperfusion. *Asia Pacific Heart J.* 1998;7:160-8.
2. Langsjoen PH, Langsjoen AM. Overview of the use of CoQ₁₀ in cardiovascular disease. *BioFactors.* 1999;9:273-84.
3. 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;18:79-89.
4. Langsjoen PH, Langsjoen AM. The clinical use of HMG CoA-reductase inhibitors and the associated depletion of coenzyme Q₁₀. A review of animal and human publications. *Biofactors.* 2003;18:101-1.
5. Koumis T, et al. Strategies for the prevention. and treatment of statin-induced myopathy: Is there a role for ubiquinone supplementation? *Am J Health-Syst Pharm.* 2004;61:515-9.
6. Chiang C, et al. Coenzyme Q₁₀ and adverse effects of statins. *J Nutr Environ Med* (Abingdon). 2004;14:17-28.
7. Kaneka Corporation. News and topics. Kaneka Corporation, Osaka, Japan. 2004: <http://www.kaneka.co.jp/kaneka-e/2004/news/>
8. Anti-Aging Products (Market Research Report R154-954). The Freedonia Group, Inc. 2003; July: <http://www.mindbranch.com/listing/product/R154-954.html>
9. Cosmeceuticals (Industry Study R154-1213). The Freedonia Group, Inc. 2003: www.mindbranch.com/reports/pdfs/R154-1213Sample.pdf
10. Yamaguchi P. Japan's Nutraceuticals Today: End of Year Japanese Nutraceutical Industry Thoughts and Looking Beyond. NPI Center. 2004 (Dec. 17): <http://www.npicenter.com/anm/templates/newsATemp.aspx?articleid=11309&zoneid=43>
11. Kwong LK, et al. Effects of coenzyme Q₁₀ administration on its tissue concentrations, mitochondrial oxidant generation, and oxidative stress in the rat. *Free Radic Biol Med.* 2002;33:627-38.

12. Pavlovic SZ, et al. The effect of coenzyme Q₁₀ on blood ascorbic acid, vitamin E, and lipid peroxide in chronic cadmium intoxication. *J Environ Pathol Toxicol Oncol*. 2001;20:133-40.
13. Abd El-Gawad HM, Khalifa AE. Quercetin, coenzyme Q₁₀, and L-canavanine as protective agents against lipid peroxidation and nitric oxide generation in endotoxin-induced shock in rat brain. *Pharmacol Res*. 2001;43:257-63.
14. Palmeira CM, et al. Enhanced mitochondrial testicular antioxidant capacity in Goto-Kakizaki diabetic rats: role of coenzyme Q. *Am J Physiol Cell Physiol*. 2001;281:C1023-8.
15. Faff J, Frankiewicz-Jozko A. Effect of ubiquinone on exercise-induced lipid peroxidation in rat tissues. *Eur J Appl Physiol*. 1997;75:413-7.
16. Stocker R, et al. Ubiquinol-10 protects human low density lipoprotein more efficiently against lipid peroxidation than does α -tocopherol. *Proc Natl Acad Sci*. 1991;88:1646-50.
17. Lass A, Sohal RS. Effect of coenzyme Q₁₀ and α -tocopherol content of mitochondria on the production of superoxide anion radicals. *FASEB J*. 2000;14:87-94.
18. Papucci L, et al. Coenzyme Q₁₀ prevents apoptosis by inhibiting mitochondrial depolarization independently of its free radical scavenging property. *J Biol Chem*. 2003;278:28220-8.
19. Iwamoto Y, et al. Deficiency of coenzyme in hypertensive rats and reduction of deficiency with coenzyme Q₁₀. *Biochem Biophys Res Commun*. 1974;58:743-8.
20. Okamoto H, et al. Effect of coenzyme Q₁₀ on structural alterations in the renal membrane of stroke-prone spontaneously hypertensive rats. *Biochem Med Metabol Biol*. 1991;45:216-26.
21. Turunen M, et al. beta2-Integrin and lipid modifications indicate a non-antioxidant mechanism for the anti-atherogenic effect of dietary coenzyme Q₁₀. *Biochem Biophys Res Commun*. 2002;296:255-60.
22. Thomas SR, et al. Dietary cosupplementation with vitamin E and coenzyme Q₁₀ inhibits atherosclerosis in apolipoprotein E gene knockout mice. *Arterioscler Thromb Vasc Biol*. 2001;21:585-93.
23. Witting PK, et al. Anti-atherogenic effect of coenzyme Q₁₀ in apolipoprotein E gene

knockout mice. *Free Radic Biol Med.* 2000;29:295-305.

