CoQH-CF™

Our Formula is the *Crystal Free* Solution

SOFT GEL
TECHNOLOGIES, INC.®

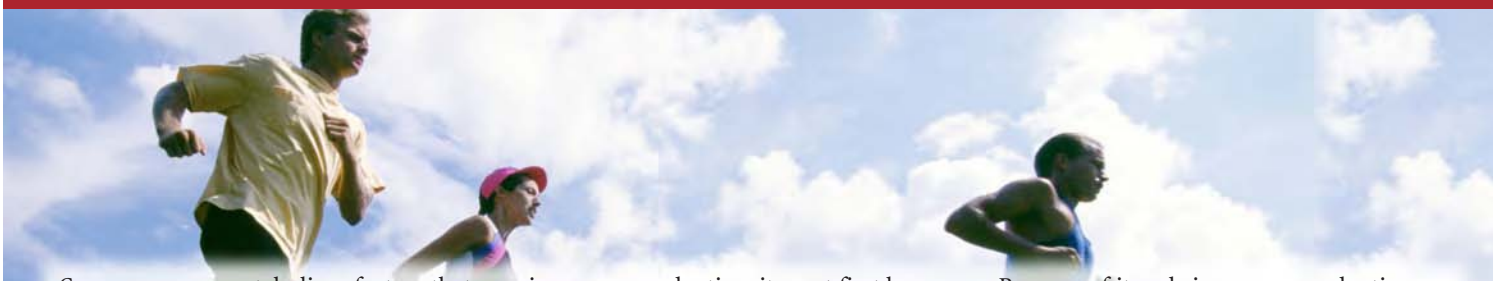
SOFT GEL TECHNOLOGIES, INC.®

One of the most common complaints in people of all ages is lack of energy. Not only does the body as a whole need energy, individual cells do as well. Many diseases are characterized by energy depletion. An individual with diabetes or heart disease may experience this depletion of energy on a cellular level. Whether reduced energy is caused by disease states, high levels of oxidative stress, or the aging process, the feelings are the same.

Coenzyme Q_{10} (CoQ_{10}) is an essential component of the body's energy-generating system found in every cell and organ. Scientific data shows that CoQ_{10} supplementation offers substantial health benefits to people suffering from a variety of health conditions. Although CoQ_{10} is classified as a fat-soluble nutrient, its degree of solubility is extremely limited. Bioavailability plays a key role in CoQ_{10} formulations. Current research strongly indicates that CoQ_{10} in soft gel form is significantly more bioavailable than the dry form. Absorption is independent of food intake. A soft gel delivery system plays a key role in enhancing the effectiveness of CoQ_{10} getting into the bloodstream. Soft gels not only improve the bioavailability of CoQ_{10}, they also provide a hermetically-sealed capsule that protects the ingredients from oxygen.

CoQH-CF™ soft gels provide a highly efficient platform for delivering the reduced form of CoQ_{10} for maximum utilization. Supplementing with this form makes CoQ_{10} more readily available to those who need it most—the late middle-aged to elderly and individuals suffering from oxidative stress conditions such as diabetes and liver disease. There is no other substitute for CoQ_{10}; without it, energy cannot be generated and longevity is hindered.

