



LifeExtension®

LE Magazine January 2007

REPORT

Has Your CoQ10 Become Obsolete?

By William Faloon



Twenty four years ago, the Life Extension Foundation introduced coenzyme Q10 to the United States. Back then, it was sold in Japan as a prescription drug to treat heart disease. Life Extension, however, provided persuasive evidence that CoQ10 could help protect against a host of age-related disorders.

Based on a large volume of favorable research, CoQ10 has become one of today's most popular dietary supplements. In recent years, new delivery systems have been developed that transport more CoQ10 into the bloodstream than original versions.

Providing greater quantities of CoQ10 to the body is of particular importance, since scientific studies show that higher CoQ10 blood levels produce superior benefits.

In what may be the most significant breakthrough in the history of the dietary supplement industry, Japan's largest CoQ10 producer has discovered a way to deliver the highest concentrations of the most biologically active form of coenzyme Q10 to the bloodstream.

As you will read in this article, this improved form of CoQ10 not only absorbs up to eight times better, but also has demonstrated unprecedented anti-aging effects compared to placebo and compared to the coenzyme Q10 you are using now.

Unlike outrageously priced prescription drugs, this new form of CoQ10 enables consumers to obtain more activated coenzyme Q10 in their bodies at a far lower cost. Based on the findings you are about to read, this novel CoQ10 compound (ubiquinol) could revolutionize how a number of age-related disorders are both prevented and treated.

Scientists long ago discovered that orally ingesting the ubiquinone form of coenzyme Q10 produced beneficial effects on the heart,¹⁻¹⁹ brain,^{1,20-24} kidneys,²⁵⁻²⁷ and other tissues.^{1,5,28-38}

What the lay literature did not discuss was the fact that in order for the ubiquinone form of CoQ10 to be properly utilized, it first must be reduced in the body to its active metabolite known as ubiquinol. While most ubiquinone is naturally reduced to ubiquinol, the optimal way to supplement with CoQ10 would be to ingest it in its ready-to-use ubiquinol form.

Since ubiquinol is highly unstable, it has been extremely difficult (until now) to make it available as a dietary

supplement. After years of painstaking research, Japan's largest producer of coenzyme Q10 has developed a patented method to stabilize ubiquinol so that it can be swallowed in a capsule for utilization by cells throughout the body.³⁹

The ramifications of widespread use of this novel form of CoQ10 are profound. For the first time, it may be possible to achieve the sustained high blood levels of biologically active ubiquinol CoQ10 needed to delay certain manifestations of aging and its related disorders.

Sharply Higher Absorption Levels

Even with today's enhanced delivery systems, achieving optimal blood levels of CoQ10 can be challenging. Those suffering from disorders that require higher blood levels have had to consume relatively large doses of CoQ10. Ideal blood levels

for those afflicted with neurological disorders (such as Parkinson's disease) or congestive heart failure are considered to be greater than 3.5 micrograms per milliliter (mcg/mL).⁴³

When CoQ10 is ingested in its reduced form as ubiquinol, higher blood CoQ10 levels can be achieved using smaller milligram doses. In assimilation studies on rats, oral feeding of ubiquinol CoQ10 was shown to increase blood levels more than twice as high as conventional CoQ10 (ubiquinone).^{44,45} Human assimilation studies are even more impressive.

WHAT MAKES UBIQUINOL DIFFERENT FROM UBIQUINONE?

Coenzyme Q10 exists in both ubiquinol and ubiquinone forms, but they have vastly different roles to play in the body. For instance, ubiquinol 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 CoQ10 that protects against toxic oxidative reactions in the body.

The chemical difference between ubiquinone and ubiquinol is that the ubiquinol compound contains two hydroxyl groups. These two hydroxyl groups enable ubiquinol to be more "hydrophilic" than ubiquinone, and thus much easier to assimilate.

The term "hydrophilic" means readily absorbable or dissolvable in water. The two hydroxyl groups on the ubiquinol compound result in its stronger bonding with water, which helps explain why it is so much more bioavailable than ubiquinone.

Today's commercial CoQ10 supplements contain ubiquinone because it remains stable longer in the capsule.

However, it is the reduced form of CoQ10 (ubiquinol) that has the ability to scavenge free radicals in mitochondria and in cell membranes, sites where free radicals inflict significant damage. The ubiquinol form of CoQ10, with its two hydroxyl groups, is what dominates in most human tissues.⁴⁰

Called a "coenzyme" because of its unique ability to participate in chemical reactions but remain at steady-state levels in the cell, coenzyme Q10 plays a central role in energy metabolism. CoQ10's ability to cycle back and forth between ubiquinone and ubiquinol accounts for many of its unique properties. This remarkable ability to cyclically accept and donate electrons, as well as to effect complementary chemical reactions in the mitochondria, accounts for CoQ10's unparalleled value to almost all life forms.

