

## the ubiquitous coenzyme Q10



Coenzyme Q10 (CoQ10) is produced by the human body and is necessary for the basic functioning of most cells. It is the spark plug for igniting the creation and release of energy production in the mitochondria.

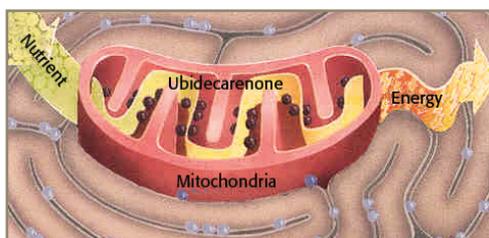
More than a billion years ago, aerobic bacteria colonised primordial eukaryotic cells that lacked the ability to use oxygen metabolically. A symbiotic relationship developed and became permanent. The bacteria evolved into mitochondria, providing the host cells with aerobic metabolism, a much more efficient way to produce energy than anaerobic glycolysis.

Within the mitochondria, coenzyme Q10 (CoQ10) is a component of the electron transport chain and participates in aerobic cellular respiration, generating energy in the form of ATP. Also known as ubiquinone, CoQ10 is an oil-soluble vitamin-like substance which is produced by the body and is necessary for the basic function of most cells.

Organs with the highest energy requirements, such as the heart and the liver, have the highest CoQ10 concentrations. CoQ10 levels decrease with age and are low in patients with chronic diseases including heart conditions, muscular dystrophies, Parkinson's disease, cancer, diabetes and HIV/AIDS. Some prescription drugs may also lower endogenous CoQ10 levels.

The actions of CoQ10 centre around three activities:

- Improved mitochondrial function
- Antioxidant activity<sup>1</sup>
- Activation of genes involved with human cell signalling, metabolism, and transport<sup>2</sup>



### Low CoQ10 = Low Energy

CoQ10 is the 'spark plug' for igniting the creation and release of energy production in the mitochondria. Deficiency of CoQ10 leads to lower production of energy in the cells. This affects not only a person's general energy level, but also muscle power, immune function, fertility and can result in serious disorders of the nervous and cardiovascular systems.

### Indications

#### Mitochondrial Disorders

Mitochondrial disorders are genetic metabolic diseases, characterised by a decrease in the ability of mitochondria to completely burn food and oxygen in order to generate energy. They can manifest as poor growth, muscle weakness, neurological disorders, learning disabilities, mental retardation, dementia, seizures and various organic diseases. Supplementation with CoQ10 may be beneficial.<sup>3</sup>

#### Cardiovascular Disease

##### Atheroma

CoQ10 has a direct anti-atherogenic effect, decreasing lipid peroxidation<sup>4,5</sup> and it has been shown to improve endothelial function in dyslipidaemic patients with type 2 diabetes.<sup>6</sup>

##### Ischaemic Heart Disease and Congestive Heart Failure

CoQ10 supplementation may ameliorate endothelial dysfunction and functional impairment of the cardiac muscle. Oral CoQ10 supplementation significantly improved the endothelium-dependent relaxation of the brachial artery, left ventricle contractility and peak VO<sub>2</sub> in a study of congestive heart failure.<sup>7</sup> CoQ10 has also been shown to increase cellular ATP production.<sup>8</sup> In patients with stable moderate congestive heart failure, oral CoQ10 supplementation was shown to ameliorate cardiac contractility and endothelial dysfunction.<sup>7</sup>

##### Cardiac Arrest

Increased survival after cardiac arrest may be achieved by the administration of CoQ10, in addition to commencing active cooling (to 32–34° Celsius).<sup>9</sup>

##### Cardiac Surgery

CoQ10 (300 mg daily) has been shown to improve mitochondrial function in patients undergoing elective cardiac surgery. Preoperative oral CoQ10 therapy in patients undergoing cardiac surgery has been shown to increase myocardial and cardiac mitochondrial CoQ10 levels, improve mitochondrial efficiency, and increase myocardial tolerance to hypoxia/reoxygenation stress.<sup>10</sup>

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## CLINICAL INFORMATION

### Hypertension

A recent meta-analysis of clinical trials of CoQ10 for hypertension examined 12 clinical trials (362 patients) comprising three randomised controlled trials, one crossover study and eight open-label studies. The research group concluded that CoQ10 has the potential in hypertensive patients to lower systolic blood pressure by up to 17 mm Hg and diastolic blood pressure by up to 10 mm Hg without significant side-effects.<sup>11</sup>

