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Coenzyme Q10: Anti-ageing by supporting and protecting the powerhouses of the cell

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The risk of various diseases increases with age. As “powerhouses of the cell”, mitochondria are of particular importance for the prevention and therapy of age-related diseases. Adenosine triphosphate (ATP) is the universal energy currency of the cell. Via oxidative phosphorylation, the energy production with oxygen consumption, more than 90 % of the energy of the organism is generated in the form of ATP in the mitochondria. Reactive oxygen compounds, so-called “free radicals”, are formed as a by-product of aerobic energy generation. Free radicals can react with and damage mitochondrial and cellular membrane and protein structures. Radical-induced damage is associated with various ageing processes. Coenzyme Q10 is a fat-soluble antioxidant that accumulates in membrane structures. In the mitochondria it serves as an electron and proton carrier between the respiratory chain proteins. As it supports mitochondrial function and is able to neutralize free radicals directly at their place of origin, coenzyme Q10 is a promising anti-ageing supplement.

Ageing is a biological process that accompanies us throughout life. Medical advances and improvements in hygienic conditions have almost doubled life expectancy of people in the western world in the past 100 years. At the same time, the frequency and severity of age-related diseases such as cancer, heart and vascular diseases, type 2 diabetes mellitus and dementia have increased.

Mitochondria are cell organelles that contain the electron transport chain. These are enzyme complexes that gradually transfer high-energy electrons to lower energy levels and finally transfer them to oxygen and protons in order to form water (so-called “controlled oxyhydrogen reaction”). Since more than 90 % of the organism’s energy is generated via the electron transport chain, mitochondria are called the “powerhouses of the cell”. Mitochondria also provide an environment that is particularly suitable for various biochemical reactions. For this reason, they are also responsible for the formation of porphyrins, which are required as key-compounds of haemoglobin, for the synthesis of steroids, for the maintenance of cellular redox homeostasis and for the initiation of programmed cell death. Mitochondria form a central hub of metabolism and offer an interesting starting point for influencing ageing processes and for the prevention and therapy of diseases that occur with increasing age.

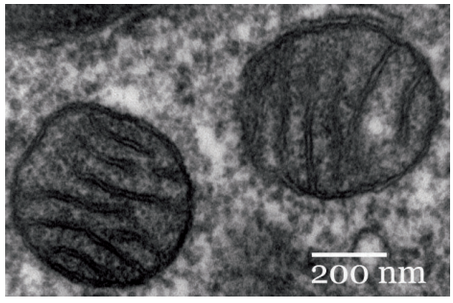

Fig. 1: Mitochondria under an electron microscope. The inner membrane structures are clearly visible.

Mitochondria are characterized by an outer and an inner membrane (Fig. 1). The outer membrane serves to delimit the environment and to control the exchange of substances with the cytosol, the inside of the cell. The inner mitochondrial membrane carries the electron transport chain. These are protein complexes that are arranged on the inner membrane or integrated into it. The electron transport chain complexes enable oxidative phosphorylation, energy generation while consuming oxygen. Aerobic energy production can produce up to 36 moles of adenosine triphosphate (ATP) from one mole of glucose, which is the universal energy currency of the cell. Compared to anaerobic glycolysis, in which only two moles of ATP can be obtained from the comparable amount of glucose, oxidative phosphorylation is characterized by its high efficiency. At the same time, the handling of oxygen poses special dangers. The transfer of electrons to oxygen creates particularly reactive compounds, so-called "free radicals". Free radicals can react with the phospholipid structures that make up cellular and mitochondrial membranes. They are also responsible for damage that occurs to proteins such as enzymes or to the respiratory chain complexes themselves. Above all, the mitochondrial genome has a rather simple structure and is therefore particularly sensitive to oxidative damage. Over time, radical-induced damage to the power houses of the cell accumulates. Together with mutations of the mitochondrial genome, there is an increased generation of radicals and reduced energy production. The decreasing availability of ATP and the increasing formation of free radicals ultimately lead to a progressive loss of cellular functions. [1]

