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Review

Coenzyme Q10 and its Effective Sources

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Abstract: Coenzyme Q10 (2,3-dimethoxy, 5-methyl, 6-decaprenyl benzoquinone, CoQ10) is naturally present in many organisms. It has key roles in several biochemical pathways. CoQ10, as an electron and proton carrier for energy coupling leads to Adenosine Triphosphate (ATP) formation. Furthermore, in medicine, the pharmacological use of CoQ10 has attracted more attention due to its benefits in treating cardiovascular and degenerative neurologic diseases. CoQ10 can be produced by chemical synthesis, extraction from biological tissues and microbial fermentation. It is found in plants such as soya bean, peanut, palm oil and litchi pericarp and in animals such as pelagic fish, beef and pork hearts. Various analytical methods have been published for the extraction and analysis of CoQ10 from different matrices. Biological production of CoQ10 offers an environmentally benign option based on the enzymatic catalysis at the cellular level. Moreover, this process due to ease of control and low production costs offers more advantages over the existing technologies.

Keywords: CoQ10, Adenosine Triphosphate (ATP), Mitochondrial Enzymes, Extraction, Microbial Fermentation

Introduction

Coenzyme Q10 (2,3 dimethoxy, 5-methyl, 6-decaprenyl benzoquinone, CoQ10) is present in many organisms (Fig. 1) (Xue *et al*., 2012). CoQ10 also known as ubiquinone or ubiquinone-10 and its active form is ubiquinol, is abundant in plants, animals and microorganisms (Yuan *et al*., 2012). It plays a crucial role in the transfer of electrons between respiratory complexes of the electron transport chain, located within the inner mitochondrial membrane (Cluis *et al*., 2012).

Recently CoQ10 found a wide range of therapeutic applications (Tokdar *et al*., 2014; Langsjoen, 1994).

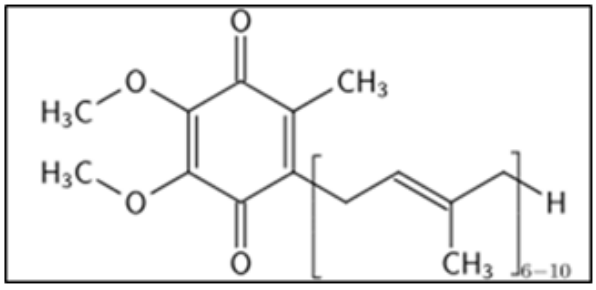

Fig. 1. Chemical structure of CoQ10 (Jankowski *et al*., 2016)

Extensive research has been conducted to increase CoQ10 production to meet growing demands for this product. CoQ10, can be produced by three methods: Chemical synthesis, extraction from biological tissues (animal and plant) and microbial fermentation (Laplante *et al*., 2009). Microbial biosynthesis offers several advantages over chemical synthesis and extraction including specificity towards the all-trans biologically active isomer of CoQ10 and the reduced production of environmentally hazardous waste based on the enzymatic catalysis at the cellular level for CoQ10 production (Cluis, 2012). Moreover, microbial fermentation found to be an attractive method for industrial production of CoQ10 (Lee *et al*., 2004; Park *et al*., 2005).

The present study aimed to discuss about importance, benefits of CoQ10 and also its effective sources and extraction methods.

Importance and Benefits of CoQ10

Application of CoQ10 in foods and animal tissue has attracted special attention owing to its crucial roles in many biochemical pathways (Rodriguez-Estrada *et al*., 2006). CoQ10 is the coenzyme for at least three mitochondrial enzymes (complexes I, II and III).