CoQ_{10} and Energy Production

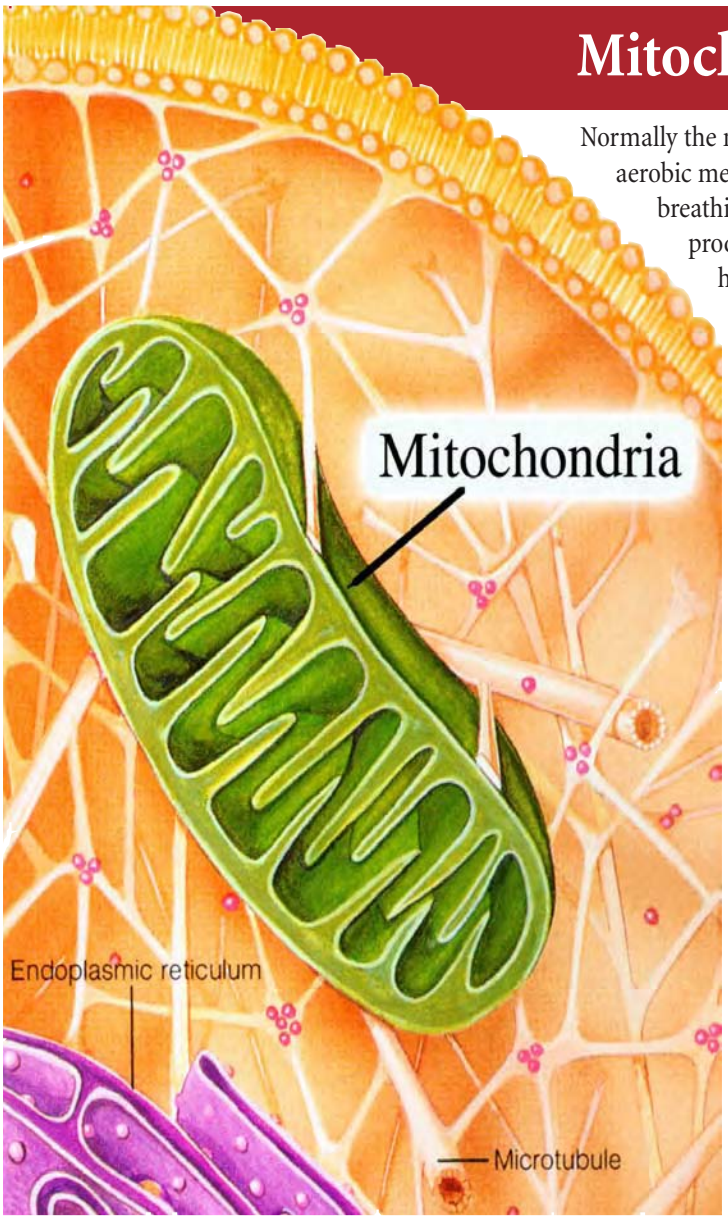


Coenzymes are metabolic cofactors that larger and more complex enzymes absolutely depend on for their function. Coenzyme Q_{10} (CoQ_{10}), or ubiquinone, is a lipid-soluble antioxidant found in every cell of the body. Present in the inner mitochondrial membrane, CoQ_{10} plays an important role in the synthesis of ATP (adenosine triphosphate)—a molecule of chemical energy upon which all cellular functions depend. It serves as a coenzyme for several key enzymatic steps to produce cellular energy and may also prevent the depletion of metabolites necessary for the resynthesis of ATP. CoQ_{10} directly regulates NADH and succinate dehydrogenase, enabling reversible reactions between these enzymes in the mitochondrial electron transport chain. In order for CoQ_{10} to wield its functions as an antioxidant and in energy production, it must first be reduced to ubiquinol.

Cells do not use nutrients from the diet for their immediate supply of energy. Instead, mitochondria—known as the "power house" of cells—produce most of the energy in cells through a process called oxidative phosphorylation. They transform oxygen and other nutrients into energy during cellular respiration. Electrons are passed along a series of respiratory enzyme complexes located in the inner mitochondrial membrane, and the energy released by this electron transfer is used to pump protons across the membrane. The resulting flow of protons into the last respiratory compartment of the electron transport chain drives the synthesis of ATP.

Because of its role in energy production, a deficiency of CoQ_{10} can aggravate many health problems. Normal blood and tissue levels of CoQ_{10} have been well established by numerous investigators around the world. Significantly decreased levels of CoQ_{10} have been noted in a wide variety of chronic health conditions in both animal and human studies. The body's ability to produce and metabolize CoQ_{10} is also reported to decrease with age. CoQ_{10} deficiency may be caused by insufficient intake of dietary CoQ_{10}, impairment in CoQ_{10} biosynthesis, excessive utilization of CoQ_{10} by the body, gene mutations, and oxidative stress. The result is less cellular energy (ATP production), slower conversion of CoQ_{10} to the reduced form and, consequently, a reduced protection against oxidation.

Mitochondrial Function and Aging



Normally the mitochondria are very efficient in producing cellular energy through aerobic metabolism. They consume over 80 percent of the oxygen obtained from breathing to release energy from food. However, oxidative phosphorylation also produces free radicals, which are toxic by-products. Because free radicals are highly unstable molecules with unpaired electrons, they react with the nearest available molecule within the cell. These electrically-charged particles not only cause oxidative damage to the mitochondria, but also to other important parts of the cell, including proteins, lipid membranes, and genes. The reactions between free radicals and cellular components lead to mitochondrial malfunction, cell membrane and DNA damage, and sometimes cause cell death.

