Nourishing and Health Benefits of Coenzyme Q_{10} – a Review

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Abstract

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Coenzyme Q_{10} is an important mitochondrial redox component and endogenously produced lipid-soluble antioxidant of the human organism. It plays a crucial role in the generation of cellular energy, enhances the immune system, and acts as a free radical scavenger. Ageing, poor eating habits, stress, and infection – they all affect the organism's ability to provide adequate amounts of CoQ_{10}. After the age of about 35, the organism begins to lose the ability to synthesise CoQ_{10} from food and its deficiency develops. Many researches suggest that using CoQ_{10} supplements alone or in combination with other nutritional supplements may help maintain health of elderly people or treat some of the health problems or diseases. Due to these functions, CoQ_{10} finds its application in different commercial branches such as food, cosmetic, or pharmaceutical industries. This review article gives a survey of the history, chemical and physical properties, biochemistry and antioxidant activity of CoQ_{10} in the human organism. It discusses levels of CoQ_{10} in the organisms of healthy people, stressed people, and patients with various diseases. This paper shows the distribution and contents of two ubiquinones in foods, especially in several kinds of grapes, the benefits of CoQ_{10} as nutritional and topical supplements and its therapeutic applications in various diseases.

Keywords: coenzyme Q_{10}; ubiquinone; food; grape; wine; nourishing; nutritional supplement; diseases; health benefits; ageing; skin

HISTORY

In 1955, Festenstein *et al.* (1955), the scientists in Morton's Laboratory in Liverpool (England) isolated an unsaponifiable lipid with a striking ultraviolet absorption at 272 nm from the intestinal mucosa of horses. Because the new substance was identified as a quinone and was found to be widely distributed in animal tissues, Morton named it *ubiquinone* (ubiquitous quinone – everywhere present quinone). Two years later in David Green's Laboratory at the University of Wisconsin (USA), Crane *et al.* (1957) observed a novel quinone in the lipid extracts of mitochondria and named it *coenzyme Q* because of its participation in the electron transport chain.

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One year later, the chemical structure of coenzyme Q_{10} (CoQ_{10}) was reported by Wolf (Olson 2001), under Dr. Folkers at Merck Laboratories. Later on the Folkers' laboratory became a centre for the purification, structural determination and synthesis of a large number of nourishing factors, besides CoQ_{10}, for example, also vitamin B_6, pantothenic acid, biotin, vitamin B_{12}, and mevalonic acid (Olson 2001).

In 1963, Professor Yamamura from Japan was the first to use coenzyme Q_7 in the treatment of a human disease: congestive heart failure. Mellors and Tappel (1966a, b) showed that reduced CoQ_6 was an effective antioxidant. In 1972 Littarru along with Folkers documented a deficiency of CoQ_{10} in human heart disease (Littarru *et al.* 1972).

Ernster (1977) from Sweden enlarged upon the importance of CoQ_{10} as an antioxidant and free radical scavenger. Peter D. Mitchell, a British biochemist, received the Nobel Prize in 1978 for his contribution to the understanding of the biological energy transfer through the formulation of the chemiosmotic theory, which includes the vital protonmotive role of CoQ_{10} in the energy transfer systems (Mitchell 1961, 1966).

In the early 1980's, there was a considerable acceleration in the number and size of clinical trials. Folkers received the Priestly Medal from the American Chemical Society in 1986 and the National Medal of Science from President Bush in 1990 for his work with CoQ_{10} and other nutrients (Olson 2001). CoQ_{10} has become a science subject of many researches.

Chemical and physical properties of CoQ_{10}

Ubiquinone, chemically 2,3-dimethoxy-5-methyl-6-polyisoprene parabenzoquinone (Figure 1), is in its natural form an orange lipophile powder, without odour and taste. Because CoQ_{10} has 10 isoprenoid units – its name is coenzyme Q_{10}. Molecular weight of CoQ_{10} is 863.34 g/mol. CoQ_{10}

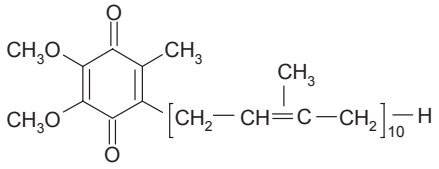


Figure 1. Chemical structure of coenzyme Q_{10} (2, 3-dimethoxy-5-methyl-6-ten-isoprene parabenzoquinone)

is not very stable and deteriorates at temperatures of about 46°C (US Patent 2005). It is a biologically active quinone; it comprises a benzoquinone ring with an isoprenoid side chain, related in structure to vitamin K and vitamin E.