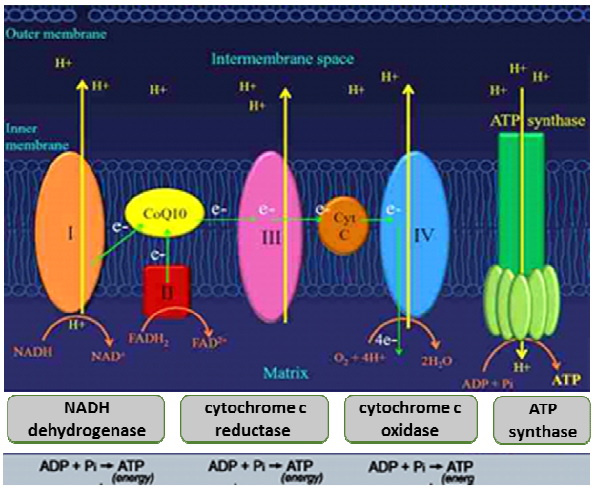

Fig. 2. Central role of CoQ10 in electron transport chain

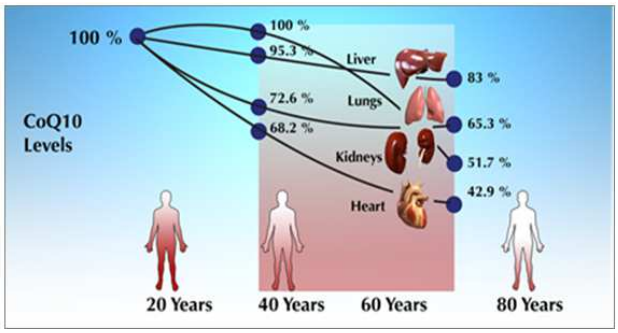

Fig. 3. CoQ10 decline with age (Littarru and Lambrechts, 2011)

CoQ10 as shown in Fig. 2 is a core component of cellular energy production. Due to its involvement in ATP synthesis, CoQ10 affects the function of every cell in the body, making it important for the health of all tissues and organs (de Dieu Ndikubwimana and Lee, 2014).

CoQ10 has been shown to have quite powerful antioxidant potential. Therefore, it can effectively defend against reactive oxygen species and free radical damage, protects the body from damage caused by harmful molecules (Ruiz-Jiménez *et al*., 2007) through protecting membranes and proteins from oxidation (Cluis, 2012). There is evidence that CoQ10 is playing a part in transcriptional regulation of genes, some of which play roles in inflammatory responses and in cholesterol metabolism (Schmelzer *et al*., 2007). Furthermore, in the medicine filed CoQ10 has received increasing attention due to its benefits in treating cardiovascular and degenerative neurologic diseases (Weant and Smith, 2005).

CoQ10 is naturally produced in the body, but its levels decrease as we age and may be low in people with cancer, genetic disorders, diabetes, heart problems and Parkinson's disease (Fig. 3). Symptoms of CoQ10 deficiency include heart failure, high blood pressure and chest pain. On the other hand, the concentration of CoQ10 in the body decreases year by year, indicating that it has a close relationship with aging (Fig. 2). For these reasons, some people rely on CoQ10 supplements. The daily intake of CoQ10 is suggested as 12 mg kg^{-1} (Rujiralai *et al*., 2014). More recently, nutraceutical supplements containing CoQ10 have gained a significant popularity in health management sections (Buettner *et al*., 2007).

Table 1. Overview of CoQ10 contents in various foods (Pravst *et al*., 2010)

Animal organ	CoQ_{10} concentration [mg/kg]
Beef	
Heart	113
Liver	39–50
Muscle	26–40
Pork	
Heart	11.8–128.2
Liver	22.7–54.0
Muscle	13.8–45.0
Chicken	
Heart	116.2–132.2
Fish	
Sardine	5–64
Mackerel	
Red flesh	43–67
White flesh	11–16
Salmon	4–8
Tuna	5

Table 2. Overview of CoQ10 contents in various plants (Pravst *et al*., 2010)

Plant	CoQ_{10} concentration [mg/kg]
Oils	
Soybean	54–280
Olive	4–160
Grapeseed	64–73
Sunflower	4–15
Pistachio nuts	20
Hazelnuts	17
Almond	5–14
Nuts	
Peanuts	27
Walnuts	19
Sesame seeds	18–23
Pistachio nuts	20
Hazelnuts	17
Almond	5–14
Vegetables	
Parsley	8–26
Broccoli	6–9
Cauliflower	2–7
Spinach	up to 10
Grape	6–7
Chinese cabbage	2–5
Fruit	
Avocado	10
Blackcurrant	3
Strawberry	1
Orange	1–2
Grapefruit	1
Apple	1

CoQ10 supplements have shown positive effects on patients suffering from conjunctive heart failure and acute myocardial infarction (Hodgson *et al*., 2002; Yang *et al*., 2010). It has been proved that CoQ10 helps treat, muscular dystrophy and periodontal disease (Yang *et al*., 2010; Mancini and Balercia, 2011).