The body can typically handle free radicals, but if antioxidants are unavailable or if free radical production becomes excessive, damage can occur. As free radical damage accumulates with age, the mitochondria become impaired, resulting in higher levels of free radicals. Poor mitochondrial function promotes a vicious cycle of oxidative stress, DNA mutation, and further impairment of mitochondrial function. Mitochondrial impairment contributes to aging by increasing free radical production and by a reduction in energy production.

Oxidative stress is a condition that can lead to and accelerate disease. It occurs when there is an imbalance of free radicals (or other pro-oxidants) and antioxidants to neutralize them, leading to oxidative damage. The degree of oxidative stress depends on the rate at which free radicals are generated, the level of antioxidant protective processes, and the turnover and repair of tissue damage resulting from free radical action. Enhanced oxidative stress is well documented in a number of degenerative diseases including Parkinson's, Alzheimer's, and diabetes. It also has an impact on the body's aging process.

Ubiquinone vs. Ubiquinol

Coenzyme Q_{10} can exist in three oxidation states:
1) the fully oxidized ubiquinone form (CoQ_{10}),
2) the partially reduced free radical semiquinone intermediate ($CoQ_{10}H\cdot$), and
3) the fully reduced ubiquinol form ($CoQ_{10}H_2$). The dominant form of CoQ_{10} in human blood and the liver (over 80%) is ubiquinol. All forms of CoQ_{10} are active redox cofactors and play important metabolic roles in their interconversion from one form to another, but they have vastly different roles to play in the body. For instance, ubiquinol—with its two hydroxyl groups—is an electron donor, while ubiquinone is an electron acceptor. The electrons that ubiquinol donates neutralize free radicals. This fact alone makes ubiquinol the form of CoQ_{10} that protects against toxic oxidative reactions in the body.

While CoQ_{10} is necessary to produce cellular energy, the body must first convert CoQ_{10} to ubiquinol. Without ubiquinol to carry electrons through the mitochondria, cellular energy cannot be produced and life cannot be sustained. Those who are young and healthy can easily convert CoQ_{10} to ubiquinol. But as we age, our ability to convert CoQ_{10} into ubiquinol often diminishes, especially for those with chronic disease states.

Researchers have been investigating the relationship between disease states marked by high levels of oxidative stress and the levels of ubiquinol in the body. Disorders of elevated oxidative stress cause major changes in the amounts of ubiquinol and ubiquinone in the body. The therapeutic opportunity is to influence the ubiquinol to ubiquinone ratio and reduce the chronic burden of oxidation at the cellular level.

To counteract oxidative stress, health-conscious people should take steps to protect themselves against the ravages of free radicals. Supplemental antioxidants offer protection against this insidious condition. The membrane-stabilizing properties of CoQ_{10} emerge from the reduction of free radicals that may cause damage to structural proteins and lipids found in membranes. CoQ_{10} supplementation replenishes diminished levels of this important antioxidant cofactor, fostering a strong protective defense against oxidative stress and age-related diseases.

Coenzyme Q_{10} can exist in three oxidation states:

1) the fully oxidized ubiquinone form (CoQ_{10})

2) the partially reduced free radical semiquinone intermediate ($CoQ_{10}H\cdot$)

3) the fully reduced ubiquinol form ($CoQ_{10}H_2$)

A Quick Primer in Antioxidant Function

Antioxidants neutralize free radicals by donating one of their own electrons, ending the electron-"stealing" reaction. The antioxidant nutrients themselves don't become free radicals by donating an electron because they are stable in either form. They act as scavengers, helping to prevent cell and tissue damage that could lead to cellular damage and disease.

CoQ_{10} Levels Diminish with Age

Normal CoQ_{10} levels in the body are maintained by biosynthesis as well as CoQ_{10} intake. The concentration of coenzyme Q_{10} in the body decreases year by year, indicating that it has a close relationship with aging. As the body ages, it not only produces less CoQ_{10}, but it is less efficient at converting ubiquinone to its reduced form, ubiquinol. This decrease in CoQ_{10} becomes apparent around 40 years of age. However, some literature suggests that CoQ_{10} begins to diminish as early as 20 years of age, with a slow but continuous decline thereafter.