Ubiquinol has a much greater bioavailability than the ubiquinone used in commercially available CoQ10 supplements.^{39,41,42} This is understandable, since ubiquinol has far greater water solubility and much better absorption into the bloodstream after ingestion.

As shown in Figure 1, a recent human trial showed that supplementing with just 150 mg per day of ubiquinol resulted in CoQ10 blood levels of 3.84 mcg/mL. In study subjects who took 300 mg per day of ubiquinol, blood CoQ10 levels reached 7.28 mcg/mL. This study showed that it took only four weeks to achieve these desirable high levels.⁴⁶

To put these blood levels in perspective, scientists have conducted human clinical trials using very high doses of conventional CoQ10 in enhanced delivery systems.

As shown in the chart above (Figure 1), one clinical study used 1200 mg per day of ubiquinone CoQ10 to achieve blood concentrations of 3.96 mcg/mL. Based on recently published absorption studies, just 150 mg per day of ubiquinol would provide virtually the same high CoQ10 blood levels as 1200 mg of enhanced-delivery ubiquinone CoQ10.^{46,47}

As indicated in Figure 1, another study used 2400 mg per day of conventional CoQ10 to reach blood levels of 7.25 mcg/mL. Just 300 mg per day of ubiquinol was shown to provide about the same amount (7.28 mcg/mL) of CoQ10 to the blood at four weeks.^{46,48}

A review of published studies on human subjects reveals that it requires very high doses of conventional CoQ10 to achieve the same levels attainable with modest amounts of ubiquinol CoQ10.⁴⁶⁻⁵⁰ Figure 1 clearly shows how little ubiquinol is needed to provide the same blood (plasma) levels that are achieved in response to far greater amounts of ubiquinone. This chart (Figure 1) reveals that it takes eight times more ubiquinone to increase CoQ10 blood levels to what can be achieved with much lower doses of ubiquinol.

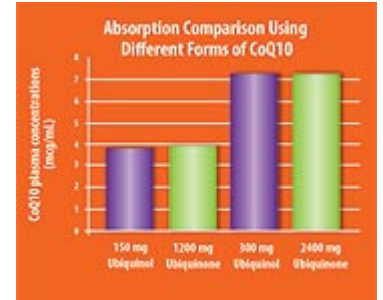


Figure 1. Human studies show that ubiquinol increases blood CoQ10 levels eight times more efficiently than ubiquinone. Note that it took 2400 mg of ubiquinone to reach CoQ10 blood levels achieved with only 300 mg of ubiquinol.

Side-by-Side Comparison of Ubiquinol and Ubiquinone

In a side-by-side single-dose human study, ubiquinol absorption was compared directly to conventional CoQ10 (ubiquinone) using the same delivery system. Subjects were given either 100 mg of ubiquinol or 100 mg of ubiquinone. To further validate the study, the subjects were crossed over, so that every participant was tested after receiving ubiquinol and later ubiquinone, and vice versa.

As shown in Figure 2 (next page), the findings showed that in aged test subjects, ubiquinol absorption was 60% greater in this single-dose side-by-side comparison.⁵¹

While single-dose oral studies have some limited value, the true picture of bioavailability occurs after people have ingested CoQ10 supplements for about four weeks. In these longer-term studies, the superior absorption of ubiquinol is most pronounced.

Ubiquinol Maintains Higher Blood Levels Longer

Animal and human studies clearly show that ubiquinol is much better absorbed than ubiquinone. What may be even more important is how long ubiquinol CoQ10 remains in the body compared to ubiquinone.

In a study of aged rats, equal amounts of ubiquinol or ubiquinone were orally administered to evaluate how long ubiquinol would remain at increased levels in the blood. The importance of this data is that it might help explain why ubiquinol exhibits superior biological effects compared to ubiquinone.



The results of this study showed that ubiquinol ingestion caused a greater than 90% increase in blood ubiquinol levels and that this elevated level persisted for the entire eight-hour duration of the study. In response to ingestion of an equal amount of ubiquinone, blood ubiquinol levels never even reached 90% of baseline.⁵²

This study also measured ubiquinol levels in micrograms per milliliter (mcg/mL) of blood. As you may recall, humans with certain disorders achieve optimal benefits when CoQ10 blood levels exceed 3.5 mcg/mL. In response to a modest amount of ubiquinol supplementation (the equivalent of 100 mg per day in humans), blood CoQ10 levels peaked at 6.0 (mcg/mL) and dropped to 4.5 after eight hours, as shown

in Figure 3 (next page). In the group receiving an equal amount of ubiquinone, peak blood levels increased to only 2.1 (mcg/mL) and declined to 1.2 eight hours later.