CoQ_{10} is the most prevalent form in humans and most mammals. It has been found also in other animals, microorganisms, and plants. CoQ_9 is the primary form found in rats and mice (Ramasarma 1985). Coenzymes Q_6, Q_7, and Q_8 (6, 7 or 8 isoprenoid units, respectively), are found in yeasts and bacteria (Overvad *et al.* 1999).

The main chemical characteristic of CoQ_{10}, responsible for its various functions, is its existence in three alternate redox states (Battino *et al.* 1990; Ernster & Dallner 1995; James *et al.* 2004):

(1) The fully oxidised *ubiquinone* form which, upon two sequential additions of hydrogen atoms, converts first into a partially reduced;
(2) *Semiquinone* – free radical form;
(3) The fully reduced *ubiquinol* form (Figure 2).

CoQ_{10} can exist in either the *cis* or the *trans* forms. Only the *trans* form is found in nature. However, both forms can be produced in a mixture by means of biofermentation or a chemical process (US Patent 2003).

Biochemistry in the human organism

In cells, CoQ_{10} is located in the middle of the phospholipids bilayer of various membranes; however, the relative amount varies in different organelles. CoQ_{10} is found in the membranes of

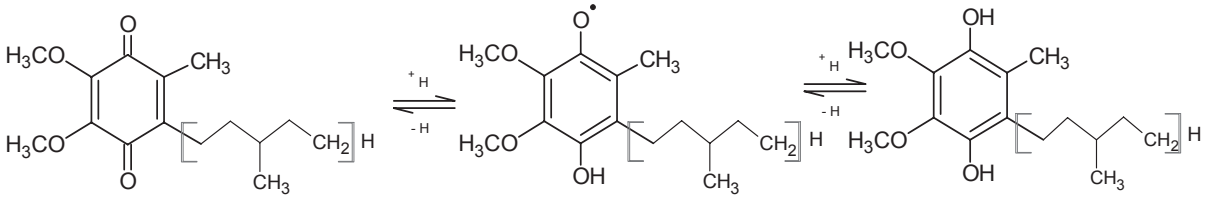


Figure 2. Three redox states of coenzyme Q_{10}

endoplasmatic reticulum, Golgi apparatus, peroxisomes, lysosomes, vesicles and notably the inner membrane of the mitochondrion in every cell in the human body (Crane *et al.* 1984). It is found in relatively higher concentrations in cells with high energy requirements, such as those of the heart, liver, muscles and pancreas.

The biosynthesis of CoQ_{10} from the amino acid tyrosine is a 17-step process (Figure 3) requiring at least eight vitamins (riboflavin, pyridoxine, niacinamide, ascorbic acid, cobalamin, folic acid, tocopherol, and pantothenic acid) and several trace elements (Hojerová 2000; Crane 2001).

Because of this biosynthesis complexity, defects in some human enzymes or regulatory proteins may cause CoQ_{10} deficiency in infantile and adult organisms (Quinzii *et al.* 2007).

CoQ_{10} is the cofactor for at least three mitochondrial enzymes (complexes I, II and III) as well as enzymes in other parts of the cell (Ernster & Dallner 1995; James *et al.* 2004).

Mitochondrial enzymes of the oxidative phosphorylation pathway are essential for the production of the high-energy phosphate, adenosine triphosphate (ATP), upon which all cellular functions depend. The electron and proton transfer functions of the quinone ring are of fundamental importance to all life forms; *ubiquinone* in the mitochondria of animals, *plastoquinone* in the chloroplasts of plants, and *menaquinone* in bacteria (Littarru 1994; Crane 2001).

Antioxidant activity

CoQ_{10} is only endogenously synthesised lipid soluble antioxidant, present in all membranes and surpassing both in the amount and efficiency other antioxidants. The protective effect is extended to lipids proteins and DNA mainly because of its close localisation to the oxidative events and the effective regeneration by continuous reduction at all locations (Bentinger *et al.* 2007).

CoQ_{10} in its reduced form as a hydroquinone (ubiquinol) (Figure 2) is a potent lipophilic antioxidant that has a great importance as a free radical scavenger. CoQ_{10} protects the stability of the cell membranes, protects DNA from free radical induced oxidative damage, and is capable of recycling and regenerating other antioxidants, such as tocopherol and ascorbate (Crane 2001). Other important functions of CoQ_{10} as e.g. cell signalling and gene expression have also been described (Bhagavan & Chopra 2006).

