

Coenzyme Q 10 – its biochemical and related aspects

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Abstract

This review analyses the findings of biochemical and related pharmacotherapeutical aspects of coenzyme Q10. Its important role in the respiratory chain is presented. Furthermore, the article presents administration of coenzyme Q10 as a supplement within preventative measures in medicine, its pharmacotherapeutical aspects and effects in a number of diseases of various aetiologies. Concurrently, it presents the issue of mutual interactions of coenzyme Q10 and its efficacy in combining supplementation with conservative therapy of selected aetiologies.

CoQ 10, respiratory chain, preventative medicine

Coenzyme Q (Q10) and its biochemical aspects

Coenzyme Q was first discovered in 1957 by Dr. F. Grane's team of scientists in Wisconsin. Biochemically it is a substance belonging to the group of ubiquinons. It is an isoprenoid coenzyme with a lateral chain; in the case of coenzyme Q10, of ten units.

Coenzyme Q is most largely found in the skeletal muscles, liver, and heart. Important biotransformation of ubiquinon 1–9 to the form of Q10 occurs in the liver, as well. This form is utilisable for humans. The capacity of biotransformation is affected by age and different loads on the organism. Individual forms of coenzyme Q, and Q1 to Q10 in particular, are represented in live organisms of various degrees of phylogenetic development.

In terms of participation in the metabolism, it has a unique role in the respiratory chain, and an antioxidant effect (Janicki and Buzala 2012; Del Pozo-Cruz et al. 2014).

The respiratory chain represents a cascade of enzymes on the inner mitochondrial membrane adjacent to the mitochondrial matrix. It is here where the hydrogen protons and electrons enter by NADH + H⁺ and FADH₂ pathways. In the mitochondrial matrix, numerous dehydrogenations (oxidations) of substrates entering mainly the cycle of citric acid and beta-oxidation of fatty acids occur. These dehydrogenations catalyse relevant dehydrogenases dependent on NAD⁺ and FAD coenzymes. By accepting the hydrogen atom they are transformed to reduced NADH + H⁺ and FADH₂ coenzymes. Thus formed NADH + H⁺ is oxidized and at the same time regenerated to NAD⁺ by the first complex of the respiratory chain, called complex I (NADH: ubiquinon oxidoreductase) (Janicki and Buzala 2012). The complex separately transfers two electrons released from two hydrogen atoms through FMN series of Fe-S centres (nonhaem iron with sulphur) to coenzyme Q.

Complete reduction of coenzyme Q to ubiquinol (QH₂, hydroquinone) which is subsequently reoxidated by another complex III. Complex III (QH₂-cytochrome c oxidoreductase) contains cytochrome c and Fe-S centres. Next one in sequence is complex IV formed by cytochrome c oxidase, catalysing oxidation of two molecules of the reduced cytochrome c produced by the previous action of complex III. Electrons are accepted by molecular oxygen (from the respiratory process) which provides endogenous water. The protons needed come from the mitochondrial matrix.

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Protons centred in the intermembrane space are transferred by means of F_0F_1 -ATPase back into the matrix. The transport of protons is thus used for ATP synthesis.

Another complex is integral part of the respiratory chain, namely complex II (succinate: ubiquinone reductase) which takes over the reduction equivalents, i.e. protons and electrons from dehydrogenases dependent on coenzyme FAD (e.g., succinate dehydrogenase in the citric acid cycle, acyl-CoA dehydrogenase from beta-oxidation of fatty acids).

It follows from the presented findings that coenzyme Q holds a key position in the energy metabolism of each somatic cell. Electron transport is connected with transport of protons into the intermembrane space; by filling the intermembrane space with protons, coenzyme Q enhances ATP formation (Janicki and Buzala 2012).

In biochemistry, coenzyme Q is also applied as an antioxidant. Its antioxidant effects manifest by the ability to catch peroxyl and alkoxyl free radicals which is an important part of defence mechanisms against oxidative stress. In terms of antioxidant effects, coenzyme Q10 is the antioxidant defence against free radicals. Firstly, the total antioxidant effect of coenzyme Q10 rests in its direct antioxidant action when ubiquinol is reoxidated to ubiquinone. During this situation, the electron is actively prevented from leaking into molecular oxygen by the formation of superoxide (a reactive form of oxygen). The study of the relationship of coenzyme Q10 and contribution to the reduction of oxidative stress state Ostman et al. (2012). Secondly, coenzyme Q10 is able to regenerate tocopherol radicals back to vitamin E, and similarly, dehydroascorbate to ascorbate (Bliznakov 1999; Tsuneki et al. 2007). In circulation, coenzyme Q10 is mostly bound to lipoproteins; largely in its reduced form of ubiquinol. Ubiquinol lowers the attack on fatty acids that during transport make part of triacylglycerols bound in lipoproteins (Bliznakov 1999; Littarru and Tiano 2007). In terms of biochemistry, there is a topical question of the relationship of coenzyme Q10 and statins when inhibitors of 3-hydroxy-3-methylglutaryl-CoA-reductase inhibit the synthesis of mevalonic acid, the primary substance for the synthesis of endogenous coenzyme Q10 (Liebermann et al. 2005).

