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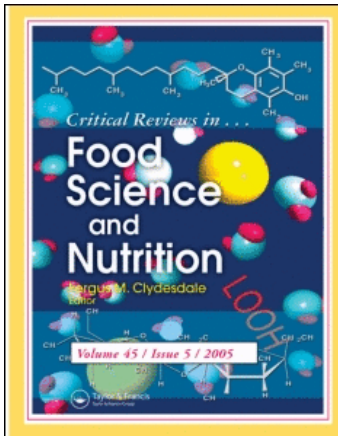
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# Coenzyme Q10 Contents in Foods and Fortification Strategies

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*Coenzyme Q10 (CoQ<sub>10</sub>) is an effective natural antioxidant with a fundamental role in cellular bioenergetics and numerous known health benefits. Reports of its natural occurrence in various food items are comprehensively reviewed and critically evaluated. Meat, fish, nuts, and some oils are the richest nutritional sources of CoQ<sub>10</sub>, while much lower levels can be found in most dairy products, vegetables, fruits, and cereals. Large variations of CoQ<sub>10</sub> content in some foods and food products of different geographical origin have been found. The average dietary intake of CoQ<sub>10</sub> is only 3–6 mg, with about half of it being in the reduced form. The intake can be significantly increased by the fortification of food products but, due to its lipophilicity, until recently this goal was not easily achievable particularly with low-fat, water-based products. Forms of CoQ<sub>10</sub> with increased water-solubility or dispersibility have been developed for this purpose, allowing the fortification of aqueous products, and exhibiting improved bioavailability; progress in this area is described briefly. Three main fortification strategies are presented and illustrated with examples, namely the addition of CoQ<sub>10</sub> to food during processing, the addition of this compound to the environment in which primary food products are being formed (i.e. animal feed), or with the genetic modification of plants (i.e. cereal crops).*

**Keywords** CoQ<sub>10</sub>, ubiquinone, ubiquinol, Q10vital, fortification, functional food, antioxidants

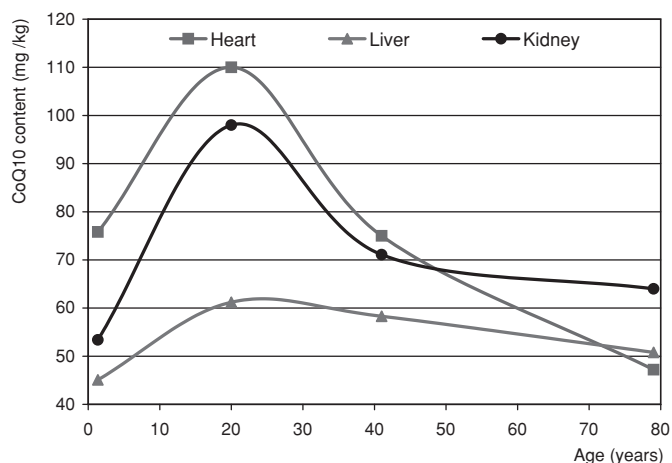
## INTRODUCTION

Coenzyme Q are natural lipophylic compounds present in each and every living cell; due to its ubiquitous occurrence in nature they are also called *Ubiquinones* (Lenaz, 1985; Lenaz et al., 1990; Kagan and Quinn, 2001; Haas et al., 2007). The predominant form in humans and most animals is Coenzyme Q<sub>10</sub>, containing 10 isoprenoid units attached to substituted benzoquinone moiety. It was first isolated from beef heart mitochondria in 1957 during an investigation of the mitochondria electron-transport system (Crane et al., 1957; review Crane, 2007). In the following years the fundamental role of CoQ<sub>10</sub> in the mitochondrial respiratory chain and in oxidative phosphorylation was determined and Peter D. Mitchell was awarded the Nobel Prize in Chemistry in 1978 for his contribution to the understanding of the role of CoQ<sub>10</sub> for biological energy transfers at the cellular level (Crane, 2007). Today it is well established that CoQ<sub>10</sub> is an essential component of the mitochondrial energy metabolism, responsible for energy conversion from carbohydrates and fatty acids into adenosine triphosphate (ATP), an

energy source involved in a multitude of physiologic functions in organisms, including muscle contraction (Crane, 2001). In the body it exists in either an oxidized (ubiquinone) or reduced form (ubiquinol and hydroquinone). Mainly in its reduced form, CoQ<sub>10</sub> is also known as a very effective antioxidant (Bentinger et al., 2007; Mellors and Tappel, 1966), protecting against lipid peroxidation, DNA, and protein oxidation and capable of functioning synergistically with other antioxidants (Challem, 2005). Recent studies show that it also cannot be discounted as a possible antioxidant when in an oxidized form (Petillo and Hultin, 2008).

Coenzyme Q<sub>10</sub> is chiefly found in the most active organs like the heart, kidney, and liver, where an even greater decline can be observed with increasing age (Fig. 1) (Kalén et al., 1989). Only up to 10% of total CoQ<sub>10</sub> is located in cytosol and about 50% in mitochondria, making it very accessible to free radicals that mainly form during the oxidative phosphorylation process (Sastry et al., 1961). In the body it is mostly present in a reduced form (ubiquinol), except in the lungs and brain where the oxidized form is predominant (Aberg et al., 1992). Continuous conversion between ubiquinone and ubiquinol (reduction–oxidation) takes place *in vivo*. Ubiquinone is also reduced during or following absorption in the intestine and over 95% of CoQ<sub>10</sub> in circulation exists in the ubiquinol form (Bhagavan

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**Figure 1** Age-related changes in CoQ<sub>10</sub> content in human organs; data source: Kalén et al. 1989.

and Chopra, 2006) and therefore its function is not affected by the form in which it is consumed. In this review, the term Coenzyme Q<sub>10</sub> (CoQ<sub>10</sub>) is used for both the oxidized and reduced forms, and ubiquinone or ubiquinol only when distinguishing between the two forms is relevant.

The important role of CoQ<sub>10</sub> has been reported in various clinical aspects (Kagan and Quinn, 2001). The beneficial effect in cardiovascular (Belardinelli et al., 2006; Pepe et al., 2007; Rosenfeldt et al., 2007; Singh et al., 2007), neurodegenerative and mitochondrial conditions (Galpern and Cudkowicz, 2007; Shults et al., 2002; Shults, 2003), diabetes (Chew and Watts, 2004), periodontal disease (Matthews-Brzozowska et al., 2007), male infertility (Balercia et al., 2004), and some other diseases is suggested in a number of case reports—preclinical and clinical studies (Dhanasekaran and Ren, 2005; Littarru and Tiano, 2005; Littarru and Tiano, 2010). A helpful effect in the treatment of cancer patients was reported either due to its antioxidant or bioenergetic activity (Lockwood et al., 1994), while an improvement in the tolerability of cancer treatment with CoQ<sub>10</sub> supplements is also under investigation (Roffe et al., 2004). It is also reported that CoQ<sub>10</sub> also reduces the formation of oxidative stress in the human skin, which is mainly connected with increasing age (Blatt et al., 1999). The human body biosynthesizes CoQ<sub>10</sub>, but its endogen tissue levels drop progressively with increasing age (Ely and Krone, 2000; Kalén et al., 1989). CoQ<sub>10</sub> deficiency was also observed in various medical conditions (Quinzii et al., 2007)—in persons with inappropriate nutrition and in smokers (Elsayed and Bendich, 2001). The intracellular biosynthesis of CoQ<sub>10</sub> begins from tyrosine through a cascade of eight aromatic precursors, which indispensably require eight vitamins, namely—tetrahydrobiopterin, vitamins B<sub>6</sub>, C, B<sub>2</sub>, B<sub>12</sub>, folic acid, niacin, and pantothenic acid (Folkers, 1996). Mevalonate is one of the precursors of CoQ<sub>10</sub>, which is also included in the biosynthesis of cholesterol. It has been shown that the endogenous synthesis of CoQ<sub>10</sub> is inhibited by cholesterol-lowering drugs (statins), which inhibit mevalonate biosynthesis, and supplementation has therefore been suggested

for some of their users (Bliznakov, 2002; Littarru and Langsjoen, 2007).