A direct demonstration of the effectiveness of coenzyme Q as an antioxidant can be shown with coenzyme Q deficient yeast. A yeast mutant defi-

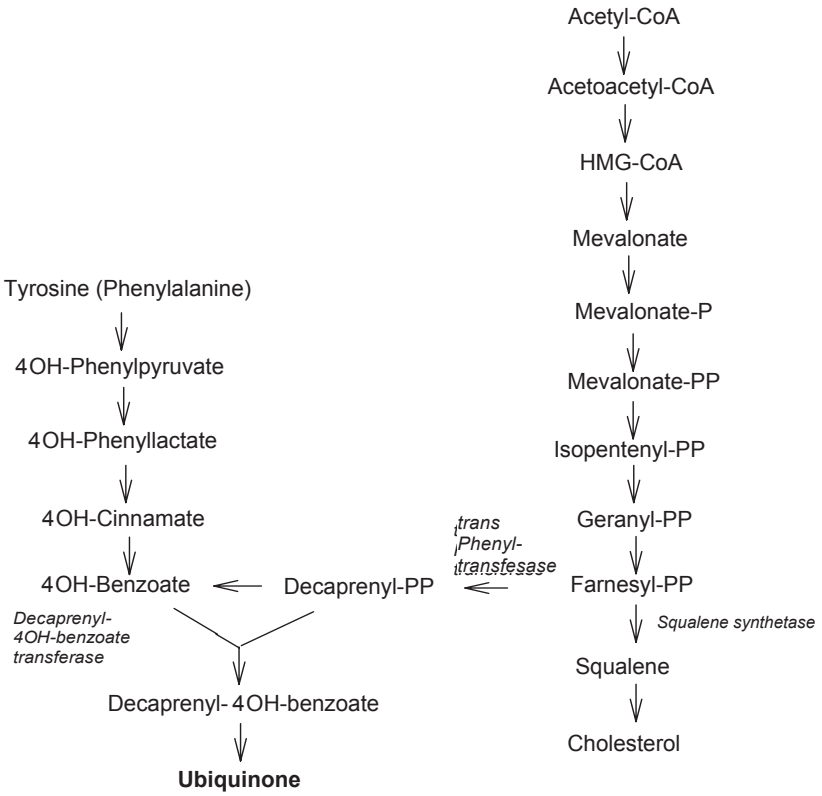


Figure 3. Biosynthesis of ubiquinone from tyrosine

cient in coenzyme Q synthesis shows more lipid peroxide formation than normal yeast (Poon *et al.* 1997). Another direct demonstration of the elimination of free radicals is shown by coenzyme Q treatment of skin in elderly subjects. Luminescence is eliminated from free radicals when a skin cream containing coenzyme Q is applied (Hoppe *et al.* 1999).

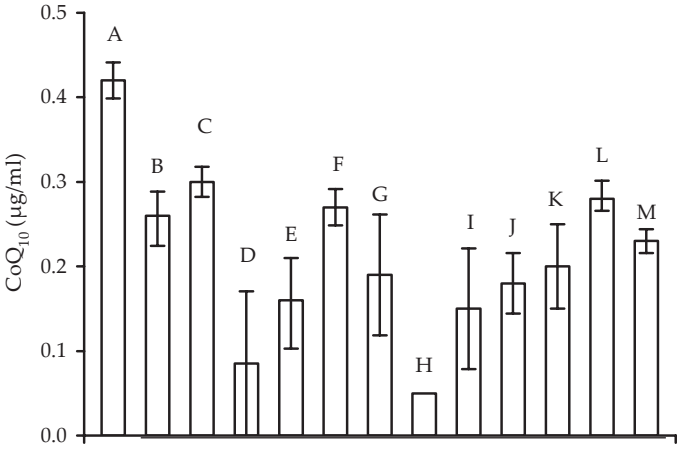
With tocopherol, ubiquinol acts as an antioxidant to stem lipid peroxidation in the inner mitochondrial membrane (Kagan *et al.* 1990; Forsmark-Andree *et al.* 1995; Lass & Sohal 1998; James *et al.* 2004). Ubiquinol can rescue tocopheryl radicals produced by the reactions with lipid or oxygen radicals by a direct reduction back to tocopherol (Arroyo *et al.* 2000). Without coenzyme Q in the membrane, regeneration of tocopherol is very slow. The regeneration of tocopherol can also be observed in low density lipoprotein where a small amount of coenzyme Q protects a larger amount of tocopherol. This function is presumably favoured by the high percentage of quinol present in the blood (Thomas *et al.* 1999; Schneider & Elstner 2000; Crane 2001).

Levels of CoQ_{10} in the human organism

The concentrations of CoQ_{10} in the human organism depend on age, sex, race, and health of the individual. In a healthy young organism is a sufficient amount of CoQ_{10}. There are some studies about plasma or serum CoQ_{10} concentrations, which are usually employed for the assessment of CoQ_{10} status in humans, primarily because of the ease of the sample collection. There are several excellent methods based on HPLC for the analysis of CoQ_{10} in plasma or serum (Lang & Parcker 1987; Grossi *et al.* 1992; Gvozdjáková *et al.* 2000; Tang *et al.* 2001).