CoQ10 Effective Sources

CoQ10, can be produced by chemical synthesis, extraction from biological tissues (plants and animal) and microbial fermentation (Laplante *et al*., 2009). In the wake of environmental awareness, the chemical options became least desirable due to inherent uses of solvents and chemicals in the process (Tokdar *et al*., 2014).

Plant and Animal Sources of CoQ10

CoQ10 is naturally present in small amounts in a wide variety of foods, but is particularly high in animal meat organs such as heart, liver and kidney, beef as well as soy oil, sardines, mackerel and peanuts (Langsjoen, 1994). The highest content is found in meat and fish tissues and viscera due to their high levels of mitochondria (Reig *et al*., 2015). Moreover, presence of CoQ10 in bee pollen was investigated (Xue *et al*., 2012). The results of CoQ10 contents in animal organs and various plants are overviewed in Table 1 and 2.

Microbial Sources of CoQ10

As summarized in Table 3, CoQ10 can be produced by microbial fermentation including fungi (e.g., *Candida, Sporidobolus, Rhodotorula, Neurospora, Aspergillus*) and bacteria (e.g., *Agrobacterium, Paracoccus, Cryptococcusi, Rhodobacter, Tricosporon*). Moreover, presence of CoQ10 in *Artemia* samples as a Crustacean was investigated (Rujiralai *et al*., 2014). Microbial production offers an environmentally benign option based on the enzymatic catalysis at the cellular level for CoQ10 assembly. Moreover, this approach is attractive to the industry because the process is easy to control at a relatively low production cost (Tokdar *et al*., 2014).

Table 3. CoQ10 production in wild types, chemical mutants and recombinant strains

Source	Specific CoQ10 content (mg/g DCW)	Reference
Wild type		
Agrobacterium tumefaciens ATTC 4452	1.9	Jeya *et al*. (2010)
Agrobacterium tumefaciens KY-8593	1.2	Cluis *et al*. (2007)
Paracoccus denitrificans ATCC 19367	0.86	Choi *et al*. (2005)
Protaminobacter ruber	1.52	Jeya *et al*. (2010)
Pseudomonas N84	1.2	Jeya *et al*. (2010)
Rhizobium radiobacter ATCC 4452	5.3	Choi *et al*. (2005)
Rhizobium radiobacter A603-35-gapA	5.27	Koo *et al*. (2010)
Rhizobium radiobacter KCCM 10413	11.84	Ha *et al*. (2009)
Rhizobium radiobacter T6102	1.95	Seo and Kim (2010)
Rhizobium radiobacter WSH 2601	1.91	Wu *et al*. (2003)
Rhodobacter sphaeroides BCRC 13100	8	Yen and Chiu (2007)
Rhodobacter sphaeroides BCRC 13100	4.5	Yen *et al*. (2010)
Rhodobacter sphaeroides FERM-P4675	2.7	Choi *et al*. (2005)
Sporidiobolus johnsonii	10.5	Dixson *et al*. (2011)
Recombinant strain		
Escherichia coli	0.29	Choi *et al*. (2005)
Escherichia coli	1.41	Choi *et al*. (2009)
Escherichia coli	2.428	Zahiri *et al*. (2006)
Escherichia coli	0.44	Huang *et al*. (2011)
Escherichia coli	0.45	Huang *et al*. (2011)
Escherichia coli	3.24	Huang *et al*. (2011)
Escherichia coli	0.51	Zhang *et al*. (2007)
Escherichia coli	0.19	Zhang *et al*. (2007)
Escherichia coli	0.77	Zhang *et al*. (2007)
Rhizobium radiobacter	5.27	Koo *et al*. (2010)
Rhizobium radiobacter	8.3	Lee *et al*. (2007)
Chemical mutants		
Agrobacterium tumefaciens AU-55	9.6	Choi *et al*. (2005)
Agrobacterium sp.	1.96	Jeya *et al*. (2010)
Agrobacterium tumefaciens KCCM 10413	8.54	Cluis *et al*. (2007)
Agrobacterium tumefaciens KCCM 10413	9.71	Jeya *et al*. (2010)
Rhodobacter sphaeroides	8.7	Jeya *et al*. (2010)
Rhodobacter sphaeroides Co-22-11 car	2.6	Cluis *et al*. (2007)
Rhodobacter sphaeroides Co-22-11	2.5	Choi *et al*. (2005)