24. Singh RB, et al. Effect of coenzyme Q₁₀ on experimental atherosclerosis and chemical composition and quality of atheroma in rabbits. *Atherosclerosis.* 2000;148:275-82.

25. Kishimoto C, et al. Anti-oxidant effects of coenzyme Q₁₀ on experimental viral myocarditis in mice. *J Cardiovasc Pharmacol.* 2003;42:588-92.

26. Murad N, et al. Coenzyme Q₁₀ exogenous administration attenuates cold stress cardiac injury. *Japan Heart J.* 2001;42:327-38.

27. Maulik N, et al. Dietary coenzyme Q₁₀ supplement renders swine hearts resistant to ischemia-reperfusion injury. *Am J Physiol Heart Circ Physiol.* 2000;278:H1084-90.

28. Ferrara N, et al. Protective role of chronic ubiquinone administration on acute cardiac oxidative stress. *J Pharmacol Exp Ther.* 1995;274:858-65.

29. Ferrante RJ, et al. Therapeutic effects of coenzyme Q₁₀ and remacemide in transgenic mouse models of Huntington's disease. *J Neurosci.* 2002;22:1592-9.

30. Matthews RT, et al. Coenzyme Q₁₀ administration increases brain mitochondrial concentrations and exerts neuroprotective effects. *Proc Natl Acad Sci U.S.A.* 1998;95: 8892-7.

31. Flint Beal M, et al. Coenzyme Q₁₀ attenuates the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) induced loss of striatal dopamine and dopaminergic axons in aged mice. *Brain Res.* 1998;783:109-14.

32. Linnane AW, et al. Human aging and global function of coenzyme Q₁₀. *Ann NY Acad Sci.*, 2002;959:396-411.

33. Ravaglia G, et al. Effect of micronutrient status on natural killer cell immune function in healthy free-living subjects aged ≥ 90 y. *Am J Clin Nutr.* 2000;71:590-8.

34. Passi S, et al. Lipophilic antioxidants in human sebum and aging. *Free Radic Res.* 2002;36:471-7.

35. Hoppe U, et al. Coenzyme Q₁₀, a cutaneous antioxidant and energizer. *Biofactors.* 1999;9:371-8.

36. Hanaki Y, et al. Ratio of low-density lipoprotein cholesterol to coenzyme Q₁₀ as a coronary risk factor. *N Engl J Med*. 1991;325:814-15 (letter).
37. Karlsson J, et al. Muscle fibers, ubiquinone and exercise capacity in effort angina. *Mol Cell Biochem*. 1996;179:179-84.
38. Butler MG, et al. Coenzyme Q₁₀ levels in Prader-Willi syndrome: comparison with obese and non-obese subjects. *Am J Med Genet*. 2003;119A:168-71.
39. Kontush A, et al. Plasma ubiquinol-10 is decreased in patients with hyperlipidemia. *Atherosclerosis*. 1997;129:119-26.
40. Gazdik F, et al. Decreased levels of coenzyme Q₁₀ in patients with bronchial asthma. *Allergy*. 2002;57:811-4.
41. Folkers K, et al. Bioenergetics in clinical Medicine- X. Survey of the adjunctive use of coenzyme Q with oral therapy in treating periodontal disease. *J Med*. 1977;8:333-48.
42. Miyake Y, et al. Effect of treatment with 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors on serum coenzyme Q₁₀ in diabetic patients. *Arzneim-Forsch/Drug Res*. 1999;49:324-9.
43. Molina JA, et al. Serum levels of coenzyme Q in patients with Lewy body disease. *J Neural Transm*. 2002;109:1195-1201.
44. Lamperti C, et al. Cerebellar ataxia and coenzyme Q₁₀ deficiency. *Neurology*. 2003;60:1206-8.
45. Mancini A, et al. Relationship between sperm cell ubiquinone and seminal parameters in subjects with and without varicocele. *Andrologia*. 1998;30:1-4.
46. Balercia G, et al. Coenzyme Q₁₀ levels in idiopathic and varicocele-associated asthenozoospermia. *Andrologia*. 2002;34:107-11.
47. Teran E, et al. Preeclampsia is associated with a decrease in plasma coenzyme Q₁₀ levels. *Free Radic Biol Med*. 2003;35:1453-6.
48. Niklowitz P, et al. Coenzyme Q₁₀ in plasma and erythrocytes: comparison of antioxidant