### Statins and CoQ10

Statins, potent inhibitors of cholesterol biosynthesis, also adversely affect CoQ10 levels since CoQ10 and cholesterol share the same common biosynthetic pathways. Statins can reduce serum levels of CoQ10 by up to 40 per cent.<sup>12</sup> The synthesis of an intermediary precursor of CoQ10, mevalonate, is also inhibited by some beta-blockers, blood pressure-lowering medication.<sup>13</sup> Supplementation with CoQ10 is recommended.<sup>1,8</sup> CoQ10 (200 mg per day) has been shown to improve blood flow and therefore overall vascular health in diabetic patients receiving statins. A randomised, double-blind, crossover study found CoQ10 improved endothelial dysfunction in statin-treated type 2 diabetic patients. The absolute improvement in blood flow in the arm of one per cent with CoQ10 supplementation, may potentially translate to a 10–25 per cent reduction in residual cardiovascular risk in these patients.<sup>14</sup>

### Exercise Performance

CoQ10 may improve exercise performance, especially in patients suffering chronic lung diseases including Chronic Obstructive Pulmonary Disease (COPD).<sup>15</sup> A study found that 100 mg CoQ10 slightly improved tolerance to higher workloads in trained cyclists.<sup>16</sup> A double-blind, crossover study of 25 Finnish top-level cross-country skiers found that 90 mg daily oral CoQ10 supplementation significantly improved measured indexes of physical performance (anaerobic threshold ( $p=0.0003$ ), aerobic threshold ( $p=0.0001$ ) and maximum oxygen capacity (0.02)) in a 12-week period. During the CoQ10 supplementation, 94 per cent of the athletes reported improvements in their performances and recovery times versus only 33 per cent in the placebo period. Lactic acid clearance had a tendency to improve during CoQ10 supplementation but was not statistically significant.<sup>17</sup> A recent study found that CoQ10 increased fat oxidation and autonomic nervous system activity during low intensity exercise. CoQ10 supplementation may benefit individuals with hyperlipidaemia or obesity by improving lipolysis.<sup>18</sup>

### Periodontal Disease

In a study of patients with periodontal disease, every one of the 29 patients who participated in the study, was shown to have 20–60 per cent reduced CoQ10 activity in gingival biopsies ( $p<0.001$ ). These results support the adjunctive use of CoQ10 with oral hygiene for improved treatment.<sup>19</sup>

### Migraine Headaches

Supplementation of CoQ10 has been found to have a beneficial effect in some patients suffering migraine headaches.<sup>20,21</sup> Dosages were 150 to 300 mg/day.

### Immune Function

Deficiency of CoQ10 is an element of ageing<sup>22</sup> and certain immune disorders.<sup>23</sup> CoQ10 may modulate immune function by improving natural killer cell activity<sup>22</sup> and increasing levels of lymphocytes and IgG. A small clinical study found CoQ10 deficiency in HIV patients and supplementation may improve T-cell helper/suppressor ratios.<sup>24</sup>

### Cancer

CoQ10 has also been shown to be an effective chemopreventive agent against colon carcinogenesis in experimental studies.<sup>25</sup> Doxorubicin is used for treating various cancers including breast cancer, Hodgkin's disease and leukaemia. Its clinical use is, however, limited due to its cumulative and irreversible cardiomyopathy side-effects. CoQ10 administration has been shown to prevent the onset and progression of doxorubicin-induced cardiomyopathy *in vivo*. CoQ10 administration further resulted in improved ECG changes and survival rates.<sup>26</sup> A recent study has found that co-administration of CoQ10 at 100 mg along with tamoxifen 10 mg twice a day to breast cancer patients reduced the level of angiogenesis markers and lipid levels.<sup>27</sup> CoQ10 may also protect against chemotherapy-induced cardiotoxicity (anthracyclines).<sup>28</sup>

### Male Fertility

CoQ10 supplementation has been shown to improve semen quality in infertile men. 212 infertile men with idiopathic oligoasthenoteratospermia (generalised abnormalities of sperm density, movement, morphology and shape), were randomly assigned to receive 300 mg of oral CoQ10 daily or placebo during a 26-week period followed by a 30-week treatment free phase. CoQ10 therapy significantly improved sperm concentration and motility (both  $p=0.01$ ). A positive correlation was found for sperm count ( $p=0.03$ ), sperm motility and morphology ( $p=0.04$ ). CoQ10 also decreases serum FSH and LH (both  $p=0.03$ ).<sup>29</sup> Male infertility may be associated with damage to the spermatozoa by reactive oxygen species. CoQ10 (200 mg/day) for six months has been shown in a study of 22 men affected by idiopathic astenozoospermia to improve sperm motility and morphology. The wives of three out of 22 patients (13.6 per cent) achieved spontaneous pregnancy within three months from the discontinuation of therapy (2.4 per cent pregnancy rate per cycle).<sup>30</sup>

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## CLINICAL INFORMATION

### Pre-eclampsia

Supplementation with CoQ10 reduces the risk of developing pre-eclampsia. Women at increased risk of pre-eclampsia were enrolled in a randomised, double-blind, placebo-controlled trial. 235 women received 200 mg of CoQ10 or placebo daily from 20 weeks of pregnancy until delivery. The overall rate of pre-eclampsia was 20 per cent (n=47). Thirty women (25.6 per cent) in the placebo group developed pre-eclampsia compared with 17 women (14.4 per cent) in the CoQ10 group (p=0.035).<sup>31</sup>