The role of coenzyme Q10 in cellular metabolism

The electron transport chain catalyses a chain of biochemical redox reactions in which electrons and protons are gradually transferred to oxygen. Coenzyme Q10, a quinone derivative that has a side chain consisting of ten isoprene units, acts as a mediator of the electron and proton flow between the respiratory chain complexes. Coenzyme Q10 is not very polar and therefore lipophilic ("fat-friendly"). It accumulates in mitochondrial and cellular membrane structures. At the same time, coenzyme Q10 is a powerful antioxidant that can neutralize free radicals. In the area of the electron transport chain, it is able to neutralize superoxide radicals directly at their place of origin (Fig. 2).

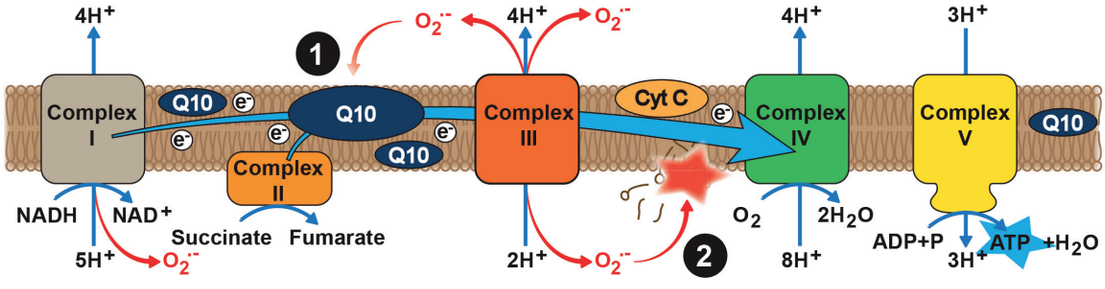

Fig. 2: Electron transport chain and radical formation: Oxidative phosphorylation occurs in the mitochondria. By this process, electrons (e-) from complex I and II of the electron transport chain are transferred to coenzyme Q10, which then transfers them to complex III and via cytochrome C to complex IV. The electrons are brought to a lower energy level and the released energy is used to pump protons (H+) through the membrane to build up an electrochemical gradient. At complex IV, the electrons are transferred to oxygen and protons to form water. The excess of protons on the inside of the membrane is broken down at complex V. The enzyme ATP-synthase located here uses the energy of the proton flow to regenerate ATP from ADP and phosphorus. Especially at complexes I and III, electrons are also transferred to oxygen, which creates superoxide radicals (O2-). The superoxide formation is estimated to be in the range of 2 % of the oxygen conversion of the oxidative phosphorylation. Oxygen radicals can be neutralized by antioxidants such as coenzyme Q10 (1). Inadequate antioxidant capacity causes radical-induced damage to protein and membrane structures (2).

The highest concentrations of coenzyme Q10 are found in organs with high metabolic activity or high energy turnover, such as the liver, kidneys and heart. Coenzyme Q10 is not a vitamin by definition, because it can be made by the body itself. The body's own coenzyme Q10 synthesis decreases with increasing age (Fig. 3). [2] With the falling tissue concentrations the anti-oxidative capacity of the organism decreases. This causes an increase in radical-induced damage, which can be detected by appropriate markers. [3]