While extensive research is in progress to confirm the role of CoQ<sub>10</sub> in these and other clinical aspects, clinical results of its beneficial effects on human health were sufficiently supported to approve CoQ<sub>10</sub> as a drug first in Japan and later also in some other countries. Further, CoQ<sub>10</sub> is now widely used as a food supplement throughout the world. We have to mention the excellent safety record of this compound as shown in many clinical trials (Hathcock and Shao, 2006). Very high and chronic exposures have also been studied. No abnormal changes in clinical parameters or serious adverse events were observed in a study in which healthy human adults chronically consumed 900 mg of CoQ<sub>10</sub> daily (Kikkawa et al., 2007). In animal studies, the lethal single-dose administration has been determined to be over 5 g/kg in rats (Hidaka et al., 2007). All available data from pre-clinical and clinical studies show that the supplementation of CoQ<sub>10</sub> is very safe.

The total amount of CoQ<sub>10</sub> in an adult human body is approximately 2 grams, whereas 0.5 grams must be replaced daily by endogenous synthesis and nourishment (food) (Bliznakov and Wilkins, 1998; Kalén et al., 1989). The average turnover rate in the body is therefore around 4 days (Ernster and Dallner, 1995) and the importance of exogenous sources increases with the impairment of endogenous synthesis. The suggested daily intake of CoQ<sub>10</sub> from exogenous sources varies from 30–100 mg for healthy people to 60–1200 mg when used as an adjunctive therapy in some medical conditions (Bonakdar and Guarneri, 2005; Challem, 2005; Jones et al., 2002).

This article aims to review the natural occurrence of CoQ<sub>10</sub> in dietary sources as these data have been scattered across many papers in different languages. Further the possibilities of fortifying both processed and primary food products are discussed and presented with some examples.

## FOOD SOURCES

Beside endogenous synthesis, CoQ<sub>10</sub> is also supplied to the organism by various foods. However, despite the scientific community's great interest in this compound (currently over 6,000 hits in the ISI Web of Science<sup>®</sup>), quite a limited number of studies have been performed to determine the contents of CoQ<sub>10</sub> in dietary components. The first reports on this issue were published in 1959 by Lester and Crane, and Folkers et al., leading researchers of this compound (Lester and Crane, 1959; Page et al., 1959), but the sensitivity and selectivity of the analytical methods at that time did not allow reliable analyses, especially for products with low concentrations. These and other early studies of the natural distribution of Coenzyme Q were reviewed in 1985 (Ramasarma, 1985). Subsequent developments in analytical chemistry, particularly in high-pressure liquid chromatography (HPLC), have enabled a more reliable determination of CoQ<sub>10</sub> concentrations in various foods (Mattila and Kumpulainen, 2001). The results of CoQ<sub>10</sub> contents in various food

**Table 1** Overview of CoQ<sub>10</sub> contents in various foods

Foods	CoQ <sub>10</sub> cont. [mg/kg] <sup>a</sup>	Notes and Ref.	Class	Foods	CoQ <sub>10</sub> cont. [mg/kg] <sup>a</sup>	Notes and Ref.	Class
<b>Meats and their processed foods</b>				<b>Fishes and shellfish</b>			
Reindeer (not spec.)	157.9	<i>h</i>	A	Horse mackerel	(3.6–130) <sup>b</sup>	[3.6], <sup>l</sup> [20.7], <sup>e</sup> [130] <sup>o</sup>	B
Beef				Sardine	(5.1–64.3) <sup>b</sup>	[5.1], <sup>l</sup> [11.9], <sup>o</sup> [64.3] <sup>e</sup>	B
- heart	113.3	<i>h</i>	A	Herring			B
- liver	39.2–50.5	[39.2], <sup>h</sup> [50.5]; <sup>o</sup> (3.8) <sup>d</sup>	B	- heart	120.0–148.4	<sup>k</sup>	
- shoulder	40.1	<sup>o</sup>	B	- flesh	14.9–27.0	[14.9–23.9], <sup>k</sup> [27.0] <sup>f</sup>	
- sirloin	30.6	<i>n</i>	B	Yellowtail	12.8–20.7	[12.8], <sup>o</sup> [20.7] <sup>e</sup>	B
- thigh	30.3	<sup>o</sup>	B	- young	33.4	<sup>o</sup>	
- tenderloin	26.5	<i>n</i>	B	Baltic herring	10.6–15.9	[14.0], <sup>g</sup> [15.9] <sup>h</sup>	B
- beef (not spec.)	16.1–36.5	[16.1], <sup>g</sup> [31.0], <sup>e,f</sup> [36.5] <sup>h</sup>	B	Mackerel		[43.3] <sup>e</sup>	B
Pork				- heart	105.5–109.8	<sup>k</sup>	
- heart	118.1–282	[118.1], <sup>n</sup> [203 (151–282)], <sup>f</sup> [127], <sup>h</sup> (64.0) <sup>g</sup>	A	- red flesh	67.5–67.7	<sup>k</sup>	
- liver	22.7–54.0	[22.7], <sup>h</sup> [54.0], <sup>n</sup> (2.7) <sup>d</sup>	B	- white flesh	10.6–15.5	[10.6], <sup>o</sup> [12.3–15.5], <sup>k</sup> (4.3) <sup>l</sup>	
- shoulder	45.0	<sup>o</sup>	B	Pollack	14.4	<sup>h</sup>	B
- sirloin	14.0	<i>n</i>	B	Eel	7.4–11.1	[7.4], <sup>n</sup> [11.1] <sup>e</sup>	B
- thigh	13.8	<sup>o</sup>	B	Rainbow trout	8.5–11	[8.5], <sup>h</sup> [11] <sup>f</sup>	B
- pork (not spec.)	24.3–41.1	[20], <sup>h</sup> [24.3–41.1] <sup>e</sup>	B	Common mussel	9.5	<sup>l</sup>	B
- lard	10.0	<sup>e</sup>	B	Cuttlefish	4.7–8.2	[4.7], <sup>o</sup> [8.2] <sup>l</sup>	C
Chicken				Salmon	4.3–7.6	[4.3], <sup>f</sup> [5.7], <sup>o</sup> [7.6], <sup>n</sup>	C
- heart	92.3–192	[92.3], <sup>j</sup> [123.2], <sup>n</sup> [192], <sup>o</sup> (10.8) <sup>d</sup>	A	Grooved carpet shell	6.6	<sup>l</sup>	C
- liver	116.2–132.2	[116.2], <sup>n</sup> [132.2], <sup>j</sup> (5.6) <sup>d</sup>	A	Albacore	6.2	<sup>l</sup>	C
- thigh	24.2–25.0	[24.2], <sup>j</sup> [25.0] <sup>o</sup>	B	Flat fish	1.8–5.5	[1.8], <sup>o</sup> [5.5] <sup>e</sup>	D
- breast/chest	7.8–17.1	[7.8], <sup>j</sup> [16.6], <sup>n</sup> [17.1] <sup>o</sup>	B	Scallop	5.0	<sup>o</sup>	C
- wing	11.0	<sup>j</sup>	B	Pike	5.4	<sup>l</sup>	C
- chicken (not spec.)	14–21	[14], <sup>h</sup> [17], <sup>f</sup> [21] <sup>e</sup>	B	Tuna	4.9	[4.9] <sup>o</sup>	C
<b>Egg</b>				- canned	14.9–15.9	[14.9], <sup>o</sup> [15.9] <sup>h</sup>	B
Chicken egg	0.7–3.7	[1.9 (1.0–2.9)], <sup>f</sup> [1.2], <sup>h</sup> [3.7], <sup>e</sup> [0.7] <sup>o</sup>	D	Striped sea bream	4.9	<sup>l</sup>	C
- yolk	5.2	<sup>j</sup>	C	Octopus	3.4	<sup>o</sup>	C
<b>Dairy products</b>				Curled picarel	4.6	<sup>l</sup>	C
Butter	7.1	<sup>e</sup>	C	Oyster	3.4–4.3	[3.4], <sup>o</sup> [4.3] <sup>l</sup>	D
Cheese		[1.4], <sup>o</sup> [2.1] <sup>e</sup>	D	Squid	3.8	<sup>n</sup>	D
- Emmental	1.3	<sup>h</sup>		Cod	3.7	<sup>o</sup>	D
- Edam	1.2	<sup>h</sup>		Bogue	3.7	<sup>l</sup>	D
Cow milk			D	Octopus	3.5	<sup>l</sup>	D
- fresh, 3.6% fat	1.9	<sup>i</sup>		Annular sea bream	3.4	<sup>l</sup>	D
- 3.5% fat	1.3	<sup>i</sup>		Common pandora	3.1	<sup>l</sup>	D
- 1.5–1.6% fat	0.7–1.2	[0.1], <sup>h</sup> [0.7–1.2] <sup>i</sup>		European hake	2.9	<sup>l</sup>	D
- UHT, 3.5% fat	1.7	<sup>i</sup>		Shrimp	1.7–2.8	[1.7], <sup>o</sup> [2.8] <sup>l</sup>	D
- UHT, 1.6% fat	1.2	<sup>i</sup>		Bondex murex	2.6	<sup>l</sup>	D
- UHT, 0.5% fat	0.5	<sup>i</sup>		Red mullet	2.6	<sup>l</sup>	D
Yogurt		[0.3], <sup>o</sup> [1.2], <sup>f</sup> [2.4] <sup>h</sup>	D	Striped mullet	2.4	<sup>l</sup>	D
- 3.2% fat	0.7–1.1	<sup>i</sup>		Red band fish	2.4	<sup>l</sup>	D
- 1.5–1.6% fat	0.7–1.4	<sup>i</sup>		Striated buccinum	2.3	<sup>l</sup>	D
- 0% fat	up to 0.1	<sup>i</sup>		Brill	1.9	<sup>l</sup>	D
Yogurt from goat and sheep milk			E	Loligo	0.4	<sup>l</sup>	E
- 6.0% fat	0.3	<sup>i</sup>		Tub gurnad	0.4	<sup>l</sup>	E
Sour milk			E	Great weever	0.3	<sup>l</sup>	E
- 3.2% fat	0.5–0.9	<sup>i</sup>		Comber	/	<sup>c.l</sup>	E
- 1.6% fat	0.5	<sup>i</sup>		Piper gurnad	/	<sup>c.l</sup>	E
- 0.1% fat	/	<sup>c.i</sup>		Sea bass	/	<sup>c.l</sup>	E
Kefir			E	Streaked gurnad	/	<sup>c.l</sup>	E
- 3.5% fat	0.9	<sup>i</sup>		<b>Oils</b>			
- 1.6% fat	0.7	<sup>i</sup>		Soybean oil			
Cream			E	- Italian studies	221–279	[221], <sup>p</sup> [279] <sup>m</sup>	A
- 35% fat	0.9	<sup>i</sup>		- Japan studies	53.8–92.3	[53.8], <sup>o</sup> [92.3] <sup>e</sup>	A
- 20–22% fat	0.5–0.9	<sup>i</sup>		- refined (Ital.)	199	<sup>p</sup>	A
Curd			E	Corn oil			
- 35% fat	0.7	<sup>i</sup>		- Italian studies	113–139	[113], <sup>p</sup> [139] <sup>m</sup>	A
- 13% fat, pressed	0.7	<sup>i</sup>		- Japan study	13.0	<sup>e</sup>	B
				- refined (Ital.)	106	<sup>p</sup>	A
				Olive oil			
				- Italian study	109	<sup>p</sup>	A