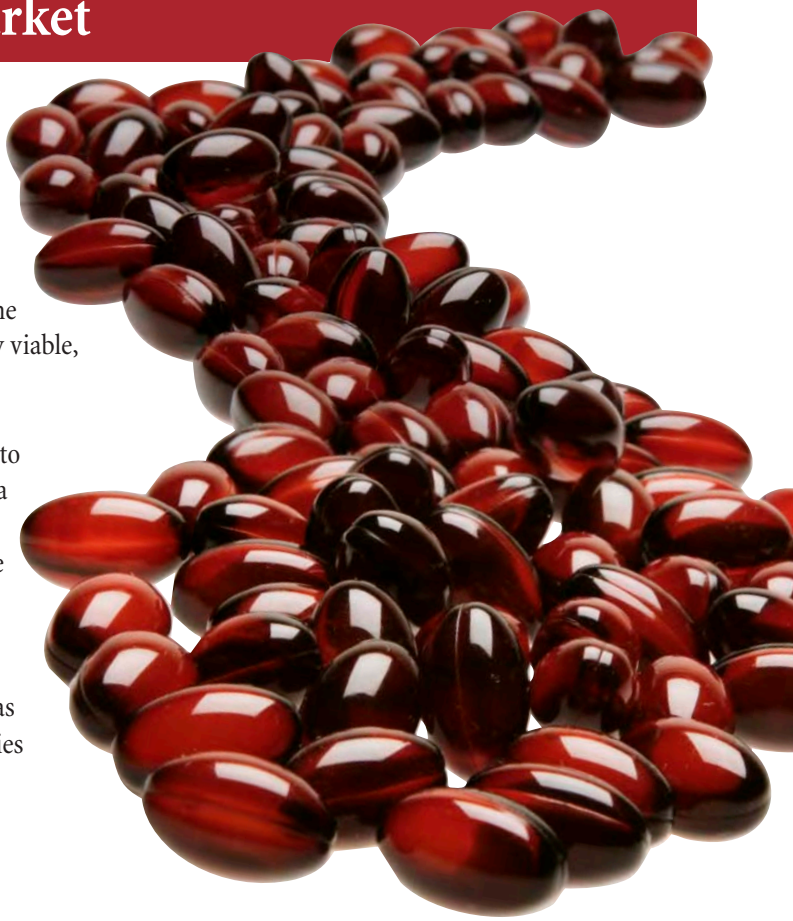
There are a number of factors that contribute to the aging process, but many age-related conditions are associated with this decline in CoQ_{10} levels. Cardiovascular disease, neurodegenerative disease, cancer, diabetes, fatigue and the reductions in stamina and energy often associated with getting older have all been linked to diminished amounts of CoQ_{10}. In these cases, not enough CoQ_{10} is biosynthesized, thereby warranting an increased intake of CoQ_{10}.

Getting a Stable Form to Market

As previously stated, in order for the ubiquinone form of CoQ_{10} to be properly utilized, it first must be reduced in the body to its active metabolite, ubiquinol. While most ubiquinone is naturally reduced to ubiquinol, the optimal way to supplement with CoQ_{10} would be to ingest it in its ready-to-use ubiquinol form. However, ubiquinol is easily oxidized in air. When it is exposed to oxygen, it quickly reverts back into the ubiquinone form of CoQ_{10}. This property has made it difficult to supply a commercially viable, stable, reduced form…until now.

KANEKA QH™

After a decade of thorough research, a patented method to stabilize ubiquinol was developed by scientists at Kaneka Corporation, a leading CoQ_{10} manufacturer. This major advancement in technology enables a commercial, stable form of ubiquinol—called Kaneka QH™—to be manufactured in bulk. Kaneka registered its ubiquinol with the Food and Drug Administration (FDA), who accepted Kaneka's NDI (new dietary ingredient) application for its Kaneka QH™ product. In addition, Kaneka has confirmed the safety of its Kaneka QH™ product in preclinical toxicity studies and a published human clinical study.