From 1996 to 2000, Gvozdjáková *et al.* (2000) measured CoQ_{10} levels in 3000 blood samples of the Slovak population. Tested were: healthy volunteers, stressed managers, two Slovak astronauts, who were getting ready for the start to Cosmos, 30 Slovak fighter pilots, people working with ionising radiation, patients with diabetes, patients with osteoporosis, patients with chronic heart disease, patients before and after heart transplantation, patients with nephropathy, and patients with myopathy. The authors reported that the blood values of CoQ_{10} in healthy volunteers ranged from 0.40 to 0.45 μg/ml (0.46 to 0.52 μmol/l). In the other blood samples of the people or patients groups, CoQ_{10} deficit was proved in comparison with healthy volunteers (Figure 4).

Kaikkonen *et al.* (2002) reported plasma CoQ_{10} values ranging from 0.40 to 1.72 μmol/l in males and 0.43 to 1.47 μmol/l in females in Finnish population. Similar data are available for the US population. Miles *et al.* (2003) reported a range from 0.50 to 1.91 μmol/l that included black and white person of both sexes. Plasma CoQ_{10} concentration ranges were higher in white males than in white females and this is consistent with the findings of Kaikkonen *et al.* (2002). In their study, black people had higher plasma CoQ_{10} values than the white people although their reference interval fitted within the reference interval for the white. The reasons for this



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A – healthy people
B – stressed people (managers)
C – 2 Slovak astronauts made ready for start to Cosmos
D – 30 Slovak fighter pilots
E – people working with ionising radiation
F – patients with insulin dependent diabetes mellitus
G – patients with non insulin dependent diabetes mellitus patients
H – patients with nephropathy
I – patients with myopathy
J – patients with osteoporosis
K – patients with chronic heart disease
L – patients with cardiomyopathy of unknown ethiology
M – patients after heart transplantation

Figure 4. Coenzyme Q_{10} in human blood (A: healthy people, B–E: stressed people, F–M: patients with some diseases) (by Gvozdjáková *et al.* 2000)

difference are not clear. By Hughes *et al.* (2002), plasma concentrations of both the total and reduced CoQ_{10} were found to be significantly lower in Asian Indian males than those in Chinese males in the Singaporean population which was presumed to be one reason for the higher risk of coronary artery disease in Asian Indians.

The distribution and contents of ubiquinones in foods

Intracellular synthesis in human body is the major but not the only source of CoQ_{10}. The rest can be synthesised in liver from the nourishment. CoQ_{10} is found in small amounts in a wide variety of foods from animal sources. Mattila and Kumpulainen (2001) reported that meat and fish (fresh sardines and mackerels) were the richest sources of CoQ_{10}. Especially, reindeer steak as well as beef and pork heart had very high contents of CoQ_{10} (113.3–157.9 μg/g). The contents in fish and other meat samples varied in ranges from 14.0 to 39.2 μg/g). Similar results were published by Weber *et al.* (1997).

There are plenty of vegetable CoQ sources – plastoquinone Q_{10} and Q_9, the richest being spinach, broccoli, peanuts, wheat germ and whole grains, although the amounts are significantly smaller than those found in meat. Kamei *et al.* (1986) determined 92.3 μg/g in corn oil and 73.4 μg/g CoQ_{10} in rapeseed oils. By Mattila and Kumpulainen (2001), rapeseed oils contain 63.5 μg/g CoQ_{10} (Table 1). Vegetables, fruits, berries, and dairy products contain relatively low levels of CoQ_{10}. In cereals, the contents of this compound were below the detection limit (Table 1).

Gvozdjáková *et al.* (1996, 2002) measured CoQ_{10} levels (as plastoquinone Q_{10}–PQ_{10}) and CoQ_9 levels (as plastoquinone Q_9–PQ_9) in several kinds of grape. The authors reported that different concentrations of the antioxidant compounds were found in their berries, skins, and pulps. Several times higher concentration of PQ_{10} was estimated in the skin and berry of St. Laurent, and of PQ_9 in the berry, skin, and pulp of Riesling × Sylvaner as compared to other grapes (Table 3).

Gvozdjáková *et al.* (2002) also found that "wine ageing" has an effect on PQ_{10} concentrations almost in all varieties of 14-week aged wine in comparison with 4-week aged wine (young wine) (Table 4).

CoQ_{10} is an interesting theme for genetic research, too. For example: in natural rice (Takahashi *et al.* 2006) and in cereals (Mattila & Kumpulainen 2001, Table 1), the major form is CoQ_9. Because of this, Takahashi *et al.* (2006) modified the lenght of the side chain of CoQ from 9 to 10 units by expressing DdsA (decaprenyl diphosphate synthetase) to produce CoQ_{10} in rice. They showed that in the leaves and seeds of transgenic rice CoQ_{10} is predominantly produced.