However, due to the limits of CoQ10 accumulation in cells, strain improvements have been made using genetic engineering (using recombinant nucleic acid technology), chemical mutagenesis and high hydrostatic pressure treatment (Kim *et al*., 2015).

Industrial production of CoQ10 have predominantly relied on bacterial and yeast mutants due to their higher CoQ10 content (Tokdar *et al*., 2014). The isolation of strains by mutagenesis and selection on inhibitors has shown to be the most successful strategy to enhance CoQ10 yields (Yen and Shih, 2009). Table 2 summarizes CoQ10 production by some wild, chemical mutants and recombinant strains.

CoQ10 Effective Extraction Methods

Liquid–liquid extraction or ultrasound extraction by using a mixture of hexane and 2-propanol found to be the most common methods for extraction of CoQ10 from different samples (Xue *et al*., 2012). For example, CoQ10 from fresh tobacco leaves and litchi pericarp was extracted using ultrasonic extraction in the presence of ethanol and hexane (Rujiralai *et al*., 2014).

The two extraction methods generate a large amount of toxic chemicals within the process, which causes a significant environmental and health impact. Therefore, it is clearly preferable to obtain extracts by eliminating the use of toxic solvents (Xue *et al*., 2012).

Accelerated Solvent Extraction (ASE) was first developed by Dionex Corporation, in 1996 and then validated on a commercially-available, automated extraction system ASE a new extraction procedure for sample preparation, combines elevated temperatures and pressures with liquid solvents. Through this method organic solvents are used at high pressures and temperatures above the boiling point. In recent years, the popularity of ASE has increased since it can provide a higher extraction efficiency with low solvent volumes and a short extraction time in comparison with some classical extraction technologies such as liquid–liquid extraction and soxhlet extraction. ASE with ethanol and an acid- thermal treatment with a petroleum ether extractant were documented for extracting CoQ10 from bee-collected pollen and *Agrobacterium tumefaciens*, respectively (Richter *et al*., 1996).

Conclusion Remarks

CoQ10, a lipid-soluble endogenous pro-vitamin found naturally in the mitochondria, is present in many organisms. It has crucial roles in many biochemical pathways and important health functions. Levels of CoQ10 decrease as we age and may be low in people with cancer, genetic disorders, diabetes, heart problems and Parkinson's disease. For these reasons, some people rely on CoQ10 supplements. CoQ10 can be produced from some microorganisms, plants and animals. It is important to establish a suitable extraction and analysis method for determining the content of CoQ10 in different foodstuffs. The most common methods for extracting CoQ10 from different samples are liquid–liquid extraction or ultrasound extraction. In recent years, the popularity of ASE has increased since it can provide higher extraction efficiency with low solvent volumes and a short extraction time in comparison with some classical extraction technologies. Microbial production offers an environmentally benign option and is attractive to the industry because of easy to control at a relatively low production cost. However the better precursors which could be combined for more CoQ10 production needs future studies. New methods for development of CoQ10 production in a better microorganism, which could produce high CoQ10 yield, could also be evaluated in the future. Finally, a type of reactor that provides high cell concentrations, high productivity and easy separation of the products could be determined from further research.

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Author's Contributions

All authors equally contributed in this work.

Ethics

This article is original and contains unpublished material. The corresponding author confirms that all of the other authors have read and approved the manuscript and no ethical issues involved.

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