Kaneka QH™ Clinical Data

Kaneka QH™ Animal Data

In a study published in *Experimental Gerontology*, it was determined whether supplementation with both forms of CoQ_{10} (ubiquinone and ubiquinol) could decelerate aging in SAMP1 mice. The senescence-accelerated mice (SAM) are a collection of inbred mouse strains developed as models of accelerated aging, compared to most laboratory strains of mice. They include nine short-lived, senescence-accelerated mouse prone strains (SAMP). The SAMP strains exhibit several features that make them interesting models of human aging, including greatly reduced physical activity, loss of hair glossiness, coarse skin, hair loss, ocular lesions, and curvature of the spine. Oxidative stress and mitochondrial dysfunction disrupt cellular metabolism in most aging cells and have been shown to occur prematurely in aging SAM.

Two month-old mice were divided into three groups—the first group (placebo) received a standard diet, the second group received a diet that contained ubiquinone, and the third group received a diet fortified with ubiquinol (Kaneka QH™). A grading score developed by the Council for Senescence Accelerated Mouse Research was used to evaluate the aging rate of the three groups of mice. The grading score increases with aging.

At three months of age, the grading score was about 0.0 for all three groups. At 12 months of age, there was a marked difference between the three groups, causing the researchers to take photos of each group. The grading score quickly increased in the placebo group, and the photos revealed mice with spinal deformities and a patchy, discolored coat. The groups receiving ubiquinone and ubiquinol slowed down the process of biological aging; although around 10 months of age, the ubiquinone group had a sharp increase in the grading score. The ubiquinol group did not experience the same spike in the grading score. The pictures of the mice who received the ubiquinol-fortified diet looked healthy, had a glossy coat, and no physical deformities or lesions. Lower scores in SAMP1 mice supplemented with ubiquinol suggest that ubiquinol may delay senescence. (See Figure 1.)

Kaneka QH™ Human Safety and Bioavailability Data

A single-blind, placebo controlled study published in *Regulatory Toxicology and Pharmacology* showed that doses of up to 300 mg ubiquinol were found to be safe with no significant adverse effects. The results also found significant absorption of ubiquinol in the gastrointestinal tract. Fifteen healthy subjects were given a single oral dose of 150 (n=10) or 300 (n=5) mg. Following its administration, ubiquinol was gradually absorbed, and mean ubiquinol concentration reached a maximum of 1.88 µg/ml for 150 mg and 3.19 µg/ml for 300 mg at 6 hours after administration. (See Table 1.) A total of 78 healthy volunteers (38 females and 40 males) completed the four-week multiple-dose study, where subjects received either a placebo (n=19), 90 (n=20), 150 (n=20), or 300 (n=19) mg for four weeks. (See Figure 2 for results and study summary.)