Table 1. Contents (μg/g fresh wt) of coenzyme Q_9 and coenzyme Q_{10} in foods (by Mattila & Kumpulainen 2001)

Food	CoQ_9	CoQ_{10}
Meat, poultry, egg		
Reindeer	8.5	157.9
Pork heart	3.1	126.8
Beef heart	n.d.	113.3
Beef liver	1.4	39.2
Pork liver	1.2	22.7
Beef	0.4	36.5
Pork ham	0.9	20.0
Chicken	0.4	14.0
Egg	n.d.	1.2
Dietary fats		
Rapeseed oil	n.d.	63.5
Fish		
Tuna, canned	0.3	15.9
Baltic herring	n.d.	15.9
Pollack, frozen	0.6	14.4
Cereals		
Bread (rye)	4.7	n.d.
Bread (wheat)	2.1	n.d.
Vegetables		
Pea	0.1	2.7
Cauliflower	0.04	2.7
Bean	0.06	1.8
Carrot	n.d.	1.7
Fruits		
Blackcurrant	0.8	3.4
Lingonberry	2.9	0.9
Strawberry	0.1	1.4
Orange	n.d.	1.4
Apple	0.2	1.3
Dairy products		
Yogurt	n.d.	2.4
Cheese Emental	n.d.	1.3
Cheese Edam	n.d.	1.2
Milk (1.5% fat)	n.d.	0.1

n.d. – not detected

Table 2. Average dietary intake of coenzyme Q_{10} and coenzyme Q_9 from different food groups (by Mattila & Kumpulainen 2001)

Food group	Consumption of food (g/day)		CoQ_{10} (mg/day)		CoQ_9 (mg/day)	
	men	women	men	women	men	women
Meat	130	79	3.02	1.9	0.09	0.05
Eggs	22	16	0.03	0.02	0	0
Fish	32	25	0.44	0.35	0.01	0.01
Dairy products	537	405	0.37	0.28	0	0
Cereals	209	150	0	0	0.47	0.33
Fruits	173	214	0.18	0.23	0.04	0.05
Vegetables	243	206	0.31	0.26	0	0
Vegetable fats	29	19	0.99	0.66	0	0

Nutritional supplement

At the present time, CoQ_{10} is very popular as a freely available dietary supplement. But there is only little relevant research into its appropriate dose and bioavailability. The recommended daily intake for CoQ_{10} has not yet been established by legislation. Generally, the suitable dose of CoQ_{10} for adult people depends an age, sex, race, and psychical and physical conditions.

By Overvard *et al.* (1999), a dose of CoQ_{10} for a nutritional supplement ranging between 30 to 150 mg/day was suggested. Higher doses of CoQ_{10} were recommended therapeutically only.

The dietary supplements of CoQ_{10} are offered in different formulations: oil-based capsules (soybean oil or other vegetable oil), capsules on hydrophilic-gel (solubilised form), powder-filled capsules, and tablets, for example effervescent. One dose of these contains usually 15, 30, or 60 mg CoQ_{10}. These are often combined in the dietary supplements with tocopherol, resveratrol, folic acid, L-carnitine, yeasts, magnesium, selenium or other mineral and trace elements.

Joshi *et al.* (2003) found that orally-administered CoQ_{10} was more rapidly delivered to the blood when formulated as an effervescent tablet or as a fast-melting tablet than in other forms. Toxicity

Table 3. Coenzyme Q_{10} (as plastoquinone PQ_{10}) and coenzyme Q_9 (as plastoquinone PQ_9) in grapes (year 2001) (by Gvozdjáková *et al.* 2002)

Sample name of grape	PQ_{10} (μg/g)			PQ_9 (μg/g)		
	berry	skin	pulp	berry	skin	pulp
Riesling × Sylvaner – white	0.926	1.16	0.474	6.64	8.97	3.27
Welsh Riesling – white	1.52	2.96	2.04	n.d.	0.415	n.d.
Pinot Blanc – white	1.27	3.09	0.624	n.d.	0.442	n.d.
Riesling – white	1.48	2.89	1.97	0.246	0.541	n.d.
Valtelin Vert – white	9.83	8.74	2.33	n.d.	1.03	0.095
Chardonnay – white	2.17	12.5	–	n.d.	1.11	n.d.
Limberger – red	2.12	4.40	1.17	0.282	1.16	n.d.
Neronet – red	1.6	3.56	1.45	0.705	3.23	0.267
St. Laurent – red	50.5	107.7	1.39	0.532	1.18	0.253
Pinot Noir – red	9.02	–	–	1.29	–	–
Cabernet Sauvignon – red	5.55	–	–	0.620	–	–