Coenzyme Q10 and selected pharmacological aspects

Coenzyme Q10 exhibits antioxidant action which is the essence of its action in a number of diseases. It is assumed that the pharmacological effects of coenzyme Q10 are mediated also via the so called “membrane stabilizing effect” based on interactions with proteins of the phospholipid bilayer. Owing to membrane stabilization, electron leakage from mitochondria is then prevented during their transport in the respiratory chain, and cell energy metabolism is normalized (Greenberg and Frishman 1990; Mortensen 1993; Rengo et al. 1992). Antioxidant issues were studied by Chapple and Matthews (2007).

In clinical practice, coenzyme Q10 is used with varying degrees of success in the treatment of many types of diseases, especially those of the cardiovascular system, and diseases aetiologically connected with the state of heightened oxidative stress (Fotino et al. 2013; Lee et al. 2012). Recommendations as to the utilisation of coenzyme Q10 and its practical application are limited to a suitable supplement to conservative therapy.

Literature also discusses the mechanism of action and supplementation of a lack of endogenous coenzyme Q10 which has been shown in a number of diseases (Gazdík et al. 2002; Shults 2005). The presumed mechanism of antihypertensive action is based on the vasodilatation mediated by the direct action of coenzyme Q10. For cardiovascular system diseases, it is presumed that coenzyme Q10 also affects the metabolism of prostaglandins, the inhibition of intracellular phospholipases and the stabilisation of slow calcium-dependent canals. Coenzyme Q10 and cardiovascular diseases were studied by Greenberg and Frishman (1990).

Studies *in vitro* and animal experiments show that coenzyme Q10 can protect the cardiac muscle against functional and structural changes following ischaemia-reperfusion injury (Whitman et al. 1997; Niborii et al. 1998; Crestanello et al. 2002).

Antihypertensive action of coenzyme Q10 consists in the mediation of a direct effect of coenzyme Q10 on the vascular endothelium of the smooth muscles of vessels. The resulting effect is lower peripheral resistance accompanied by the lowering of blood pressure (Digiesi et al. 1992). A study focused on utilisation of coenzyme Q10 in the therapy of hypertension shows that Q10 lowers systolic blood pressure (Rosenfeldt et al. 2007). Until the following retrospective studies, Q10 may be considered only as a good supplement to conservative therapy of hypertension.

The issue of interactions between coenzyme Q10 and statins has also been studied, in relation to the inhibition of 3-hydroxy-3-methylglutaryl-CoA reductase, and subsequently, mevalonic acid synthesis (Liebermann et al. 2005). Statins and endogenous Q10 were studied by Folkers et al. (1990), De Pinieux et al. (1996), and Liebermann et al. (2005). Caso et al. (2007) mention in their study that complementary therapy using coenzyme Q10 moderates expressions of myopathy during statin therapy and can be recommended to patients using statins for muscle pain.

In 1975, a case was published relationship of coenzyme Q10 in the therapy of periodontitis (Wilkinson et al. 1975). Other authors, however, question the use of coenzyme Q10 in periodontitis therapy (Watts 1995). Some authors deem it necessary to conduct further controlled clinical studies (Chapple and Matthews 2007).

Other studies of coenzyme Q10 evaluate the use of the supplement in the therapy of migraine. Coenzyme Q10 probably stabilizes nervous functions and lowers hyperexcitability as it helps maintaining homeostasis of macroergic phosphates and decreases the influence of free radicals on the nervous tissue (Ramadan and Buchanan 2006). Supplementation with Q10 can lead to improving migrainous states (Rozen et al. 2002; Sándor et al. 2005).

In relation to neurodegenerative diseases, the effect of long-term use of coenzyme Q10 has not yet been sufficiently investigated (Shults 2005). According to studies published so far, Q10 could help restore normal functioning of aerobic metabolism in the brain tissue, and thus slow down the progression of neurodegenerative diseases (Koroshetz et al. 1997; Strijks et al. 1997; Shults 2005).

Coenzyme Q10 has also been studied in relation to sperm activity. Due to infection and inflammation, the antioxidant capacity of the seminal plasma may be decreased, which may cause heightened oxidative burden on the sperm and a decrease in their motility. Increasing sperm motility probably consists in the proper general antioxidant effect of Q10 (Safarinejad et al. 2012).

In conclusion, we note that although results of more extensive studies and clinical data have accrued, coenzyme Q10 remains primarily a supplement of conservative therapy of some diseases.

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