(Continued on next page)

**Table 1** Overview of CoQ<sub>10</sub> contents in various foods (Continued)

Foods	CoQ <sub>10</sub> cont. [mg/kg] <sup>a</sup>	Notes and Ref.	Class	Foods	CoQ <sub>10</sub> cont. [mg/kg] <sup>a</sup>	Notes and Ref.	Class
- Japan study	4.1	<sup>e</sup>	D	Broccoli	5.9–8.6	[6.6 (5.9–7.7)], <sup>f</sup> [7.0], <sup>o</sup>	C
- extra virgin (Ital.)	114–160	[114], <sup>m</sup> [160] <sup>p</sup>	A			[8.6] <sup>e</sup>	
Rapeseed oil	63.5–73.4	[63.5], <sup>h</sup> [73.4] <sup>e</sup>	A	Rape (flower cluster)	6.7–7.4	[6.7], <sup>o</sup> [7.4] <sup>e</sup>	C
Peanut oil	77	<sup>m</sup>	A	Cauliflower	(1.4–6.6) <sup>b</sup>	[1.4], <sup>e</sup> [2.7], <sup>h</sup> [4.9], <sup>f</sup> [6.6] <sup>o</sup>	DE
Sesame oil	32.0	<sup>e</sup>	B	Chinese cabbage	2.1–4.5	[2.1], <sup>e</sup> [2.7], <sup>n</sup> [4.5] <sup>o</sup>	D
Cottonseed oil	17.3	<sup>e</sup>	B	Sorrel	3.6	<sup>d</sup>	D
Sunflower oil				Sweet potato	3.0–3.6	[3.0], <sup>o</sup> [3.6] <sup>e</sup>	D
- Italian studies	10–15	[10], <sup>p</sup> [15] <sup>m</sup>	B	Garlic	2.7–3.5	[2.7], <sup>e</sup> [3.5], <sup>o</sup>	D
- Japan study	4.2	<sup>e</sup>	C	Sweet pepper	3.3	<sup>e</sup>	D
- refined	15	<sup>p</sup>	B	Japanese radish			
Safflower oil	4.0	<sup>e</sup>	D	- leaves	3.3	<sup>e</sup>	D
Rice bran oil	/	<sup>c,e</sup>	E	- root	0.7–1.0	[0.7], <sup>o</sup> [1.0] <sup>e</sup>	F
Coconut oil	/	<sup>c,e</sup>	E	Cabbage	1.0–3.1	[1.0], <sup>d</sup> [1.6], <sup>e</sup> [3.1] <sup>o</sup>	D
<b>Nuts and seeds</b>			B	Pea	2.3–2.7	[2.3], <sup>o</sup> [2.7] <sup>h</sup>	D
Peanuts (roasted)	26.7	<sup>e</sup>	B	Asparagus	2.2	<sup>o</sup>	D
Sesame seeds (roast.)	17.6–23.0	[17.6], <sup>o</sup> [23.0] <sup>e</sup>	B	Carrot	up to 2.2	[<0.2], <sup>f</sup> [1.7], <sup>h</sup> [2.2] <sup>e</sup>	D
Pistachio nuts (roast.)	20.1	<sup>e</sup>	B	Eggplant	1.0–2.2	[1.0], <sup>o</sup> [2.1], <sup>e</sup> [2.2] <sup>n</sup>	D
Walnuts (raw)	19.0	<sup>e</sup>	B	Mustard spinach	2.0	<sup>o</sup>	D
Hazelnuts (roasted)	16.7	<sup>e</sup>	B	Bean	1.8	<sup>h</sup>	D
Almond	5.0–13.8	[5.0], <sup>o</sup> [13.8] <sup>e</sup>	BC	Japanese taro	1.8	<sup>o</sup>	D
Chestnuts (raw)	6.3	<sup>e</sup>	C	Welsh onion	1.1	<sup>o</sup>	DF
<b>Cereals</b>				Potato	0.5–1.1	[0.5], <sup>d,f,h</sup> [1.0], <sup>e</sup> [1.1] <sup>o</sup>	D
Corn				Lotus root	1.0	<sup>o</sup>	DF
- whole grain	/	<sup>c,e</sup>	E	Onion	0.7–1.0	[0.7], <sup>o</sup> [1.0] <sup>e</sup>	F
- corn germ	7.0	<sup>d</sup>	C	Brussels sprout	0.9	<sup>d</sup>	F
Wheat				Tomato	up to 0.9	[/], <sup>c,o</sup> [0.2], <sup>f</sup> [0.9] <sup>h</sup>	F
- whole grain	/	<sup>c,e</sup>	E	Cucumber	up to 0.1	[/], <sup>c,f,h</sup> [0.1] <sup>o</sup>	F
- wheat germ	3.5–6.8	[3.5], <sup>e</sup> [6.8] <sup>d</sup>	CD	Basella	/	<sup>c,e</sup>	F
Rice				Button mushroom	/	<sup>c,o</sup>	F
- whole wheat	/	<sup>c,e,f</sup>	E	Edible burdock	/	<sup>c,e</sup>	F
- rice bran	4.9	<sup>e</sup>	D	Garland chrysanthemum	/	<sup>c,e</sup>	F
Japan. barnyard millet	1.4	<sup>e</sup>	E	Lettuce	/	<sup>c,e</sup>	F
(whole grain)				Okra	/	<sup>o</sup>	F
Buckwheat (whole gr.)	1.1	<sup>e</sup>	E	Pumpkin	/	<sup>c,e,o</sup>	F
Job's tears (whole gr.)	0.6	<sup>e</sup>	E				
Barley (whole gr.)	/	<sup>c,e</sup>		<b>Fruits, berries and their proceeded foods</b>			
Oats (whole gr.)	/	<sup>c,e</sup>		Avocado	9.5	<sup>o</sup>	B
<b>Pulses, vegetables, mushrooms, and their proceeded foods</b>				Blackcurrant	3.4	<sup>h</sup>	D
Parsley	(7.5–26.4) <sup>b</sup>	[7.5], <sup>o</sup> [26.4], <sup>n</sup>	B	Strawberry	1.4	<sup>h</sup>	D
Soybean				Orange	1.0–2.2	[1.0], <sup>o</sup> [1.4], <sup>h</sup> [2.2] <sup>f</sup>	D
- whole, dry	6.8–19.0	[6.8], <sup>o</sup> [19.0] <sup>e</sup>	B	- juice	0.3	<sup>h</sup>	E
- green (raw)	18.7	<sup>e</sup>	B	Grapefruit	1.3	<sup>o</sup>	D
- boiled	12.1	<sup>e</sup>	B	Apple	1.1–1.3	[1.1], <sup>f</sup> [1.2], <sup>o</sup> [1.3] <sup>h</sup>	D
- natto (fermented)	5.6–10.0	[5.6], <sup>o</sup> [10.0] <sup>e</sup>	C	Lingonberry	0.9	<sup>h</sup>	E
- sprout	1.1	<sup>o</sup>	D	Clementine	0.9	<sup>h</sup>	E
- tofu	2.9	<sup>o</sup>	D	Banana	0.8	<sup>o</sup>	E
- soy drink (milk)	up to 2.5	[<0.1], <sup>i</sup> [2.5] <sup>o</sup>	E	Persimmon	0.8	<sup>o</sup>	E
- soy yogurt	<0.1	<sup>i</sup>	E	Kiwi	0.5	<sup>f</sup>	E
Perilla (leaves)	(2.1–10.2) <sup>b</sup>	[2.1], <sup>o</sup> [10.2] <sup>e</sup>	CD	Strawberry	0.5	<sup>o</sup>	E
Spinach	(0.4–10.2) <sup>b</sup>	[0.4], <sup>o</sup> [4.9], <sup>d</sup> [10.2] <sup>e</sup>	CD				