Table 4. Concentration of coenzyme Q_{10} (as plastoquinone PQ_{10}) in wine in dependence on "wine ageing" (October 2001– February 2002) (by Gvozdjáková *et al.* 2002)

Sample name of wine	PQ_{10} (μg/l)	
	4-weeks aged (young) wine	14-weeks aged wine
Riesling × Sylvaner – white	3.92	3.79
Welsh Riesling – white	8.63	1.82
Pinot Blanc – white	n.d.	3.00
Riesling – white	n.d.	1.82
Valtelin Vert – white	3.52	n.d.
Limberger – red	3.92	1.04
Neronet – red	4.71	1.82
St. Laurent – red	3.14	1.04
Pinot Noir – red	1.96	n.d.
Cabernet Sauvignon – red	12.8	n.d.

and side effects have not been encountered in several decades of clinical use at doses up to several hundred mg a day (Joshi *et al.* 2003).

Because of its hydrophobicity and large molecular weight, the absorption of dietary CoQ_{10} is slow and limited. Gvozdjáková *et al.* (1999, 2002, 2004, 2005) following their research reported high bioavailability of CoQ_{10} in capsules in its hydrosoluble form. According to US Patent (2003) good absorption of CoQ_{10} is in capsules in its oil-water emulsion form. As CoQ_{10} is not toxic (no side effects were reported), no medical conditions known preclude it use. In the case of dietary supplements, solubilised CoQ_{10} formulations show enhanced bioavailability (Bhagavan & Chopra 2006). Most suppliers recommend to take CoQ_{10} may be taken with fatty foods.

Topical supplement

CoQ_{10} along with vitamin E, vitamin C and superoxiddismutase plays a key role in the skin protective network. In the skin, the reduced form of CoQ_{10} (ubiquinol) acts as an antioxidant with 10-fold higher levels in the epidermis than in the dermis (Shindo *et al.* 1994). By Hojerová (1999), ageing, poor eating habits, stress, and infection – they all affect the ability to provide adequate amounts of CoQ_{10} in the skin. After the age of 35, the organism begins to lose its ability to synthesise CoQ_{10} from food and its deficiency develops (Hojerová 2000). Hoppe *et al.* (1999) estimated CoQ_{10} increases in the skin of the human skin from childhood to maturity and then decreases with age and under irradiation with UVA rays. Therefore, oral supplementation with CoQ_{10} may be very helpful for the skin health.

During the last decade, CoQ_{10} has reached a leading position in the topical products, too. There are numerous topical formulations containing CoQ_{10}, claiming to possess of antioxidant effects, skin repair and regeneration abilities as well as anti-wrinkling and anti-ageing capability (Hojerová *et al.* 2006). Vinson and Anamandla (2006) demonstrated *in vivo* antioxidative effects in the skin of young and middle-aged subjects of two forms of CoQ_{10} after a single dose and after a long-term supplementation.

Although many scientific articles on the medical benefits of CoQ_{10} have been presented, little has been published on pharmacokinetics during its topical administration. Koprda *et al.* (2005) monitored CoQ_{10} penetration across snakes skins. Since CoQ_{10} is a large thermolabile and highly lipophilic molecule, the topical bioavailability is not very great. The carrier system is one of the important factors to determine pharmacokinetic of the skin penetration. The latest technical developments by Zulli *et al.* (2006) repeal that the encapsulation of CoQ_{10} in liposomes or nanoemulsions results in a significantly enhanced bioavailability.

CoQ_{10} and diseases

Normal blood and tissue levels of CoQ_{10} have been established by numerous investigators. Significantly decreased levels of CoQ_{10} have been noted in a wide variety of diseases in both animal and human studies. CoQ_{10} deficiency may be caused by an insufficient dietary CoQ_{10} intake, the impairment in CoQ_{10} biosynthesis, excessive utilisation of CoQ_{10} by the body, or any combination of the three. A decreased dietary intake is presumed in chronic malnutrition and cachexia (Littarru *et al.* 1991).

Animal data show that CoQ_{10} in large doses is taken up by all tissues including the heart and brain mitochondria. This fact has implications for therapeutic applications in human diseases, and evidence exists for its beneficial effects in cardiovascular and neurodegenerative diseases (Bhagavan & Chopra 2006).