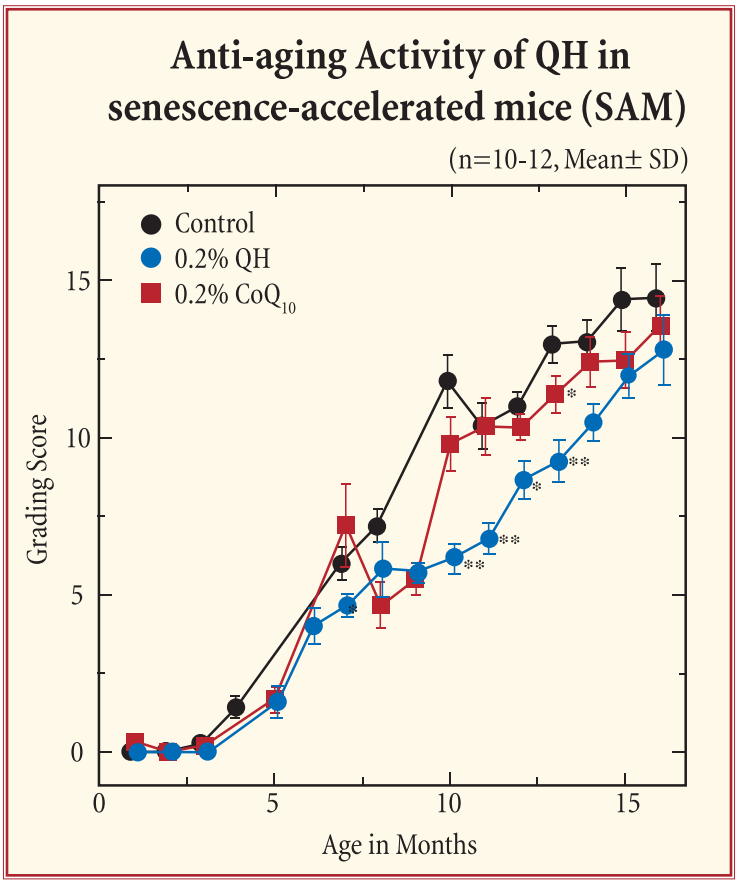


Figure 1.

Kaneka QH™ Human Plasma Concentration Single Dose Summary

	150 mg	300 mg
n (subjects)	5 men; 5 women	5 men
C_{max} (µg/ml)	1.88	3.19
T_{max} (hr)	6	6
AUC (µg•hr/ml)	74.61	91.76

Table 1.

CoQH-CF™

The Next Generation of CF Technology

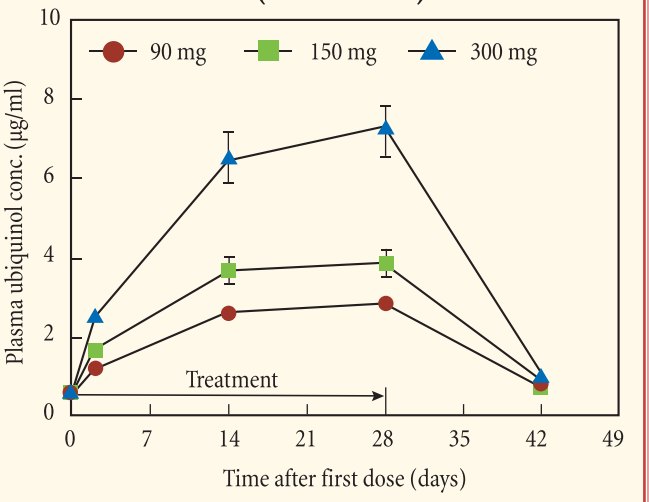
Extreme care must be taken to prevent the introduction of oxygen when manufacturing supplements containing Kaneka QH™. Soft Gel Technologies, Inc.® has developed a patent-pending formula to protect ubiquinol from being oxidized. Using Soft Gel's crystal-free (CF) technology, CoQH-CF™ was created. This unique soft gel delivery system with Kaneka QH™ allows individuals who are unable to process CoQ_{10} effectively on their own (primarily baby boomers and those with disorders of elevated oxidative stress) to increase plasma levels of CoQ_{10} in its reduced form. Ubiquinol from the supplement is readily available to enter the energy production process.

CoQH-CF™ soft gels contain a liquid inner fill of Kaneka QH™, alpha lipoic acid, d-limonene, and capric and caprylic acid. This solution protects the Kaneka QH™ material from oxidation and crystallization. Alpha lipoic acid (ALA) is a versatile antioxidant, plays a critical role in energy production and metabolism, and is universally soluble. Citrus fruits contain d-limonene, an essential oil extracted from the fruit peels. (The FDA has approved d-limonene as GRAS—generally recognized as safe—for human consumption as a synthetic flavoring substance.) The properties of d-limonene enable it to serve as a solubilizing agent for the ubiquinol, without causing significant chemical interactions or degradation. The two fatty acids, capric and caprylic acid, help dissolve the ALA. CoQH-CF™ is a completely solubilized CoQ_{10} formula that resists recrystallization and improves dissolution. Exclusively available from Soft Gel Technologies, Inc.®, CoQH-CF™ is offered in 50 and 100 mg soft gels.

A Targeted Antioxidant Solution

CoQH-CF™ soft gels with Kaneka QH™ provide a stabilized and protected form of ubiquinol. Due to the fact that ubiquinol is already in a reduced form, the body does not have to process the nutrient. This means that as soon as it is swallowed, it is ready to enter the energy production process as it is. Unlike traditional ubiquinone, the Kaneka QH™ ubiquinol does not require initial enzymatic reduction, thereby providing for the maximum utilization of CoQ_{10}. Supplementing with ubiquinol increases plasma levels of CoQ_{10} efficiently, particularly in individuals who are unable to process CoQ_{10} effectively on their own. CoQH-CF™ specifically addresses the needs of the 40+ age group and those suffering from various diseases and symptoms of lifestyle related conditions such as fatigue, stress and lack of stamina or energy. It is especially important for individuals with conditions of extreme oxidative stress, including diabetics and those with liver disease, to supplement with CoQH-CF™.