<sup>a</sup> If more than one reference is available, the CoQ<sub>10</sub> content interval is stated. Data that differentiate significantly from the majority of reliable studies are not stated in the CoQ<sub>10</sub> content column, but are included in the Notes and References column in parentheses.

<sup>b</sup> Food items with a large CoQ<sub>10</sub> content interval (min. 8 mg/kg and three times difference between higher and lower reliable CoQ<sub>10</sub> content) are stated in round brackets and need to be re-evaluated.

<sup>c</sup> Below the detection limit.

<sup>d</sup> (Kraszner-Berndorfer and Kováts, 1972); determination of the oxidized form.

<sup>e</sup> (Kamei et al., 1986); determination of the oxidized form.

<sup>f</sup> (Weber et al., 1997); determination of the oxidized form.

<sup>g</sup> (Mattila et al., 2000); determination of the oxidized form with an electrochemical detector.

<sup>h</sup> (Mattila and Kumpulainen, 2001); determination of the oxidized form.

<sup>i</sup> (Stražičar et al., 2005); determination of the oxidized form.

<sup>j</sup> (Prošek et al., 2007); determination of the oxidized form.

<sup>k</sup> (Souchet and Laplante, 2007); determination of the oxidized form.

<sup>l</sup> (Passi et al., 2002); total CoQ<sub>10</sub> after determination of the oxidized and reduced form.

<sup>m</sup> (Cabrini et al., 2001); total CoQ<sub>10</sub> after determination of the oxidized and reduced form; recalculated to mg/kg with an approximation of oil density: 0.92 g/cm<sup>3</sup>.

<sup>n</sup> (Kettawan et al., 2007); total CoQ<sub>10</sub> after determination of the oxidized and reduced form.

<sup>o</sup> (Kubo et al., 2008); total CoQ<sub>10</sub> after determination of the oxidized and reduced form.

<sup>p</sup> (Pregolato et al., 1994); total CoQ<sub>10</sub> after determination of the oxidized and reduced form; recalculated to mg/kg with an approximation of oil density: 0.92 g/cm<sup>3</sup>.

**Table 2** Classes of CoQ<sub>10</sub> levels in food sources

Class	Approx. CoQ <sub>10</sub> content	Description
<b>A</b>	over 50 mg/kg	very rich CoQ <sub>10</sub> source
<b>B</b>	10–50 mg/kg	rich CoQ <sub>10</sub> source
<b>C</b>	5–10 mg/kg	modest CoQ <sub>10</sub> source
<b>D</b>	1–5 mg/kg	poor CoQ <sub>10</sub> source
<b>E</b>	below 1 mg/kg	very poor CoQ <sub>10</sub> source

products as determined in studies since 1985 are overviewed comprehensively in Table 1, together with some interesting earlier reports after 1970. The reviewed results should be employed carefully as significant variations of reported CoQ<sub>10</sub> content in similar products are reported in some cases. Possible reasons for these differences lie in variations seen around the world, different types of analyzed tissues, or their treatment along with different sample species. All analytical procedures include a phase in which CoQ<sub>10</sub> has to be extracted from a food matrix to a non-polar solvent; in practice, this process cannot be completely quantitative. Further, a certain difference between analyses can also be generated due to differences in analytical methods; a difference of about 15% was noted when the same samples were analyzed with LC and LC/MS determination (Stražičar et al., 2005). It should also be mentioned that the uncertainty of the analytical results has been neglected in many studies, even though up to  $\pm 50\%$  uncertainty is reported in samples with a low CoQ<sub>10</sub> content (Stražičar et al., 2005). Due to the mentioned variations in CoQ<sub>10</sub> content, we have assigned food items into 5 classes (A, B, C, D, E) depending on their CoQ<sub>10</sub> level; products that are the richest in CoQ<sub>10</sub> (over approx. 50 mg/kg) are assigned to class A, while class E represents its very poor sources (below approx. 1 mg/kg) (Table 2).

Kraszner-Berndorfer and Kováts studied the levels of CoQ<sub>10</sub> of several food items by column chromatography and determined some other bioquinones, such as vitamin K<sub>1</sub>-phylloquinone, vitamin K<sub>2</sub>-menaquinone, plastoquinone, and tocopheryl quinone (Kraszner-Berndorfer and Kováts, 1972). While their reports of CoQ<sub>10</sub> levels in vegetables are mostly in line with later reports (Table 1), the results for meats and oil appears to be too low (i.e. 1.0 and 3.8 mg/kg for sunflower oil and beef liver, respectively, 4 to 13-times lower than in subsequent reports). The first extensive study of Coenzyme Q levels in food products was published in Japan in 1986; CoQ<sub>10</sub> and CoQ<sub>9</sub> were determined in over 70 samples using the HPLC technique (Kamei et al., 1986). The intake of CoQ<sub>10</sub> in the average Danish diet was then investigated on the basis of analytical results for selected 25 food items; CoQ<sub>9</sub> and  $\alpha$ -tocopherol were also determined and the effect of cooking studied (Weber et al., 1997). No detectable destruction of CoQ<sub>10</sub> was observed by boiling, while 14–32% destruction occurred by frying. A Finnish research group analyzed some food samples during their comparison of different detectors in determinations of CoQ<sub>10</sub> (Mattila et al., 2000). The same group further determined CoQ<sub>10</sub> and CoQ<sub>9</sub> levels in 35 selected food items and studied dietary intake in Finns (Mattila and Kumpulainen, 2001). CoQ<sub>10</sub> contents were studied