CoQ_{10} and cardiovascular diseases. CoQ_{10} is known to be highly concentrated in the heart muscle cells due to the high energy requirements

of this cell type. For the past 14 years, the great bulk of clinical work with CoQ_{10} has focused on heart disease. Specifically, congestive heart failure (from a wide variety of causes) has been strongly correlated with significantly low blood and tissue levels of CoQ_{10}. The heart failure was found to correlate with the deficiency of CoQ_{10}, which may well be the primary etiologic factor in some types of heart muscle dysfunction, while in others it may be a secondary phenomenon. The majority of clinical studies concerned the treatment of heart disease and they were remarkably consistent in their conclusions: the treatment with CoQ_{10} significantly improved the heart muscle function while producing no adverse effects or drug interactions. There are many studies reporting positive results of oral administration of CoQ_{10} as adjunctive therapy in the treatment of congestive heart failure (Kaikkonen *et al.* 2002; Gazdík *et al.* 2003). In Japan and other countries, CoQ_{10} is an approved treatment for several cardiovascular conditions. CoQ_{10} may be useful in treating congestive heart failure as well as other heart conditions (Folkers *et al.* 1992). Many studies have confirmed that CoQ_{10} is safe. One of them, which evaluated the effects of CoQ_{10} supplementation on 2500 patients diagnosed with congestive heart failure (50–150 mg of CoQ_{10} daily for three months), reported that the patients showed a remarkable improvement in clinical signs and symptoms, without adverse side effects (Baggio *et al.* 1994). This study and many others conclude that CoQ_{10} supplementation is safe and effective.

By Gvozdjáková *et al.* (1999), CoQ_{10} whole blood levels in patients after heart transplantation were significantly lower in comparison with healthy persons. The level decreased significantly with incipient rejection in comparison with patients without signs of rejection.

CoQ_{10} and hypertension. The results of several small, uncontrolled studies in humans suggest that CoQ_{10} supplementation could be beneficial in the treatment of hypertension. More recently, two short-term placebo-controlled trials found that CoQ_{10} supplementation resulted in moderate blood pressure decreases in hypertensive individuals. Mortensen (1993) found that the addition of 120 mg/day of CoQ_{10} to conventional medical therapy for 8 weeks in patients with hypertension and coronary artery disease decreased systolic blood pressure by an average of 12 mm Hg and diastolic blood pressure by an average of 6 mm Hg as compared to a placebo containing B-complex vitamins. In patients with isolated systolic hypertension, the supplementation with 120 mg per day of coenzyme Q_{10} and 300 IU/day of vitamin E for 12 weeks resulted in an average decrease of 17 mm Hg in systolic blood pressure compared with 300 IU/day of vitamin E alone.

Low blood levels of CoQ_{10} have been found in people with hypertension but it is not clear if CoQ_{10} deficiency is the cause of the high blood pressure. Research suggests that CoQ_{10} causes small decreases in the blood pressure (Digiesi *et al.* 1990).

Greenberg and Frishman (1990) from the Sinai Hospital and Medical Centre in New York reported that the cardiovascular importance of CoQ_{10} is being evidenced in clinical trials worldwide. In humans, a deficiency of CoQ_{10} was found in 39% of patients with hypertension, compared to 6% of those with normal blood pressure. Providing these patients with 60 mg of CoQ_{10} for eight weeks resulted in a 10% or greater decrease in blood pressure. Yamagami *et al.* (1986) in a double-blind study found that 20 hypertensive subjects with low serum CoQ_{10} levels and receiving 100 mg of CoQ_{10} per day for 12 weeks showed a significant reduction in systolic and diastolic blood pressures.

CoQ_{10} and cancer. CoQ_{10} may also have potential as an anticancerogenic and immune-stimulating agent. CoQ_{10} in conjunction with conventional medical treatment and other antioxidant nutrients showed an increased survival rate and regression of cancer incidence. Numerous studies have noted the incidence of CoQ_{10} deficiency in a variety of cancers including breast, lung, prostate, pancreatic, and colon cancer (Lockwood & Mosegaard 1994; Folkers & Osterborg 1997).

Lockwood *et al.* (1994) described a research in which thirty-two women with metastatic breast cancer received 90 mg of CoQ_{10} daily, along with vitamins C and E, β-carotene, and essential fatty acids. In six cases, the tumor diminished. During the 18-month treatment period, none of the patients died and none showed signs of further distant metastases.

Two patients with metastatic breast cancer were treated with 390 mg/day of coenzyme Q_{10}. One of the patients was a 44-year-old woman with numerous liver metastases. After taking CoQ_{10} for 11 months, all of the liver metastases had disappeared and the patient was reported to be in excellent health. The other patient was a 49-year-old woman with breast cancer that had metastasised to the pleural cavity.

After six months of CoQ_{10} therapy, all of the pleural fluid was gone and the patient was reported to be in excellent health (Folkers *et al.* 1993).