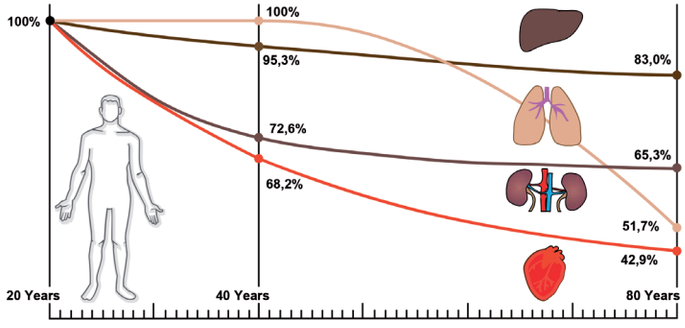

Fig. 3: Since coenzyme Q10 can be produced by the body itself, it is therefore not a vitamin by definition. With increasing age, the formation of the coenzyme decreases. A decrease in the Q10 concentrations manifests itself in varying degrees in different tissues. The most obvious is the decrease in the heart muscle tissue. At the age of 40 about 70 % of the concentrations could still be measured, which could be measured at the age of 20. By contrast, values of only around 43 % were measured at the age of 80. [2]

Coenzyme Q10 as an anti-ageing supplement

An additional supply of coenzyme Q10 leads to an accumulation of the active substance in the tissues. It could be demonstrated that after oral supplementation in heart failure patients, an accumulation in the heart tissue occurs [4], as well as in mitochondria extracted from tissue samples [5]. Coenzyme Q10 supplementation can alleviate the damage caused by the ageing process and significantly improve mitochondrial function, which weakens with increasing age. With regard to its anti-ageing effect, the active ingredient has been studied very well in the context of skin ageing. As an enveloping organ, the skin is exposed to a wide range of environmental influences, of which the ultraviolet portion of solar radiation has a significant influence on ageing. Because of its longer-wave character, UVA radiation can penetrate deeper into the skin and induce the formation of free radicals. In addition to cells of the epidermis, it can also damage fibroblasts of the dermis. The short-wave UVB radiation, on the other hand, is almost completely absorbed in the epidermis. The energy released can primarily damage DNA and proteins of epidermal keratinocytes.

In addition, photostress also influences the function of the mitochondria of the skin cells. A decrease in ATP formation and a decrease in mitochondrial membrane potential can be clearly measured after irradiation of human skin fibroblasts with UV light. This has a markedly negative impact on cell metabolism, since repair capacity, like most other biochemical processes, depends on sufficient ATP formation. It could be demonstrated that incubation of skin cells with coenzyme Q10 promotes regeneration after UV radiation. Coenzyme Q10 accelerates the restoration of cellular ATP levels and mitochondrial membrane potential. Coenzyme Q10 also helps to limit light-induced chromosome damage by stimulating enzymes that repair damaged DNA. [6] As in all tissues, the energy formation of the skin cells decreases continuously with increasing age. The reduction in mitochondrial respiration and the synthesis of energy in the form of ATP could be clearly demonstrated by measuring the respiratory quotient of skin cells from donors of different ages.

The respiratory parameters improved markedly after the cells were incubated with coenzyme Q10 (Fig. 4). [1] A recent study (2017) also showed that oral supplementation of coenzyme Q10 affects visible signs of ageing in a positive way. In the investigation, 33 study participants received either 50 or 150 mg of a coenzyme Q10 formulation with improved bioavailability. After 12 weeks, participants in both groups showed a reduction in wrinkles and microrelief lines and an improvement in skin smoothness. The participants who received the higher dose of the active ingredient also demonstrated an additional improvement in nasolabial folds, corners of the mouth and upper radial lip lines. [7]

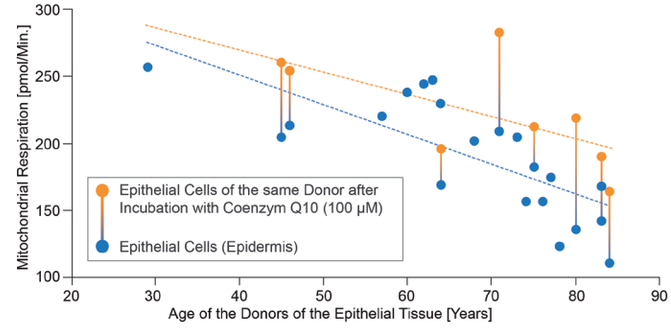

Fig. 4: Effect of coenzyme Q10 on the mitochondrial respiration rate of epithelial tissue with trend lines. Mitochondrial respiration and ATP synthesis decrease with age. Incubation of the tissue with coenzyme Q10 led to a significant increase in respiration, which was attributed to an improvement in electron transport chain function. [1]

Coenzyme Q10 in age-related diseases

Many mitochondria are found in tissues with high energy consumption. In cardiac muscle cells, their volume share reaches more than a third. The capacity of the energy production in the heart muscle depends on sufficiently high coenzyme Q10 concentrations in the mitochondria of the heart muscle cells, so that even small deficits can result in a deterioration of cardiac function.