in detail as regards many Slovenian and other European dairy products such as milk, yogurt, sour milk, probiotics, cream, and curd (over 50 samples) as well as soy products (Stražičar et al., 2005). The same group also performed an interesting investigation of different poultry tissues, revealing CoQ<sub>10</sub> variations in different tissues of the same animal species (Prošek et al., 2007). Seasonal variations of CoQ<sub>10</sub> content in different tissues of pelagic fish like mackerel and herring were recently studied in Canada (Souchet and Laplante, 2007; Laplante et al., 2009). Due to the rapid oxidation of ubiquinol to ubiquinone during sample preparation and extraction, CoQ<sub>10</sub> content has usually been measured by a determination of the ubiquinone content. However, the separate determination of ubiquinone and ubiquinol in food products is also possible and the results of those studies are included in Table 1 as total CoQ<sub>10</sub> content. Two Italian research groups determined the contents of the reduced and oxidized forms of CoQ<sub>9</sub> and CoQ<sub>10</sub> in samples of edible oils (olive, peanut, soybean, corn, and sunflower oil) (Cabrini et al., 2001; Pregnolato et al., 1994). Another Italian group further studied the Coenzyme Q content in the muscle tissue of 30 different marine species of fish and shellfish, together with levels of vitamin E and various fatty acids; they determined that the ubiquinol versus the ubiquinone ratio is relatively high in fresh species, therefore this parameter was suggested as being useful as an index of fish freshness (Passi et al., 2002). Thirteen food items were recently analyzed in Japan during an assessment of the quality of CoQ<sub>10</sub>-containing dietary supplements (Kettawan et al., 2007). The dietary intake of ubiquinone and ubiquinol was recently established for the Japanese population; analyses of 70 food items showed that the intake of ubiquinol accounts for 46% of the total CoQ<sub>10</sub> intake (Kubo et al., 2008).

As expected, meats and fishes are the richest source of dietary CoQ<sub>10</sub> due to their relatively high levels of fats and mitochondria (Mattila and Kumpulainen, 2001). The compound is non-equally distributed among different tissues of the same animal source depending on its function, e.g. heart, liver, muscle, etc. (Kalén et al., 1989). For this reason, the origin of analyzed tissue is stated in Table 1 where such information is available. The highest tissue level of CoQ<sub>10</sub> was determined in reindeer meat (158 mg/kg), beef, pork, and chicken heart and chicken liver (class A: over 50 mg/kg). Contents in most other beef and pork tissues (except liver) are lower (14–45 mg/kg), while lard only contains 10 mg CoQ<sub>10</sub>/kg. Substantial differences in CoQ<sub>10</sub> content within different tissues of chickens were also confirmed by several authors; while liver and heart are rich in CoQ<sub>10</sub>, much lower levels were determined in the thighs, breasts, and wings (below 25 mg/kg). Nevertheless, together meats represent the most important source of dietary CoQ<sub>10</sub> [64% in Danes (Weber et al., 1997), 55% in Finns (Mattila and Kumpulainen, 2001) and 44% in Japanese (Kubo et al., 2008)].

The CoQ<sub>10</sub> concentration in chicken eggs was also determined, yet substantial differences can be observed between different studies (1–4 mg/kg); only egg yolk can be regarded as a modest CoQ<sub>10</sub> source (5 mg/kg). Dairy products are also much poorer in CoQ<sub>10</sub>, when compared to animal tissues. Modest

content was found in butter (7 mg/kg). A connection was found between the technological processing of food, its fat content and concentration of CoQ<sub>10</sub> (Stražičar et al., 2005)—namely, less processed products and foods with a higher amount of fat usually have greater amounts of CoQ<sub>10</sub>, e.g. full-fat fresh milk (3.6% fat: 1.9 mg/kg) contains more CoQ<sub>10</sub> than UHT milk with reduced milk fat content (1.2 and 0.5 mg/kg for 1.6% and 0.5%, respectively). Similarly, fermented products such as yogurts (3.2% fat: 0.7–1.1 mg/kg), sour milk (3.2% fat: 0.5–0.9 mg/kg), and kefir (3.5% fat: 0.7–0.9 mg/kg) only contain approximately 2/3 of the CoQ<sub>10</sub> in milk with the same content of milk fat (3.5% fat: 1.3–1.9 mg/kg), while the content is even lower in products with reduced milk fat; yogurts with declared 0% of milk fat only contain negligible concentrations of CoQ<sub>10</sub>. Interestingly, a lower content was found in yogurt from goat and sheep milk (0.3 mg/kg) despite their much higher fat content (6%). Similarly, very low levels are present in cream (0.9 mg/kg) despite its high fat content (35%).

Within fish, substantial differences in reported CoQ<sub>10</sub> content were observed in some cases, particularly in horse mackerel (3.6–130 mg/kg) and sardine (5.1–64.3 mg/kg). Mackerel and herring were recently studied in detail; the highest CoQ<sub>10</sub> concentration was found in the heart (over 100 mg/kg) (Souchet and Laplante, 2007). In mackerel, a 5-times higher concentration of CoQ<sub>10</sub> in red flesh as compared with white flesh was explained mainly by the higher abundance of mitochondria in red flesh and since red flesh is generally used for continuous swimming activities and obtains its energy from oxidative phosphorylation, whereas white flesh is mostly active during vigorous movements and mainly acquires its energy from anaerobic glycolysis; slight seasonal variations in CoQ<sub>10</sub> levels were also determined in white flesh (Souchet and Laplante, 2007). Lower contents of CoQ<sub>10</sub> were observed in bottom fish, for example flat fish and eels (2–6 and 7–11 mg/kg) and interestingly also in salmon (4–8 mg/kg), despite its significant fat content. On average, a higher CoQ<sub>10</sub> content was found in the *Crustacea* subphylum than in the *Teleostei* infraclass (Passi et al., 2002). The consumption of fish and shellfish is very different throughout the world and their importance for the dietary intake of CoQ<sub>10</sub> is estimated to range from 9% in Northern European countries (Mattila and Kumpulainen, 2001; Weber et al., 1997) to 22% in Japan (Kubo et al., 2008).

Looking at products of non-animal origin, the highest CoQ<sub>10</sub> levels have been observed within oils. The composition of oils is of course closely connected to the composition of the source plants—CoQ<sub>10</sub> is dominant in oils from plants belonging to the *Brassicaceae* and *Fabaceae* family, while CoQ<sub>9</sub> prevails in grasses (*Poaceae*) and plants belonging to *Asteraceae* (Kamei et al., 1986). Two independent Italian research groups determined much higher levels of CoQ<sub>10</sub> in soybean, corn, and olive oil (199–279, 106–139, and 109–160 mg/kg, respectively) (Cabrini et al., 2001; Pregnolato et al., 1994) than two groups in Japan (54–92, 13, and 4 mg/kg, respectively) (Kamei et al., 1986; Kubo et al., 2008). It is known that the content of some components in natural oils differs significantly with regard to the

region in which the source plants were grown, but no such studies have yet been performed for CoQ<sub>10</sub>. The different concentrations observed in the mentioned oils may indicate that the level of Coenzyme Q in oils is also strongly connected with the geographical and climatic origin of plants, yet further investigations are needed to confirm this hypothesis. Such an investigation would also be very useful for evaluating the quality of oils. Moving on to other oil samples, rapeseed oil is also very rich in CoQ<sub>10</sub> (63–73 mg/kg). About half of that level can be found in sesame oil (32 mg/kg) and about a quarter in cottonseed and sunflower oil (17 and 4–15 mg/kg, respectively). It should be noted that some of these oils, particularly corn oil (186–405 mg/kg), are very rich in CoQ<sub>9</sub> (Cabrini et al., 2001; Kamei et al., 1986). The content of CoQ<sub>10</sub> in rice bran and coconut oil were below the detection limit.