CoQ_{10} and periodontal disease. The gingival biopsies in patients having diseased periodontal tissue showed a deficiency of coenzyme Q_{10}, in contrast to those with normal periodontal tissue who showed no deficiency (Littarru *et al.* 1971). In some studies, CoQ_{10} supplements caused faster healing and tissue repair (Inwamoto *et al.* 1981; Hanioka *et al.* 1994). Additional studies are needed to evaluate the effectiveness of CoQ_{10} when used together with the traditional therapy for periodontal disease.

CoQ_{10} and bronchial asthma. CoQ_{10} may be helpful in the treatment of respiratory diseases, especially asthma. Gazdík *et al.* (2002) described significantly decreased levels of CoQ_{10} and α-tocopherol both in plasma and blood in patients with bronchial asthma, as compared with healthy subjects.

Gvozdjáková *et al.* (2005) did a study which showed that patients with corticosteroid-dependent bronchial asthma had low plasma CoQ_{10} concentrations which might contribute to their antioxidant imbalance and oxidative stress. The reduction in the dosage of corticosteroids required by the patients following the antioxidant supplementation means a lower incidence of adverse effects due to the drugs.

CoQ_{10} and diabetes. The role of CoQ_{10} in the energy formation also relates to how the body uses carbohydrates. Preliminary research suggests that a close relative of this nutrient lowered blood sugar levels in a group of people with diabetes. People with type 2 diabetes were found to have significantly lower blood levels of CoQ_{10} as compared with healthy people (Miyake *et al.* 1999).

The supplementation with 100 mg/day of CoQ_{10} for 3 months neither improved glycemic control nor decreased insulin requirements in Type 1 diabetics compared to placebo. Similarly, 200 mg/day of CoQ_{10} supplementation for 6 months did not improve glycemic control or serum lipid profiles in Type 2 diabetics. The authors of both studies concluded that CoQ_{10} supplements could be used safely in diabetic patients (Eriksson *et al.* 1999; Henriksen *et al.* 1999).

CoQ_{10} and renal failure. CoQ_{10} was studied in a small pilot study involving 21 patients with chronic renal failure. Researchers administered CoQ_{10} to 11 of the subjects while 10 received a placebo capsule. After 4 weeks the number of patients on dialysis was significantly lower in the CoQ_{10} group (36.2%) while 90.0% of patients in the placebo group were on dialysis at the end of the study (Singh *et al.* 2000). Lippa *et al.* (1994) measured the levels of CoQ_{10} in a group of 48 patients on chronic hemodialysis, in 15 uremic patients, and in a control group of healthy subjects. CoQ_{10} levels were significantly lower (< 0.001) in both hemodialytic and uremic patients as compared with the normal group.

CoQ_{10} and Parkinson disease. CoQ_{10} showed some promise for slowing down the progression of Parkinson's disease in the early stage (Muller *et al.* 2003). The research by Schultz showed that mitochondrial function is impaired in patients with Parkinson's disease and CoQ_{10} levels are reduced in the mitochondria of Parkinsonian patients. Shults *et al.* (1999) in a national clinical trial including 80 patients with Parkinson's disease who did not require treatment for their disability, the patients who were given CoQ_{10} supplements showed signs that the disease was progressing less rapidly than would have been expected. The greatest benefit was seen in everyday activities of the patients, such as feeding, dressing, bathing, and walking. CoQ_{10} was safe and well tolerated at the dosages of up to 1200 mg/day (Shults *et al.* 2002).

CoQ_{10} and rheumatoid arthritis. By a study of Bauerová and Bezek (1999) and that of Jaswal *et al.* (2003), oxidative stress is one of the primary factors involved in the pathogenetic changes during rheumatoid arthritis. Antirheumatic treatment affecting the level of CoQ_{10} was found able to slow down the progression of this disease (Comstock *et al.* 1997; Knekt *et al.* 2000).

Mitochondrial function in the heart and skeletal muscle and effectivity of supplementation with CoQ_{10} was dependent on the severity of the induced adjuvant arthritis. The results with solubilised CoQ_{10} (hydrosoluble form) indicate its cardioprotective effect in the experimental model of adjuvant arthritis. They are thus of potential significance in the treatment of patients with rheumatoid arthritis (Gvozdjáková *et al.* 2004; Kucharská *et al.* 2005; Bauerová *et al.* 2008).

CONCLUSIONS

The exciting new findings by scientific researchers suggest that CoQ_{10} is an important antioxidant readily used by the body and delaying various the progress of diseases under medical supervision.

CoQ_{10} is very popular as a freely available dietary supplement, too. But only little has been published on its recommended daily intake and bioavailability. More researches are needed to examine the appropriate dose, effectiveness, and bioavailability of orally-administered and topically-administered coenzyme Q_{10}. In our present experimental research study, we are working on the determination of the topical absorption of coenzyme Q_{10} using *in vitro* OECD 428 method.

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