Ubiquinol is an important nutrient that should be seriously considered for optimum health, longevity, and vitality.



Study Summary:

- **Plasma ubiquinol concentration was reached to over 7 µg/ml at a dose of 300 mg/day**
- **Plasma ubiquinol concentration was increased in a dose-dependent manner**
- **Plasma ubiquinol concentration reached a plateau after two weeks**
- **Plasma ubiquinol concentration was immediately decreased when QH supplementation was stopped**

Figure 2.

References

Folkers K. Heart Failure is a dominant deficiency of coenzyme Q10 and challenges for future clinical research on CoQ_{10}. *J Mol Med* 1993;71 (suppl 8):S51-4.

Greenberg S *et al.* Co-enzyme Q_{10}: a new drug for cardiovascular disease. *J Clin Pharmacol* 1990;30:596-608.

Hosoe K *et al.* Study on safety and bioavailability of ubiquinol (Kaneka QH™) after single and 4-week multiple oral administration to healthy volunteers. *Reg Tox Pharmacol* 2007;47:19-28.

Kalen A *et al.* Age-related changes in the lipid compositions of rat and human tissues. *Lipids* 1989;24(7):579-84.

Kontush A *et al.* Plasma ubiquinol-10 as a marker for disease: is the assay worthwhile? *Biofactors* 1999;9(2-4):225-9.

Palamakula A *et al.* Preparation and In Vitro Characterization of Self-Nanoemulsified Drug Delivery Systems of Coenzyme Q_{10} Using Chiral Essential Oil Components. *Pharm Tech* 2004;Oct:74–88.

Yan J *et al.* Reduced coenzyme Q_{10} supplementation decelerates senescence in SAMP1 mice, *Exp Geront* 2006;41:130-140.

CoQH-CF™: Innovation in Nutrition Technology

- The cells of the heart, brain, muscles, liver, immune system, and gastrointestinal lining contain the greatest number of mitochondria. Mitochondria are a primary site of free radical activity.
- Free radicals have been implicated in the etiology of many chronic degenerative diseases.
- Many theories exist regarding the aging process. While scientists continue to explore and debate the theories of how people age, a leading hypothesis proclaims that aging is a product of oxidative damage inflicted by free radicals.
- Aging causes changes at the cellular level that predispose people to disease and disability.
- Coenzyme Q_{10} (CoQ_{10}) concentrations in the body decrease with age.
- Ubiquinol is the next generation of CoQ_{10} available. It is CoQ_{10} that has been metabolized, or essentially processed by the body, for use in the cellular respiration process.
- Ubiquinol is freely diffusible in the inner mitochondrial membrane, shuttling electrons between the less mobile complexes of the electron transport chain. Without ubiquinol to carry electrons through the mitochondria, cellular energy cannot be produced and life cannot be sustained.
- Since ubiquinol is highly unstable, it has been extremely difficult (until now) to make it available as a dietary supplement. Ubiquinol is highly oxidative, meaning that when exposed to air, it quickly reverts back into CoQ_{10}. Oxidation makes it very difficult to stabilize ubiquinol as an ingredient.
- Kaneka QH™ is a commercially available, patented form of ubiquinol that has all of the benefits associated with CoQ_{10} (ubiquinone), but is the more potent reduced form of CoQ_{10}.
- Patent-pending CoQH-CF™ soft gels contain Kaneka QH™ and keep the ubiquinol protected and stable from oxidation.
- Supplementation with CoQH-CF™ is an effective way to increase CoQ_{10} levels for those who cannot efficiently convert ubiquinone to ubiquinol on their own.
- The baby-boomer generation, those who are affected by chronic disease, and individuals who experience excessive oxidative stress should utilize CoQH-CF™ for their specific CoQ_{10} supplementation needs.

SOFT GEL
TECHNOLOGIES, INC.®
800.360.7484
sales@soft-gel.com
www.soft-gel.com