Various nuts and seeds are also quite rich in CoQ<sub>10</sub> with peanuts, sesame seeds, and pistachio nuts being the richest representatives (over 20 mg/kg). While walnuts and hazelnuts are also relatively rich in CoQ<sub>10</sub> (17–19 mg/kg), less than half of that content can be found in chestnuts. Two quite different results are reported for almonds, namely 14 mg/kg (roasted sweet almond) and 5 mg/kg.

In most cereals CoQ<sub>9</sub> is dominant (4–23 mg/kg) and the contents of CoQ<sub>10</sub> were below or near the detection limit (Kamei et al., 1986). Interestingly, while rice bran and wheat germ contain high levels of Coenzyme Q when compared to brown rice or whole grain wheat, it was suggested that these compounds localize upon germs (Kamei et al., 1986). Similarly to corn oil, a high CoQ<sub>9</sub> level was found in whole grain corn (23 mg/kg) while its CoQ<sub>10</sub> content was below the detection limit. Some CoQ<sub>10</sub> can be found in whole-grain Japanese barnyard millet, buckwheat, and Job's tears (1.4, 1.1 and 0.6 mg/kg, respectively), while its content in barley and oats was not detected.

Soybeans are relatively rich in CoQ<sub>10</sub> (8–19 mg/kg), while much less CoQ<sub>10</sub> can be found in their processed products such as in tofu, soy milk and yogurts. Within vegetables, high CoQ<sub>10</sub> was also recently found in parsley (26 mg/kg), but this value has to be reevaluated as a much lower level was previously reported (8 mg/kg). Something similar applies to perilla and spinach as very large CoQ<sub>10</sub> content intervals are available in the literature (2.1–10.2 and 0.4–10.2 mg/kg, respectively). Broccoli, rape, and cauliflower are modest sources of CoQ<sub>10</sub>, while concentrations below 5 mg/kg were found in other analyzed samples. No CoQ<sub>10</sub> has been found in plants of *Asteraceae*, *Cucurbitaceae*, and *Basellaceae* family, while concentrations of CoQ<sub>9</sub> are 1–5 mg/kg (Kamei et al., 1986).

Most fruits and berries represent a poor to very poor source of CoQ<sub>10</sub>, with the exception of avocado where the relatively high CoQ<sub>10</sub> content (9.5 mg/kg) is probably connected with its high fat content. Blackcurrant is another exception with a modest CoQ<sub>10</sub> level (3.4 mg/kg), while concentrations in other samples were determined to be below 1.4 mg/kg.

The CoQ<sub>10</sub> content in people's diets in the developed world was determined to be 3–6 mg per day, primarily derived from meat, whereas cereals, fruit, and vegetables only make up a



minor contribution (Kubo et al., 2008; Mattila and Kumpulainen, 2001; Weber et al., 1997). Such CoQ<sub>10</sub> intake is not sufficient to either compensate age-related CoQ<sub>10</sub> decline or the lack of it due to other reasons. A greater CoQ<sub>10</sub> intake can be achieved with the consumption of substantially increased amounts of CoQ<sub>10</sub>-rich food products, but even when looking at just the few richest CoQ<sub>10</sub> sources (class A), over 0.5 kg of these products would need to be consumed daily for an intake of 30 mg CoQ<sub>10</sub>. Additional intake of exogenous CoQ<sub>10</sub> is therefore beneficial and can be consumed either in the form of food supplements or, more naturally, with functional food fortified with CoQ<sub>10</sub>, or both.

### COENZYME Q<sub>10</sub> AND FUNCTIONAL FOODS

The functional foods concept started in Japan in the early 1980s with the launch of three large-scale government-funded research programs on “systematic analyses and development of functional foods,” “analyses of physiological regulation of the functional food,” and “analyses of functional foods and molecular design.” In 1991 a category of foods with potential benefits in a nutritional effort to reduce the escalating cost of health care was established (Foods for Specified Health Use – FOSHU) (Ashwell, 2002). In the United States, evidence-based health or disease prevention claims have been allowed since 1990 when the Nutrition Labeling and Education Act was adopted; claims have to be approved by the Food and Drug Administration (FDA) (Arvanitoyannis and Houwelingen-Koukaliaroglou, 2005). In the European Union, the harmonized Health and Nutrition Claims Regulation was accepted in 2006 and will reach its full affect the European market in 2011 (EC Regulation no. 1924/2006) when all nutritional and health claims will require specific authorization by the European Commission through the Comitology procedure, following scientific assessment and verification of a claim by the European Food Safety Authority (EFSA).

The definition of functional foods is an ongoing issue and many variations have been suggested by different organizations (Arvanitoyannis and Houwelingen-Koukaliaroglou, 2005). A consensus on the functional foods concept was reached in the European Union in 1999 when a working definition was established whereby a food can be regarded as functional if it is satisfactorily demonstrated to beneficially affect one or more target functions in the body beyond adequate nutritional effects in a way that is relevant to either an improved state of health and well-being or a reduction of disease risk. Functional foods must remain foods and demonstrate their effects when consumed in daily amounts that can be normally expected (Ashwell, 2002). Examples of such functional foods are products fortified with a sufficient amount of an active component to provide evidence-based health benefits for consumers. Regardless of the various definitions, the main purpose of functional food should be clear—to improve health and well-being. Current legislation concerning this matter is progressing very slowly and the reg-

ulations often allow manufacturers to imply that a food item promotes health without providing proper scientific evidence or ban claims that food prevents disease, even when it does (Katan and De Roos, 2004). The basic problem is that marketing such “healthy” foods to otherwise healthy people is very successful and therefore this area should be sufficiently regulated and carefully watched by the scientific community. Special attention should be paid to the adequate scientific background of health claims which as part of product labeling present important information to consumers (Hooker and Teratanavat, 2008).

On the basis of the reported health benefits of the supplementation of CoQ<sub>10</sub> to human nutrition, quite some time ago scientists started thinking about fortifying foods with Coenzyme Q<sub>10</sub> (Borekova et al., 2008). In addition to the relatively high price of CoQ<sub>10</sub> two main problems are closely connected with this issue: (a) the diverse legislation and regulation of health claims within different countries; and (b) fortification technology.

At least three classes of health claims are in proceedings at the European Food Safety Authority (EFSA) on the proposal of the European Federation of Associations of Health Product Manufacturers (EHPM); energy metabolism, heart health, and antioxidant properties are currently being addressed. In the United States, CoQ<sub>10</sub> is regulated as a food component, meaning that the approval of products that contain this compound is not required by the FDA unless specific health claims are made; to our knowledge, no food health claims have been accepted or declined. In respect of extensive scientific work and the determined important role of CoQ<sub>10</sub> in various clinical aspects we believe that further human efficacy studies will allow the world-wide approval of CoQ<sub>10</sub> health claims, but any prediction of what will or might be claimed about related contents could at this stage be very speculative. Nevertheless, the important role of CoQ<sub>10</sub> in cellular bioenergetics and its antioxidant properties are beyond question and its use in neurodegenerative disorders is clinically recommended (i.e. for slowing down the functional decline in patients with Parkinson’s disease), while its value in other conditions is under further clinical investigation (Bonakdar and Guarneri, 2005). We should also add that health claims are not always the main marketing tool for sales growth. The perception of customers to the beneficial effects of CoQ<sub>10</sub> is in many countries already at such a high level that the “fortified with Coenzyme Q<sub>10</sub>” statement can convince customers to purchase fortified products. This sometimes allows the manufacturer to mislead customers with the addition of very low quantities of CoQ<sub>10</sub> (i.e. 1 mg/L) to their products. Even though there are no regulations to prevent these marketing tools in most countries, such manipulative techniques should be persistently rejected, at least by the scientific community.

