PERSECPTIVE

## Coenzyme Q<sub>10</sub>: A Miracle Nutrient Advances in Understanding

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In the past several years, there have been some important breakthroughs in understanding coenzyme  $Q_{10}$ 's biological effects and how to achieve maximum therapeutic benefits from Co $Q_{10}$  supplementation.

The purpose of this article is to provide a brief overview of the history of  $CoQ_{10}$  and the role it plays in the prevention and treatment of cardiovascular disease. After this brief introduction, I will mention newer areas of therapeutic potential and then end by addressing the following two very important  $CoQ_{10}$  topics: a) the issue of crystallization and absorption and, b) the difference between ubiquinone and ubiquinol, and which form is best.

#### History

In 1957, University of Wisconsin biochemist Fred Crane isolated a yellowish substance from beef hearts. He sent samples to a colleague, biochemist Dr. Karl Folkers who worked at the pharmaceutical company Merck, Sharpe and Dohme. in 1958, Dr. Folkers successfully determined the chemical structure of  $CoQ_{10}$  and conducted some preliminary studies, which led him to believe that  $CoQ_{10}$  had enormous potential as a cardiovascular drug. At the time, Merck executives were not interested in developing a new cardiovascular drug. Consequently, the patent rights to  $CoQ_{10}$  were sold to a company in Japan.

It took Japanese scientists about ten years to develop industrial fermentation technology that resulted in the production of commercial quantities of  $\text{CoQ}_{10}$ . This enabled the initiation of the first clinical trials in which  $\text{CoQ}_{10}$  was used to treat patients with heart failure in Japan. In 1976,  $\text{CoQ}_{10}$  was approved in Japan as a drug to treat cardiovascular disease, and it remained one of the top-selling cardiovascular drugs in Japan for over twenty years.

In the 1970s, Dr. Folkers and his colleague, Dr. Gian-Paolo Littarru of Italy published data they had collected with tissue biopsies from 200 patients, which revealed that patients with heart disease and patients undergoing heart surgery had blood and tissue Coenzyme  $Q_{10}$  levels significantly below normal levels.<sup>1</sup>

In 1978, British biochemist Peter Mitchell was awarded the Nobel Prize in Chemistry for discovering the key role coenzyme  $Q_{10}$  plays in the electron transport chain in mitochondrial membranes, which results in the generation of cellular energy in the form of ATP.<sup>2</sup> Folkers' early work along with Mitchell's Nobel prize dramatically increased scientific interest in CoQ<sub>10</sub> around the world.

## Biosynthesis of CoQ<sub>10</sub>

The biosynthesis of  $CoQ_{10}$  from the amino acid tyrosine is a multistage process requiring at least eight vitamins and several trace elements. Considering the widespread consumption of nutrient-deficient fast foods and highly processed foods and the fact that nutritional content of our commercial food supply has been steadily declining since the end of World War II, due to the use of toxic chemicals, artificial fertilizers and other destructive farming practices, it is easy to see why many people have nutritional deficiencies that hinder the body's ability to synthesize coenzyme  $Q_{10}$ .

#### **Drug-Induced Nutrient Depletions**

I am the author of *The Drug-Induced Nutrient Depletion Handbook.*<sup>3</sup> In this handbook, I present peerreviewed scientific studies which document that 11 different classes of drugs deplete coenzyme  $Q_{10}$ . The classes of drugs that deplete  $CoQ_{10}$  are oral contraceptives, hormone replacement therapy (HRT), tricyclic antidepressants, adrenergic stimulants, thiazide diuretics, antipsychotics, statins, most chemotherapy drugs, beta-blockers and oral hypoglycemics: both sulfonylureas and biguanides.

Thus, it is easy to see why many people are coenzyme  $Q_{10}$  deficient due to poor nutrient intake from poor diets and the fact that many people may be taking one or more drugs that deplete coenzyme  $Q_{10}$ .