In heart failure, coenzyme Q10 supplementation can contribute to a significant improvement in symptoms. It could be shown that patients with severe heart failure usually have low coenzyme Q10 plasma levels. With right heart failure and global insufficiency, there

is often abdominal oedema that worsens the absorption of nutrients. If these patients receive high doses of coenzyme Q10 as ubiquinol, significant improvements in ejection performance and the severity of heart failure can usually be observed. [8] Ubiquinol is the bioactive form of the coenzyme, which is characterized by improved bioavailability.

In people with high blood pressure, coenzyme Q10 has a normalizing effect on blood pressure, which also relieves stress on the heart muscle. As a lipophilic ("fat-friendly") substance, it accumulates in the cell membranes and protects them from oxidative damage. It improves the integrity and fluidity of the membranes of the blood cells. This makes them more fluid and mobile and allows them to pass through the narrow capillaries of the vascular system more easily. In people with high blood pressure, an antihypertensive effect in the range of 17 mmHg systolic and 8 mmHg diastolic could be demonstrated. [9]

With increasing age, the risk of developing type 2 diabetes mellitus also increases. According to estimates, about 15 % of 55–74 year olds in Germany are affected by the disease. It is expected that this number will continue to increase until 2030. Type 2 diabetes mellitus is usually associated with a high oxidative burden on the metabolism. The high glucose concentrations lead to saccharification of the body's own protein structures. In diabetes, saccharified hemoglobin ("HbA1c") is used as a marker for the quality of blood sugar control over the past eight to twelve weeks. Like hemoglobin, other structures are saccharified that are broken down by the immune system. Immune cells such as macrophages generate superoxide radicals with the aim of dissolving damaged structures. The radical formation also attacks "healthy" structures and leads to an enormous oxidative burden on the organism. [10] Supplementation with antioxidants such as coenzyme Q10 is therefore particularly suitable for people with diabetes. In addition to an improvement in markers that show oxidative damage, it was also possible to demonstrate improvements in the function of the β-cells and insulin resistance. [11] Positive effects on diabetic polyneuropathy could also be shown following a supplementation of coenzyme Q10 [12].

Coenzyme Q10 should be supplemented when taking medications that interfere with the body's synthesis of the coenzyme. Endogenous biosynthesis depends on the precursor mevalonic acid, from

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which the side chain of the coenzyme is formed. Mevalonic acid is also required for the body's own cholesterol synthesis and rate of synthesis is reduced by taking statins. The cholesterol-lowering medication therefore simultaneously leads to a reduction in the level of coenzyme Q10 in the tissues. A decrease in the coenzyme Q10 blood level by up to 40 % could be measured. [13] Coenzyme Q10 was investigated as a complementary therapy together with statins in clinical settings, in doses between 100 and 600 mg daily. A significant reduction in statin-associated side effects such as muscle pain, muscle weakness and cramps could be shown. [14]

Conclusion

As a fat-soluble antioxidant, coenzyme Q10 accumulates in membrane structures. In the "power houses of the cell", the mitochondria, it serves as an electron and proton carrier between the electron transport chain complexes. Here it can also neutralize free radicals directly at their place of origin. The concentration in the tissues decreases with increasing age. A supplementation of coenzyme Q10 can support the function of the mitochondria and protect the body's own tissues from the harmful effects of free radicals. As a body's own substance, coenzyme Q10 is extremely well tolerated.

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