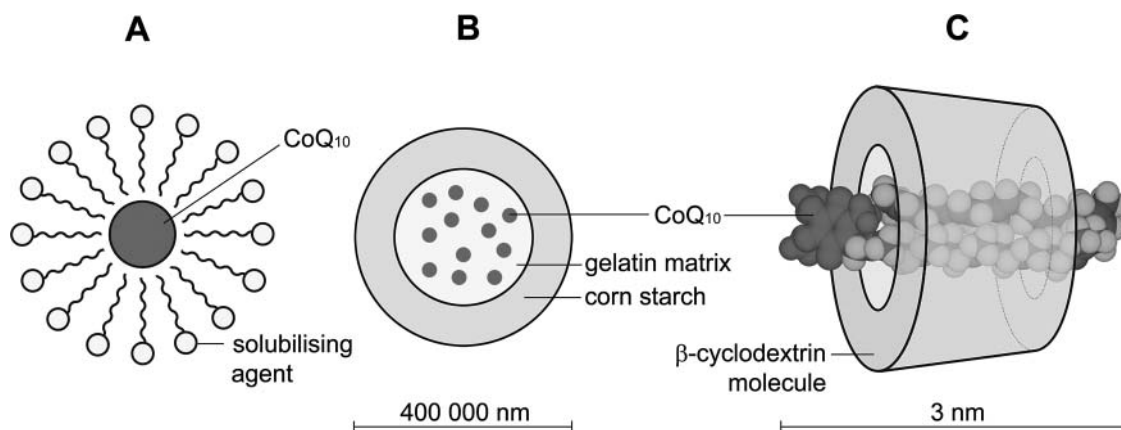
Until recently, the fortification of most food products with CoQ<sub>10</sub> was not easily achievable due to the compound’s molecular structure and physical properties. In pure form, CoQ<sub>10</sub> is a crystalline powder. Its lipophilicity and high molecular weight ( $M_r = 863$ ) makes it insoluble in water, which represents the main limitation on the fortification of foods, particularly those with a low fat content. In most food products very small increase

in the CoQ<sub>10</sub> level can be achieved with the use of a crystalline compound, which is reflected in the negligible effect of such foods on human health when consumed in normally expected daily amounts and such products therefore cannot be considered to be functional food. New forms of CoQ<sub>10</sub> have been developed to solve this problem and will be discussed in the following chapter. In addition to insolubility in water, the solubility of CoQ<sub>10</sub> in lipids is also limited and CoQ<sub>10</sub> is thus very poorly absorbed (Bhagavan and Chopra, 2007). The absorption can be improved by food intake (Ochiai et al., 2007), by dividing the daily dose into smaller dosages throughout the day (Singh et al., 2005) and by increasing the solubility of CoQ<sub>10</sub> in water (Bhagavan and Chopra, 2007; Žmitek et al., 2008a). The stability of CoQ<sub>10</sub> presents a problem at increased temperatures or when products are stored in light (UV irradiation) (Matsuda and Masahara, 1983; Milivojević Fir et al., 2009). Despite the antioxidant properties of CoQ<sub>10</sub>, ubiquinone or ubiquinol cannot be used alone to preserve food; it has been determined that ubiquinol reacts with peroxidizing lipid forming the corresponding semiquinone radical, yet it is rapidly transformed into ubiquinone in the air (Lambelet et al., 1992).

### ENHANCING THE WATER-SOLUBILITY OF COQ<sub>10</sub>

The increased water-solubility of otherwise insoluble compounds not only allows the fortification of aqueous-based products but also contributes to their improved absorption, which is a common pharmaceutical strategy (Liu, 2008). A number of different approaches have been developed to achieve this goal with CoQ<sub>10</sub>, although many of them have been developed mainly for cosmetic or pharmaceutical use. An example of such an approach are the liposomal or micellar aggregates of CoQ<sub>10</sub> derivatives that have been formed in aqueous media for use in cosmetics (dermal application) (Zappia and De Rosa, 1989). Further, nanomicelles have been successfully formed with conjugated polyethylene glycol and proposed as a drug carrier system (Scheme 1: A) (Borowy-Borowski et al., 2004) and aqueous

pharmaceutical solutions of CoQ<sub>10</sub> for injectable preparations have been prepared with the use of a hydrogenated lecithin containing at least 85% of phospholipid components (Ohashi et al., 1984). Polisorbates have also been used as solubilizing agents and suggested for medical use for perfusion solutions (Masterson, 1998). Pharmaceutical formulations have also been prepared by the solubilization of CoQ<sub>10</sub> with polyethoxylated 40 hydrogenated castor oil as a non-ionic surfactant (Seghizzi et al., 1993) or with decaglycerol stearate (Shibusawa et al., 2000); 3–30% of emulsifier and high pressure homogenization was needed in the latter case. The aqueous dispersion of solid CoQ<sub>10</sub> has also been developed and non-ionic liquid polymer tyloxapol has been used for its stabilization (Westesen and Siekmann, 2001). Technological solutions achieved without additives are most desired by the food industry which would like to avoid unnecessarily expanding product ingredient lists, particularly with compounds that are new and unknown to customers, even though the safety of such compounds is sometimes not in question. If additives have to be used, recognized and widely used compounds such as starch or its derivatives are very convenient. Starch-based hydrophilic coatings have been successfully used for stable solutions or dispersions of CoQ<sub>10</sub> in water. In one such attempt, small CoQ<sub>10</sub> beadlets were finely dispersed into a water-soluble fish gelatine matrix and coated with starch-based granules (Scheme 1: B) (Chen et al., 2004). While these beadlets include a number of CoQ<sub>10</sub> molecules, a further breakthrough was achieved by the use of cyclodextrins (CD) (Moldenhauer and Cully, 2003; Prošek et al., 2005). Among the latter,  $\beta$ -cyclodextrin ( $\beta$ -CD) has been found to be very convenient as this starch derivative is already commonly used in the food industry and as a drug carrier system (Uekama et al., 1998) due to its proven safety, round-the-world approval, and easy accessibility. An inclusion complex can be formed in which a molecule of CoQ<sub>10</sub> is associated with one  $\beta$ -CD (CDQ<sub>10</sub>, Scheme 1: C) (Prošek et al., 2005). The stability, solubility in diverse aqueous media, and easy handling with such a form of CoQ<sub>10</sub> in addition to the unchanged organoleptic properties of fortified foods has led to a breakthrough in CoQ<sub>10</sub>-fortification and the number of



**Scheme 1** Schematic models of various novel forms of CoQ<sub>10</sub>: (A) nanomicelles, (B) CoQ<sub>10</sub> beadlets finely dispersed in a water-soluble fish gelatine matrix and coated with starch-based granules (Chen et al. 2004), (C) CDQ<sub>10</sub> - inclusion complex of CoQ<sub>10</sub> in  $\beta$ -cyclodextrin (Prošek et al. 2005).

fortified products is rising rapidly. In the last few years, many products such as dairy (milk, yogurt, kefir, etc.), fruit nectars and juices, syrups, and other beverages, honey, tea etc. have been launched in different markets around the world. These novel forms of CoQ<sub>10</sub> have also allowed the development of new pharmaceutical formulations like syrups and effervescent tablets. It should also be mentioned that the better *in vivo* absorption of some forms of CoQ<sub>10</sub> with increased water-solubility has been determined, resulting in improved bioavailability (Bhagavan and Chopra, 2007; Prošek et al., 2008; Žmitek et al., 2008a; Žmitek et al., 2008b).

### FORTIFICATION STRATEGIES

The novel forms of CoQ<sub>10</sub> allow the fortification of diverse food products. Fortification can be theoretically achieved by three main strategies: (1) the addition of CoQ<sub>10</sub> to food during processing; or (2) with the addition of this compound to the environment in which primary food products are formed (animal feed etc.), or (3) with the genetic modification of plants. All three strategies are presented below with some examples.