In this particular study, ubiquinol was present in the blood at a 3.75-fold greater concentration after eight hours compared to ubiquinone.⁵²

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Retarding the Aging Process

If all that ubiquinol did was assimilate so much better than ubiquinone, this alone would make the ubiquinol form of CoQ10 the preferred choice. What has scientists most excited, however, are the superior anti-aging effects demonstrated by the ubiquinol form of CoQ10 as compared to ubiquinone.

Aging humans suffer a precipitous decline in coenzyme Q10 synthesis that correlates with increased risks of multiple degenerative diseases.^{23,53-73} Gerontologists have long theorized that if one could maintain youthful mitochondrial energy levels, many deleterious effects of aging could be postponed. CoQ10 is a critical factor involved in healthy mitochondrial energy production.

To ascertain the age-retarding effects of ubiquinol, scientists conducted a meticulous study of senescence-accelerated mice.⁷⁴ One reason this mouse model is used is that it enables researchers to quickly identify compounds that may slow aging. Senescence-accelerated mice grow normally, but show early signs of aging, including reduced physical activity, loss of hair glossiness, coarse skin, hair loss, ocular lesions, and curvature of the spine.

In this study, the senescence-accelerated mice were divided into three groups. Starting at two months of age, the first group continued to receive standard lab chow, while the second group's lab chow was fortified with conventional (ubiquinone) CoQ10, and the third group's lab chow was fortified with ubiquinol CoQ10.⁷⁴

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. A higher grading score means that biological aging is occurring faster. At three months of age, the grading score was about 0.0 for all three groups.⁷⁴

As would be expected, the aging rate spiked sharply higher in the control group (not receiving any CoQ10) starting

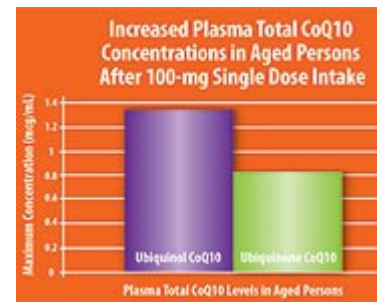


Figure 2. CoQ10 blood levels 60% higher after only one dose in humans taking ubiquinol compared to ubiquinone.

around three months of age. Mice receiving ubiquinol or ubiquinone CoQ10 showed a slower rate of aging after three months compared to the placebo group, as shown in Figure 4 (next page).⁷⁴

When middle age set in (at about nine months of age), the placebo group grading score spiked up to 10.0, whereas the grading score of the groups receiving ubiquinol or ubiquinone increased to only 5.5. This translates into a 45% slower rate of aging for mice receiving ubiquinol or ubiquinone compared to placebo.⁷⁴

So at nine months, it is clear that either form of CoQ10 (ubiquinol or ubiquinone) markedly slowed measurements of aging. At 10 months of age, however an incredible divergence was observed. As shown in Figure 4, the placebo group's grading score spiked to 12, the ubiquinone group score reached 9.9, whereas the ubiquinol group score only increased to 5.9. Therefore, at a point that translates into late middle age, mice receiving ubiquinol aged 51% slower than placebo and 40% slower than the group receiving the ubiquinone form of CoQ10.⁷⁴

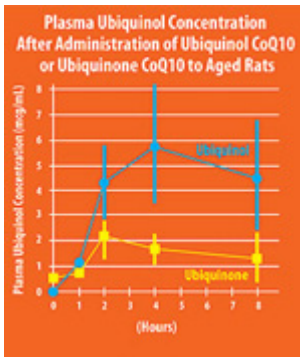


Figure 3. CoQ10 blood levels 3.75 times higher after eight hours in rats receiving ubiquinol compared to ubiquinone.

At 12 months of age, the difference in the groups was so remarkable that the researchers decided to take photos of the mice in each group. As can be seen by the photos on the next page, a mouse receiving ubiquinol appears to be perfectly healthy, whereas a mouse receiving ubiquinone has suffered noticeable degenerative changes. The mouse receiving neither form of CoQ10 looks absolutely ghastly.