### Cystic Fibrosis

Patients with cystic fibrosis are at high risk for malabsorption and malnutrition, and as a result may have low serum values of CoQ10 as well as other fat-soluble vitamins and antioxidants. CoQ10 plays a vital role in the maintenance of an adequate redox balance in the lung. Deficiency may potentially impact overall outcomes in paediatric cystic fibrosis. Supplementation with CoQ10 may be beneficial.<sup>32</sup>

### Fibromyalgia and Chronic Fatigue Syndromes

Fibromyalgia is a common chronic pain syndrome accompanied by other symptoms such as fatigue, headache, sleep disturbances and depression. Fibromyalgia is partly due to a defect in the distribution and metabolism of CoQ10 in cells and tissues and supplementation may be beneficial.<sup>33</sup> Supplementation may also be beneficial for patients suffering chronic fatigue.<sup>34,35</sup>

### Psoriasis

The levels of vitamin E, CoQ10 and selenium are lower than normal in chronic inflammatory skin disorders such as psoriasis and atopic dermatitis. A combination of conventional therapy and supplementation with vitamin E, CoQ10 and selenium has been shown to improve the clinical conditions of patients with severe forms of psoriasis.<sup>36</sup>

### Ageing

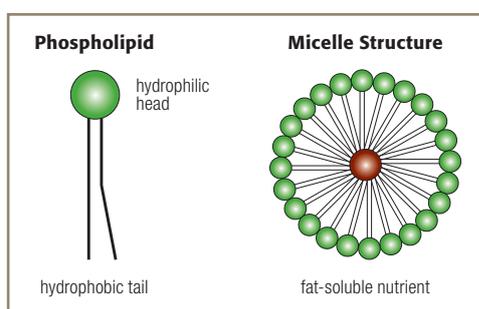
Ageing and ischaemic diseases are related in their aetiological degeneration of the mitochondrial respiratory chain. Reactive oxygen species (ROS) induce a progressive peroxidation of mitochondrial phospholipids. This could lead to a loss of facilitated electron channelling and mitochondrial dysfunction. CoQ10 supplementation may be beneficial.<sup>37</sup>

### Parkinson's Disease

Studies have reported decreased levels of CoQ10 in plasma and platelets, as well as in the cortex brain region of Parkinson's patients.<sup>38</sup> Mitochondrial dysfunction may result in excessive production of reactive oxygen species, triggering the apoptotic death of dopaminergic cells in Parkinson's disease. The addition of high dose CoQ10 in early Parkinson's disease may be beneficial.<sup>39,40</sup>

### Enhanced Absorption

The absorption of CoQ10 can be greatly improved by increasing its solubility in water. A study has shown that CoQ10 in a complex micelle form has a much higher bioavailability when compared to powdered CoQ10.<sup>41</sup> In a micelle, the CoQ10 is located within the phospholipid hydrophobic centre, upon entering the blood stream, the enzyme is readily integrated into various lipoproteins for transport and incorporation into target tissues.



### Drug Interaction

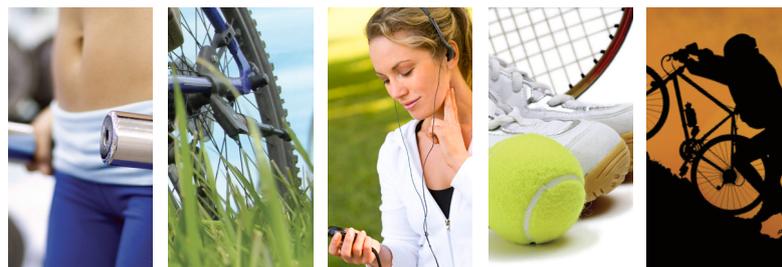
CoQ10 may prevent or reduce adverse effects of Beta-1-adrenoreceptor antagonists and related antihypertensive medications. Administration of CoQ10 is recommended before, during and after chemotherapy with anthracyclines, particularly doxorubicin. It is also known that certain drugs including statins, hypoglycaemic drugs, tricyclic antidepressants have a negative impact on CoQ10 levels and co-administration is recommended.<sup>42</sup>

### Dosage

The recommended adult dose for CoQ10 supplementation is 150 to 300 mg daily. CoQ10 is fat-soluble so should be taken with a meal containing fat for optimal absorption. Although there have been reports of interaction with warfarin, it is unlikely that under normal circumstances CoQ10 will have any interaction with warfarin.<sup>43</sup>

### Importance of Coenzyme Q10

- **Needed for energy conversion**
- **An essential antioxidant**
- **Regenerates other antioxidants**
- **Stimulates cell growth and inhibits cell death**



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## CLINICAL INFORMATION

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