The Drug-Induced Nutrient Depletion Handbook is out-of-print. However, I have created a *Quick Reference Guide to Drug-Induced Nutrient Depletions*. As part of my commitment to help people improve their health, I am offering this Quick Reference Guide FREE to everyone. Use the link below to get your free copy of the Quick Reference Guide to Drug-Induced Nutrient Depletions and feel free to distribute this offer to your patients, family and friends. LINK: naturalpharmacist.net/dind Let's Make Good Health Go Viral...!!!<sup>TM</sup>

## Coenzyme Q<sub>10</sub> Exists in Two Forms

Ubiquinone is the oxidized form, which has a molecular weight of 864. Ubiquinol, which is the reduced form, has two more hydrogen molecules in its structure, giving it a molecular weight of 866. Ubiquinone and ubiquinol are a redox pair (oxidation-reduction) that can be rapidly converted from one form to the other in cells, lymph or blood depending on the demand for their various functions.

## CoQ<sub>10</sub>'s Antioxidant Functions

The reduced form of  $\text{CoQ}_{10}$ , ubiquinol, is a powerful lipid-soluble antioxidant that provides critical antioxidant protection in the lymph and blood throughout the body.<sup>4</sup> Ubiquinol is the only known fat-soluble antioxidant that human cells can synthesize.<sup>5</sup> In its reduced form, ubiquinol coenzyme  $Q_{10}$  plays a major role in preventing oxidation in both the lipids that make up much of the structure of cellular membranes in cells throughout the body and also in lipoprotein lipids present in circulation.<sup>6</sup> Coenzyme  $Q_{10}$  can also recycle or regenerate other antioxidants such as vitamin  $E^7$  and vitamin C.<sup>8</sup>

#### **Cellular Energy Production**

The oxidized form of  $CoQ_{10}$ , ubiquinone, is required for energy production in the mitochondria of all cells except the red blood cells. Specifically,  $CoQ_{10}$  is required in several steps of the electron transport chain in mitochondrial inner membranes, which is where cellular energy, known as ATP, is produced. This is the work that earned Peter Mitchell his 1978 Nobel Prize.

#### Bi-directional Conversion of Ubiquinone to Ubiquinol

When ubiquinone is taken orally, it is converted to ubiquinol during absorption and remains in its reduced form in the lymph and in blood.  $CoQ_{10}$  is not needed to

produce energy when it is circulating in the lymph or blood. This conversion takes place so that reduced ubiquinol form of  $CoQ_{10}$  can provide antioxidant protection as it is being circulated throughout the body.

For decades, physicians have prescribed statin drugs in the belief that elevated LDL-cholesterol is a major risk factor for cardiovascular disease. This is unfortunate because LDL-cholesterol is not a "bad" molecule. However, when LDL-cholesterol becomes oxidized, it becomes a "damaged" molecule that is capable of causing vascular endothelial injury which contributes to atherosclerosis and cardiovascular disease.<sup>9</sup>

A 1997 study by cardiologist Svend Aage Mortensen made the following important statement. Dr. Mortensen announced that  $CoQ_{10}$  is an antioxidant that is "packaged into the LDL & VLDL fractions of cholesterol." This means that LDL cholesterol is the "carrier" that transports coenzyme  $Q_{10}$  around the body. It also means that when  $CoQ_{10}$  is being transported on the LDL cholesterol molecule, its antioxidant properties enable it to protect LDL cholesterol against oxidative damage. This explains why  $CoQ_{10}$  helps prevent the formation of oxidized LDL cholesterol, which is one important way that  $CoQ_{10}$ 

#### CoQ<sub>10</sub> Studies

In this section I will present some selected studies that show coenzyme  $Q_{10}$ 's therapeutic benefits in various medical conditions.

#### CoQ<sub>10</sub> & Cardiovascular Disease

Over the past 40 years, the results of many clinical trials confirm that coenzyme  $Q_{10}$  supplementation is useful in the prevention and treatment of many aspects of cardiovascular disease such as congestive heart failure, hypertension, ischemic heart disease, cardiac arrhythmias.<sup>11</sup>

#### The 2014 Q-Symbio Study<sup>12</sup>

Chronic heart failure patients (average age: 63 years) administered  $3 \times 100$  mg of ubiquinone coenzyme  $Q_{10}$  or matching placebo daily for two years along with patient's conventional heart failure medicine.