As can be seen in Figure 4, at 12 months, there is relatively little difference between the placebo and ubiquinone groups in grading scores, whereas the group receiving ubiquinol shows a 22% slower rate of aging. The most startling data this chart shows, however, is that mice receiving ubiquinol dramatically slowed the rate at which age-induced degenerative changes occurred in mid-life and to a lesser degree in later life.

Video Footage of 12-Month-Old Mice

The still pictures of 12-month-old mice that received ubiquinol, ubiquinone, or the control (placebo) speak for themselves. What is even more impressive is video footage comparing the different groups of mice.

A video shows that in response to no supplemental CoQ10, the mouse is essentially immobile and unresponsive, exhibiting lesions in and around the eye, with spinal and limb deformities as well as a patchy, discolored coat. Many of these pathological events seen in mice not supplemented with CoQ10 are classic signs of degenerative aging suffered by elderly humans.

The 12-month-old mouse supplemented with ubiquinol, on the other hand, is shown to be alert, responsive, and energetic, with no physical lesions or deformities and a glossy coat resembling that of a young, healthy mouse.

Anti-Fatigue Effects of Ubiquinol in Aged Rats

A universal pathological effect inflicted by aging on living organisms is mitochondrial energy depletion that manifests outwardly as fatigue. The primary mechanism by which CoQ10 protects against age-related degeneration is helping to maintain mitochondrial energy output.³

To compare the anti-fatigue effects of the ubiquinol and ubiquinone forms of CoQ10, scientists took a group of aged rats and measured how long they could run on a treadmill. In this crossover study, the control group receiving no CoQ10 showed a slight decline in treadmill running time, whereas running times increased 60% in the group receiving ubiquinone and an astounding 150% in the group receiving the ubiquinol form of CoQ10, as shown in Figure 5 (next page).⁷⁵

Ubiquinol Levels Lower in Disease States

As humans age, there is a sharp reduction in coenzyme Q10 synthesis, with a corresponding reduction in blood ubiquinol levels. Figure 6 shows the reductions in various coenzyme Q10 tissue levels that occur with normal aging.

In examining humans suffering from various pathological conditions, blood ubiquinol levels are uniformly lower.⁵³⁻⁷³ In those with diabetes, ubiquinol levels have been shown to be 74% lower than in control subjects.⁷⁶ Ubiquinol decreases of 6.5% to 12.5% have been observed in those with hepatitis, liver cancer, and amyotrophic lateral sclerosis (Lou Gehrig's disease).^{59-61,69}

Ubiquinol's Effect on Mitochondrial Function

In healthy human blood, more than 90% of coenzyme Q10 exists in its reduced ubiquinol form. An analysis of published research indicates that ubiquinol is the form of CoQ10 that most effectively suppresses free radicals and increases mitochondrial energy output.^{54,57,77-81}

Only ubiquinol effectively scavenges lipid peroxy radicals and prevents chain-reaction-causing oxidative damage to polyunsaturated fatty acids of biological membranes. Ubiquinol forms an important first line of antioxidant defense in atherogenic lipoproteins such as low-density lipoprotein (LDL), and is capable of regenerating alpha-tocopherol vitamin E.^{54,78,79}

Supplementation with the ubiquinol form of CoQ10 not only elevates blood levels of ubiquinol, but also increases the ratio of ubiquinol to total CoQ10 concentration. For example, when ubiquinol is supplemented, the ubiquinol to total CoQ10 ratio increases to 96-98.5%, compared to approximately 80-85% when ubiquinone is supplemented. Moreover, the ratio remained unchanged during administration of ubiquinone.^{80,81}

An increase in the ratio of ubiquinol in blood, by even small percentages, may indeed have profound implications. With enzymes, a boost of as little as 3-5% can translate into powerful biological effects. Ubiquinol supplementation results in an impressive 12% increase in the ubiquinol to total CoQ10 ratio.

The term "hydrophilic" means readily absorbable or dissolvable in water. Ubiquinol is the more hydrophilic form of CoQ10, which has been shown to be more stable in lipid bilayers of the cell and therefore could be very well dispersed in the mitochondria.⁸²

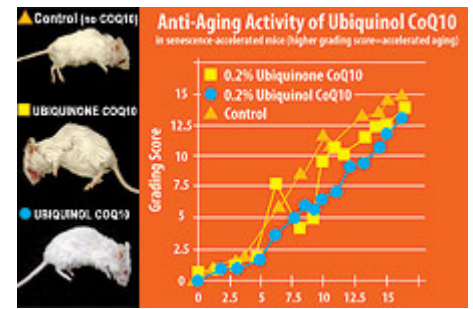


Figure 4. At 12 months of age, the mouse receiving ubiquinol (bottom) appears to be perfectly healthy. The mouse receiving ubiquinone (middle) has suffered noticeable degenerative changes. The mouse receiving neither form of CoQ10 exhibits lesions, deformities, discoloration, and other signs of degenerative aging.