- levels in healthy probands after oral supplementation and in patients suffering from sickle cell anemia. *Clin Chim Acta*. 2002;326:155-61.
49. Siciliano G, et al. Coenzyme Q₁₀, exercise lactate and CTG trinucleotide expansion in myotonic dystrophy. *Brain Res Bull*. 2001;56:405-10.
50. Rötig A, et al. Quinone-responsive multiple respiratory-chain dysfunction due to widespread coenzyme Q₁₀ deficiency. *Lancet*. 2000;356:391-5.
51. Palan PR, et al. Plasma concentrations of coenzyme Q₁₀ and tocopherols in cervical intraepithelial neoplasia and cervical cancer. *Eur J Cancer Prev*. 2003;12:321-6.
52. Folkers K, et al. Biochemical deficiencies of coenzyme Q₁₀ in HIV-infection and exploratory treatment. *Biochem Biophys Res Commun*. 1988;153:888-96.
53. De Luca C, et al. Blood antioxidant status and urinary levels of catecholamine metabolites in β -thalassemia. *Free Radic Res*. 1990;30:453-62.
54. Laaksonen R., et al. The effect of Simvastatin treatment on natural antioxidants in low-density lipoproteins and high-energy phosphates and ubiquinone in skeletal muscle. *Am J Cardiol*. 1996;77:851-4.
55. Palomäki A, et al. Ubiquinone supplementation during lovastatin treatment: effect on LDL oxidation ex vivo. *J Lipid Res*. 1998;39:1430-7.
56. Folkers K, et al. Lovastatin decreases coenzyme Q levels in humans. *Proc Natl Acad Sci*. 1990;87:8931-4.
57. Aberg F, et al. Gemfibrozil-induced decreased in serum ubiquinone and α - and γ -tocopherol levels in men with combined hyperlipidaemia. *Eur J Clin Invest*. 1998;28:235-42.
58. Rundek T, et al. Atorvastatin decreases the coenzyme Q₁₀ level in the blood of patients at risk for cardiovascular disease and stroke. *Arch Neurol*. 2004;61:889-92.
59. Passi S, et al. Statins lower plasma and lymphocyte ubiquinol/ubiquinone without affecting other antioxidants and PUFA. *Biofactors*. 2003;18:113-24.
60. Dlugosz A, Sawicka E. The chemopreventive effect of coenzyme Q on lipids in the paint and lacquer industry workers. *Int J Occup Med Environ Health*. 1998;11:153-63.

61. Singh RB, Niaz MA. Serum concentration of lipoprotein(a) decreases on treatment with hydrosoluble coenzyme Q₁₀ in patients with coronary artery disease: discovery of a new role. *Int J Cardiol.* 1999;68:23-9.
62. Lankin VZ, et al. Antioxidant decreases the intensification of low density lipoprotein in vivo peroxidation during therapy with statins. *Mol Cell Biochem.* 2003;249:129-40.
63. Tran MT, et al. Role of coenzyme Q₁₀ in chronic heart failure, angina, and hypertension. *Pharmacotherapy.* 2001;21:797-06.
64. Baggio E, et al. Italian multicenter study on the safety and efficacy of coenzyme Q₁₀ as adjunctive therapy in heart failure. *Mol Aspects Med.* 1994;15(suppl):S287-94.
65. Singh RB, et al. Effect of hydrosoluble coenzyme Q₁₀ on blood pressure and insulin resistance in hypertensive patients with coronary artery disease. *J Hum Hypertens.* 1999;13:203-8.
66. Langsjoen P, et al. Treatment of essential hypertension with coenzyme Q₁₀. *Mol Aspects Med.* 1994;15(suppl):S265-72.
67. Burke BE, et al. Randomized, double-blind, placebo-controlled trial of coenzyme Q₁₀ in isolated systolic hypertension. *South Med J.* 2001;94:1112-7.
68. Hodgson JM, et al. Coenzyme Q₁₀ improves blood pressure and glycaemic control: a controlled trial in subjects with type 2 diabetes. *Eur J Clin Nutr.* 2002;56:1137-42.
69. Playford DA, et al. Combined effect of coenzyme Q₁₀ and fenofibrate on forearm microcirculatory function in type 2 diabetes. *Atherosclerosis.* 200;168:169-79.
70. Singh RB, et al. Effect of coenzyme Q₁₀ on risk of atherosclerosis in patients with recent myocardial infarction. *Mol Cell Biochem.* 2003;246:75-82.
71. Singh RB, et al. Randomized, double-blind placebo-controlled trial of coenzyme Q₁₀ in patients with acute myocardial infarction. *Cardiovasc Drugs Ther.* 1998;12:347-53.
72. Morisco C, et al. Effect of coenzyme Q₁₀ therapy in patients with congestive heart failure: A long-term multicenter randomized study. *Clin Invest.* 1993;71(8, suppl):S134-6.