**RESULT:** significantly improved symptoms and survival in the coenzyme  $Q_{10}$  group. Sub-group analysis of just the European study participants showed significantly improved ejection fraction in the coenzyme  $Q_{10}$  treatment group.<sup>13</sup>

#### The 2013 KiSel-10 Study

Community living senior citizens (average age: 78 years) administered  $2 \times 100$  mg of ubiquinone CoQ<sub>10</sub> in combination with 200 mcg of selenium or matching placebo daily for four years.

**RESULT:** significantly reduced risk of death from heart disease and improved heart function in the active treatment group.<sup>14</sup>

#### Langsjoen Hypertension Study

Cardiologist Peter Langsjoen selected 109 patients with essential hypertension. Patients added high-dose  $CoQ_{10}$  (average dose 225 mg/day) to their existing antihypertensive drugs.

**RESULT:** New York Heart Association (NYHA) functional class improved from a mean of 2.40 to 1.36, and 51% of patients came completely off from 1 to 3 blood pressure meds within average of 4.4 months after starting high-dose  $\text{CoQ}_{10}$ .<sup>15</sup>

#### CoQ<sub>10</sub> & Cancer

Studies reveal that cancer patients have low levels of coenzyme  $Q_{10}$ .<sup>16</sup> Thomas Seyfried, MD has written an important book titled *Cancer as a Metabolic Disease: On the Origin, Management and Prevention of Cancer.*<sup>17</sup> Seyfried explains that cancer is a metabolic disease that initiates with damage to mitochondrial DNA, which hinders the ability of cells to produce adequate energy. This causes the metabolic shift from oxygen to glucose for energy production, which is the hallmark of cancer cell metabolism. Coenzyme  $Q_{10}$  in its reduced form—ubiquinol plays a critically important role in mitochondrial DNA (mtDNA) from free radical damage.<sup>18</sup>

**Breast Cancer.** In a small study, 32 advanced breast cancer patients with lymph metastasis were treated with 390 mg of  $CoQ_{10}$  daily. Either partial or complete tumor regression was documented in 6 of the 32 women.<sup>19</sup>

**Prostate Cancer.** In men with prostate cancer, treatment with high-dose  $CoQ_{10}$  resulted in substantial reductions in PSA and tumor size. An important finding was that the men did not begin to show any signs of response until about 90 days into the trial.<sup>20</sup>

**Reducing Chemotherapy Side Effects.** clinical trials have also reported that coenzyme  $Q_{10}$  substantially protects against and/or reduces side effects in patients undergoing various forms of chemotherapy.<sup>21</sup>

**Neurological Conditions.** Reduced levels of coenzyme  $Q_{10}$  are associated with several neurological diseases and its ability to reduce oxidative stress suggests that  $CoQ_{10}$  may be able to slow the progression and in some cases, possibly provide some therapeutic benefit. Conditions in which  $CoQ_{10}$  may play a role include Parkinson's disease<sup>22</sup>, Huntington's disease<sup>23</sup> and Alzheimer's disease.<sup>24</sup>

**Life Extension.** Coenzyme  $Q_{10}$ 's ability to protect mitochondria against excessive free radical damage makes it a candidate for consideration as a life extension nutrient. Although studies in animal models have had mixed results, a study conducted by Emile Bliznakov, MD has fascinating implications.

Dr. Bliznakov started his experiment with 100 "old" female white mice 16 to 18 months of age, which is equivalent to humans in their 60s to 70s. Being elderly, these mice were already beginning to show some signs of

decreased immunity and aging bodily functions.<sup>25</sup> Fifty mice regularly received  $CoQ_{10}$ ; the other 50 old mice served as controls. All mice were maintained on optimally nutritious diets.

- At 36 weeks into the study, 100% of the control mice were dead while 40% of the CoQ<sub>10</sub>-treated mice were still alive, active and not showing the normal signs of physical deterioration commonly associated with advanced age.
- At week 56, 10% of the CoQ<sub>10</sub>-treated mice were still alive and thriving. This is 2X longer than these mice would normally be expected to survive beyond the beginning of the experiment.
- At the 80th week 4 mice were still alive; at the 82nd week, the last mouse died. In human terms, this is a life span of roughly 130 years of age! (the last control mouse died at week 36).