#### Fortification of Processed Foods

The fortification of many essential processed foods can be achieved today with the use of the novel CoQ<sub>10</sub> forms. For example, milk and dairy products were determined to be very suitable for this purpose (Stražičar et al., 2005). The concentration of CoQ<sub>10</sub> in them is low (below 2.5 mg/kg), while their consumption by the average population is quite high. Further, it was shown that their CoQ<sub>10</sub> content can be increased significantly by using appropriate forms of CoQ<sub>10</sub> with enhanced solubility in aqueous media, without affecting the product stability or organoleptic properties (Prošek et al., 2005). Processed cow milk is such an example (Table 3). While unfortified milk (3.5% fat, Ljubljanske mlekarne dairy, Slovenia) contains 1.7 mg CoQ<sub>10</sub>/kg, a relatively small increase can be achieved by saturation with a crystalline compound (3.2 mg/kg). On the contrary, even as high as a 5000-times increase in the initial CoQ<sub>10</sub> concentration can be accomplished (8500 mg/kg) by using the water-soluble CDQ<sub>10</sub> form (Prošek et al., 2005). Such a high concentration is, of course, not of practical importance for the food industry but reflects the impact of the development of

**Table 3** Concentrations of CoQ<sub>10</sub> in milk before and after the addition of various forms of CoQ<sub>10</sub> (Prošek et al. 2005)

Milk sample	mg CoQ <sub>10</sub> /kg
Regular, 3.5% fat (no CoQ <sub>10</sub> added)	1.7
Saturated with crystalline CoQ <sub>10</sub> , 3.5% fat	3.2
Saturated with CDQ <sub>10</sub> , 3.5% fat	8500
Example of fortified milk in stores, 1.6% fat*	50

\*UHT milk "Alpsko mleko Q<sub>10</sub>," produced by Ljubljanske mlekarne dairy (Slovenia)

new forms of CoQ<sub>10</sub>. This approach has already been successfully implemented and used by several dairies in the production of fortified milk; usual concentrations of CoQ<sub>10</sub> in such products are around 50 mg/kg, about 30 times more than the natural content in milk.

The fortification of yogurts and other dairy products, fruit juices, nectars, and several other beverages was also achieved simply by the addition of the water-soluble form of CoQ<sub>10</sub> to the product upon stirring. In an analogous manner, CoQ<sub>10</sub> in an appropriate form with increased solubility in aqueous media can be added to semi-solid products such as liver pâté, honey, marmalade, jam etc. (Prošek et al., 2005), but sufficient homogenization should be assured as to which liquid or semi-liquid forms of CoQ<sub>10</sub> are the most convenient.

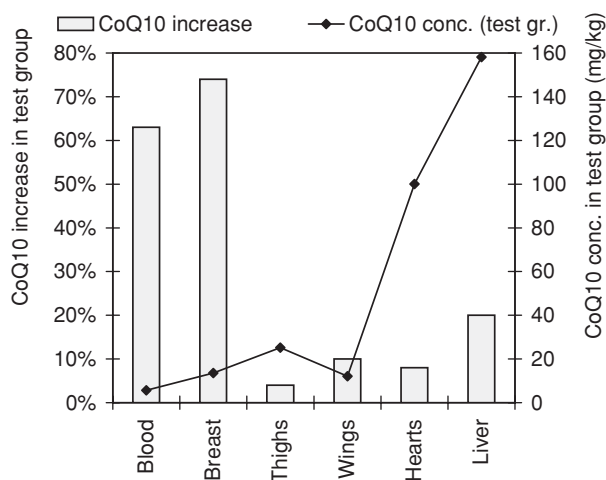
While the fortification of many products seems very simple, great care has to be taken with the composition and homogeneity of the final product. Products have to contain the declared CoQ<sub>10</sub> content throughout the time period in which they should be used. Stability studies are therefore necessary, particularly for types of products for which stability with the used CoQ<sub>10</sub> form has not yet been confirmed, or where interactions with other components and materials such as primary packaging materials could occur. Very recently a stability study of Coenzyme Q<sub>10</sub> in various fortified foods was published (Pravst et al., 2009).

#### Fortification of Unprocessed Foods

The addition of CoQ<sub>10</sub> to foods during processing is, however, not usable for the enrichment of primary foods, i.e. meat. While the fortification of animal feed with CoQ<sub>10</sub> is reported to have beneficial health effects for animals (Geng et al., 2004), up until recently this method has not been used for the fortification of meat. This fortification strategy is presented in the following example.

Poultry is quite convenient for fortification with CoQ<sub>10</sub>. Within the meats it has the lowest CoQ<sub>10</sub> level, a relatively low fats and cholesterol level, and in many countries its consumption is at a high level and growing quicker than with beef and pork. The fortification of poultry was recently successfully achieved with broiler chickens (Prošek et al., 2007). Twenty days prior to slaughter, chickens were fed with CoQ<sub>10</sub>-fortified feed (test group) with about 5 mg of a water-soluble formulation of CoQ<sub>10</sub> (CDQ<sub>10</sub>) per kg of body weight daily. Concentrations of CoQ<sub>10</sub> in the animal tissues significantly increased in comparison to the reference group given non-fortified feed (Fig. 2). An almost doubled increase was observed in breast meat (7.8 and 13.6 mg/kg for the reference and test groups, respectively), while a smaller increase is typical of tissues with naturally higher concentrations of CoQ<sub>10</sub>. At the same time, a higher CoQ<sub>10</sub> ratio towards cholesterol was observed in the test group, especially in breast meat (0.022 and 0.044 for the reference and test groups, respectively). The content of CoQ<sub>10</sub> in meat has been further increased by gradually increasing the amount of CoQ<sub>10</sub> in the feed.

Chicken eggs can also be fortified if hens are fed with CoQ<sub>10</sub>-fortified feed; a 67% increase in CoQ<sub>10</sub> content in yolk



**Figure 2** Comparison of the average CoQ<sub>10</sub> increase in chickens fed with CoQ<sub>10</sub>-fortified feed (CDQ<sub>10</sub>) for 20 days (test group) in comparison to the reference group given non-fortified feed, and the average content of CoQ<sub>10</sub> in the test group; data source: Prošek et al. 2007.

(8.7 mg/kg) has been achieved after three weeks of feeding hens with about 7 mg of water-soluble CoQ<sub>10</sub> (CDQ<sub>10</sub>) (Prošek et al., 2007). Even a higher CoQ<sub>10</sub> content in egg yolk was recently achieved (22 mg/kg) with a much higher addition of CoQ<sub>10</sub> to the feed of laying hens (800 mg CoQ<sub>10</sub> per day of 28 days) (Kamisoyama et al., 2010).

Another option for the enrichment of foods with CoQ<sub>10</sub> is development plants with increased Coenzyme Q10 content by genetic modification. This strategy is most interesting when used on crops. Very recently CoQ<sub>10</sub>-enriched rice was successfully produced with CoQ<sub>10</sub> levels as high as 35 mg/kg (Takahashi et al., 2009; Takahashi et al., 2010).

## CONCLUSIONS

Coenzyme Q<sub>10</sub> is a natural substance present in all human cells. It plays a fundamental role in cellular bioenergetics and is an effective antioxidant. Beside endogenous synthesis, food is also a source of CoQ<sub>10</sub>. Meat, fish, nuts, and certain oils are the richest nutritional sources, while much lower levels can be found in most dairy products, vegetables, fruits, and cereals. Large variations of CoQ<sub>10</sub> content in some food products of different geographical origin have been found, especially within oils. The average dietary intake of CoQ<sub>10</sub> is only 3–6 mg, about half of it being in reduced form. Numerous health benefits of CoQ<sub>10</sub> supplementation have been reported which, in addition to the growing demand for CoQ<sub>10</sub> as a food supplement, has also been reflected in the growing demand for its use in functional foods. The latter have been becoming more popular and widely used since forms of CoQ<sub>10</sub> with enhanced water-solubility have been developed which enable the fortification of low-fat aqueous-based products and exhibit improved bioavailability. Three main strategies have been used for fortifi-

cation purposes. Processed food can be fortified by the addition of the compound during food processing; dairy products have been determined to be especially suitable for this purpose. For example, Coenzyme Q<sub>10</sub> content in milk can now be increased significantly over its natural level without negative effects on product stability and taste. Similarly, the fortification of other dairy products along with fruit juices, nectars, and several other beverages has been also performed. Analogously, CoQ<sub>10</sub> can also be added to semi-solid products such as pâté, honey, marmalade, etc. However, this strategy is not usable for the enrichment of primary foods, i.e. meat. The content of CoQ<sub>10</sub> in animal tissues can be improved by the use of fortified feed, as shown with poultry. The biggest increase in CoQ<sub>10</sub> content has been observed in tissues in which the concentrations of CoQ<sub>10</sub> are naturally low. Using the same approach, an increase in CoQ<sub>10</sub> content has also been reported for egg yolk. Another option for the enrichment of foods is the genetic modification of plants to increase their Coenzyme Q<sub>10</sub> content. This strategy was recently successfully used on rice.

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