73. Belardinelli R, et al. Coenzyme Q₁₀ potentiates the effect of exercise training on the endothelium-dependent relaxation of the brachial artery in chronic heart failure. *Circulation*. 2003;108:IV-739 (abstr).
74. Huang CC, et al. Rapid visual recovery after coenzyme Q₁₀ treatment of Leber hereditary optic neuropathy. *J Neuro-ophthalmol*. 2002;22:66 (letter).
75. Folkers K, Simonsen R. Two successful double-blind trials with coenzyme Q₁₀ (vitamin Q₁₀) on muscular dystrophies and neurogenic atrophies. *Biochem Biophys Acta*. 1995;1271:281-6.
76. Van Maldergem L, et al. Coenzyme Q-responsive Leigh's encephalopathy in two sisters. *Ann Neurol*. 2002;52:750-4.
77. Di Giovanni S, et al. Coenzyme Q₁₀ reverses pathological phenotype and reduces apoptosis in familial CoQ₁₀ deficiency. *Neurology*. 2001;57:515-8.
78. Musumeci O, et al. Familial cerebellar ataxia with muscle coenzyme Q₁₀ deficiency. *Neurology*. 2001;56:849-55.
79. Müller T, et al. Coenzyme Q₁₀ supplementation provides mild symptomatic benefit in patients with Parkinson's disease. *Neurosci Lett*. 2003;341:201-4.
80. Shults CW, et al. Effects of coenzyme Q₁₀ in early Parkinson disease: evidence of slowing of the functional decline. *Arch Neurol*. 2002;59:1541-50.
81. Suzuki S, et al. The effects of coenzyme Q₁₀ treatment on maternally inherited diabetes mellitus and deafness, and mitochondrial DNA 3243 (A-G) mutation. *Diabetologia*. 1998;41:584-8.
82. Watts GF, et al. Coenzyme Q₁₀ improves endothelial dysfunction of the brachial artery in Type II diabetes mellitus. *Diabetologia*. 2002;45:420-6.
83. Balercia G, et al. Coenzyme Q₁₀ supplementation in infertile men with idiopathic asthenozoospermia: An open, uncontrolled pilot study. *Fertility Sterility*. 2004;81:93-8.
84. Blatt T, et al. [Modulation of oxidative stresses in human aging skin]. *Z Gerontol Geriatr*.

1999;32:83-8 (in German with English abstr).

85. Hanioka T, et al. Effect of topical application of coenzyme Q₁₀ on adult periodontitis. *Mol Aspects Med.* 1994;15(suppl):S241-8.

86. Williams KD, et al. 52-week oral gavage chronic toxicity study with ubiquinone in rats with a 4-week recovery. *J Agric Food Chem.* 1999;47:3756-63.

87. Schiavino D, et al. Rush desensitization with ubiquinone. *Allergy.* 1997;52:783-4.

88. Malm C, et al. Supplementation with ubiquinone-10 causes cellular damage during intense exercise. *Acta Physiol Scand.* 1996;157:511-12.

89. Shinozawa S, et al. Tissue concentration of doxorubicin (adriamycin) in mouse pretreated with Alpha-tocopherol or coenzyme Q₁₀. *Acta Medica Okayama.* 1991;45:195-200.

90. Zhou Q, Chowbay B. Effect of coenzyme Q₁₀ on the disposition of doxorubicin in rats. *Eur J Drug Metab Pharmacokinet.* 2002;27:185-92.