I spoke with Dr. Bliznakov personally, and he explained the following remarkable visual differences between the two groups of mice at 30 weeks, when some of the control mice were still alive. The fur on the controls was dull, coarse, matted and on some mice, clumps of hair had fallen out, leaving bald patchy spots. All the remaining control mice were very listless and spent most of their time lying around and not socializing. On the other hand, the fur in the coats of the  $CoQ_{10}$ -treated mice remained smooth and soft, and they maintained a much greater level of activity and socialization.

#### Ubiquinone vs Ubiquinol

 $CoQ_{10}$  is poorly absorbed because of its lipophilic nature and its large molecular weight. In 2006, Kaneka Corporation in Japan began marketing the ubiquinol (reduced) form of  $CoQ_{10}$  with claims that it was better absorbed than ubiquinone and hence, more effective. This has been a very successful marketing strategy for Kaneka, but actually, the claims are not scientifically accurate.

Ubiquinol  $CoQ_{10}$  products are substantially more expensive than ubiquinone  $CoQ_{10}$  products. However, when ubiquinol is ingested, it is oxidized by gastric acid to ubiquinone before it is absorbed.<sup>26</sup> Hence, people pay more for ubiquinol, but really do not get added benefit(s). Research has shown that it is not necessary to take ubiquinol in order to significantly increase ubiquinol levels in plasma and in plasma lipoproteins. Taking a ubiquinone supplement will do the same.<sup>27</sup>

#### **Dosing Advice**

The following advice pertains to all  $CoQ_{10}$  products, regardless of the type of  $CoQ_{10}$  being taken. Coenzyme  $Q_{10}$  is a fat-soluble nutrient and humans do not absorb fat-soluble nutrients very efficiently.  $CoQ_{10}$  supplements should be taken at a meal that contains some fat. This enhances the absorption of the  $CoQ_{10}$ .

The following data was gathered from multiple human clinical trials. On average, participants' pre-test  $CoQ_{10}$  blood levels were 1.09 ug/ml. After ingestion of a single 100 mg dose of  $CoQ_{10}$ , blood levels increased to 2.33 ug/ml. However, when people ingested 200 mg of  $CoQ_{10}$  in a single dose, the blood level only increased to 2.35 ug/ml—almost no different than the blood level following a 100 mg dose. However, when individuals took 100 mg of  $CoQ_{10}$  in divided doses, twice daily, blood levels rose to 3.47 ug/ml.

Because coenzyme  $Q_{10}$  is a large molecular weight, fat-soluble compound, its absorption is slow and limited. This explains why better blood levels are achieved with divided doses rather than taking a large single dose of coenzyme  $Q_{10}^{28}$ .

#### The Crystallization Problem

 $CoQ_{10}$ 's melting point is 10°C higher than human body temperature, which equates to about 118° F. Consequently, at temperatures below 118° F, single molecules of  $CoQ_{10}$  dissolved in water or oil begin to clump into crystals. We cannot absorb  $CoQ_{10}$  crystals; we can only absorb single molecules. Upon microscopic examination, many  $CoQ_{10}$  softgel capsules contain crystals, which partially explains why many  $CoQ_{10}$  products have low absorbability. Even  $CoQ_{10}$  products that are dissolved in oil recrystallize in the body, which prevents absorption.

#### **Absorption Studies**

Until recently, there was a lack of standardization in most CoQ<sub>10</sub> absorption studies, which made it difficult to make product comparisons. However, a recently published, head-to-head study that compared the absorption of variously formulated ubiquinone products with a well-formulated ubiquinol product, revealed conclusively that a well-formulated ubiquinone product is about 200% better absorbed than ubiquinol products.<sup>29</sup> However, this is not the end of the story.

#### The Oil Matrix

William Judy, PhD, has been a highly respected coenzyme  $Q_{10}$  scientist for over 40 years. In the past several years, he has focused on  $CoQ_{10}$  absorption issues and conducting  $CoQ_{10}$  absorption studies. Dr. Judy's absorption studies have led him to realize that the form of coenzyme  $Q_{10}$  in a product (ubiquinone or ubiquinol) is less important than the oil matrix that the  $CoQ_{10}$  is dissolved in. Most coenzyme  $Q_{10}$  products are not simply  $CoQ_{10}$ , they contain other ingredients such as various oils or a substance like piperine, which is a compound derived from black pepper. These substances may enhance the absorption of coenzyme  $Q_{10}$ .

#### Formulation is More Important Than Form

Dr. Judy's research has revealed that the following two important factors determine the absorption (and

effectiveness) of coenzyme  $Q_{10}$ . One is the composition of the oil matrix in which the  $CoQ_{10}$  is dissolved and the second factor is the heating and cooling process used prior to filling the coenzyme  $Q_{10}$ /oil mixture into the soft-gel capsules. These are the factors that differentiate between a crystal free  $CoQ_{10}$  product vs a product with  $CoQ_{10}$ crystals.

### Crystal Free CoQ<sub>10</sub>

Numerous companies that produce coenzyme  $Q_{10}$  products are engaged in research to develop their own patented delivery system that keeps their  $CoQ_{10}$  in solution, both in the capsule and after it has been ingested. These are called Crystal Free coenzyme  $Q_{10}$  products.

Pharma Nord is a Denmark-based company that that has been committed to producing quality coenzyme  $Q_{10}$ products for over 30 years. During the 1990s they funded numerous absorption and bioavailability studies on their **Bio-Quinone<sup>TM</sup>** Active CoQ<sub>10</sub> GOLD product. These studies confirmed that their patented oil mixture provided a crystal free product that is well absorbed.<sup>30,31,32</sup>

#### **Industry Acceptance**

Pharma Nord's willingness to fund studies that document the superior absorbability of their Bio-Quinone  $CoQ_{10}$  resulted in their products being selected to be used in a majority of the large clinical trials conducted around the world. To date, 78 human studies have been conducted using *Bio-Quinone Active CoQ\_{10} GOLD*, and 26 of these studies are randomized, double-blind, placebo-controlled studies with 30 or more participants.

#### CoQ<sub>10</sub> & Immunity

The global COVID-19/coronavirus pandemic has made people much more conscious about taking steps to boost their immune system. Coenzyme  $Q_{10}$  supports and/ or enhances immune function in the following ways: stimulates production of red blood cells and hemoglobin<sup>33</sup>, improves ratio between T4/T8 lymphocytes<sup>34</sup>, increases production of natural killer cells<sup>35</sup> and stimulates the production of antibodies.<sup>36</sup> Thus, coenzyme  $Q_{10}$  should be considered along nutrients like vitamin C and vitamin D, as important natural therapies to enhance immune function.

#### **Bio-Quinone's Superior Absorbability**

One of the world's leading coenzyme  $Q_{10}$  scientists, Dr. Guillermo Lopez-Lluch of Spain, conducted a bioavailability study with seven of the leading coenzyme  $Q_{10}$ formulations on the market. In this double-blind, crossover study, individuals were given a single 100 mg dose of  $CoQ_{10}$  and plasma  $CoQ_{10}$  levels were measured 48 hours after ingestion. Pharma Nord's Bio-Quinone was found to be from 3 to 10 times better absorbed than the other 6 brands tested.<sup>37</sup> This explains why Pharma Nord's Bio-Quinone has been the  $CoQ_{10}$  product selected to be used

# Pharma Nord's CoQ10 Stays in Solution



Bio-Quinone CoQ10's superior bioavailability is due to the unique technique used to dissolve the CoQ10 in oil. CoQ10 that is not exposed to any pre-treatment forms crystals, which prevents efficient absorption.



Bio-Quinone Q10 undergoes a special heat treatment that changes crystals into snowflake-like structures with greater surface area which stay in solution

in the majority of large coenzyme  $Q_{10}$  clinical trials around the world over the past thirty years.

The slide/image above shows how Pharma Nord's patented process keeps their coenzyme  $Q_{10}$  in solution, which results in a product that is largely crystal free. Coenzyme  $Q_{10}$  is an incredibly important nutrient, but in order to be effective, it must be well absorbed and bioavailable. That's why I use and recommend Pharma Nord's *Bio-Quinone Active CoQ*<sub>10</sub> *GOLD*.

**To Order:** Practitioners, if you would like to get product information or order Pharma Nord's Bio-Quinone for yourself or for your patients, send a request to: practitioner@pharmanord.com

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Most formulations contain CoQ10 crystals in oil. Humans can not absorb crystals, we can only absorb single molecules.



These "snowflakes" completely dissolve at body temperature and remain in solution, which provides better absorption and higher plasma CoQ10 levels

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