Ubiquinol's greater hydrophilic properties probably enable it to be taken up better by cells, which might result in specifically targeting the mitochondria within cells.⁸³ In other words, since ubiquinol is more hydrophilic (that is, less capable of dissolving in fats), it would theoretically tend to be less retained in cell membranes, while achieving more significant intracellular concentrations.⁸⁴ This may offer a plausible mechanism whereby ubiquinol might accumulate more effectively within mitochondria than exogenous ubiquinone, thereby exerting a greater contribution to mitochondrial energy production.

Scientists are still seeking to identify the exact mechanisms by which ubiquinol so effectively enhances mitochondrial function. The ability of ubiquinol to remain at constantly higher levels in the bloodstream is one likely reason why it has demonstrated such remarkable anti-aging effects compared to ubiquinone.

What is the Optimal Human Dose of Ubiquinol?

Video Footage of 12-month-old mice. Pictures of senescence-accelerated mouse not supplemented with CoQ10 (upper frame) compared to mouse supplemented with ubiquinol CoQ10 (lower frame).

Healthy people seeking to maintain more youthful coenzyme Q10 blood levels usually supplement with around 100 mg of conventional CoQ10 (ubiquinone) daily. Based on side-by-side comparative research, if these individuals were to switch to 100 mg of ubiquinol instead, they would enjoy a significant increase of CoQ10 in the blood. This alone makes ubiquinol the logical choice.

Those seeking to replicate the incredible anti-aging findings of the study performed on senescence-accelerated mice should consider supplementing with 200-300 mg of ubiquinol a day. These higher doses have produced the most remarkable benefits of ubiquinol CoQ10 compared to ubiquinone CoQ10. In other words, at a dose of 100 mg per day, the benefit of

ubiquinol over ubiquinone is only about 1.5-fold, whereas at higher doses, bioavailability increases up to a remarkable 8-fold.

The reason for this phenomenon is that once one exceeds 100 mg using conventional ubiquinone, the linear increase in CoQ10 blood levels slows. This is probably due to absorption saturation limitations inherent to this form of CoQ10. When doses of 150-300 mg of ubiquinol are ingested, there is an exponential increase in blood CoQ10 levels. Not only is there a greater initial spike, but there is also a greater sustained level of blood CoQ10 over an eight-hour period.

Based on the totality of published research about coenzyme Q10, it would appear desirable for adults over the age of 30 to seek a minimum sustained blood level of more than 3 mcg/mL of blood. This level could be achieved by supplementing with two to three 50-mg ubiquinol capsules daily, depending on one's age, daily calorie intake, and body weight. Ideally, one would take ubiquinol in two divided doses to achieve consistent blood levels throughout the day.

Therefore, for those seeking CoQ10's classic documented benefits, supplementing with 100-150 mg a day of ubiquinol would appear to be appropriate. Those who want to emulate the successful anti-senescence mouse study should consider a dose of 200-300 mg a day of ubiquinol. Since the anti-senescence study dose was based on food intake, those who restrict their calorie intake to around one kilo (2.2 pounds) a day would need only about 200 mg of ubiquinol, while those who consumed more calories would need to take 250-300 mg of ubiquinol.

Reducing one's food intake (without inducing malnutrition) is the single best-documented anti-aging therapy.⁸⁵⁻⁹¹ In the case of ubiquinol requirements, those who eat sensibly would require less of this supplemental nutrient.

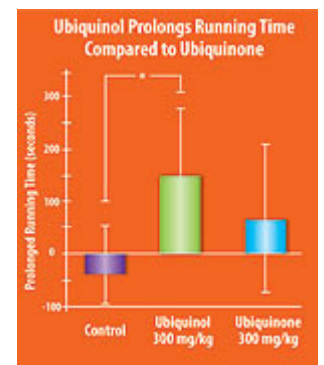


Figure 5. Prolonged treadmill running time of older rats (aged 61-63 weeks) two hours after administration of the human equivalent of 300 mg of ubiquinol compared to 300 mg of ubiquinone. Ubiquinol increased running time 2.5-fold more than ubiquinone.

Summary

The lay public recognizes CoQ10 as a nutrient that protects heart health, yet provocative research indicates that CoQ10 may have a wide range of benefits that include preventing skin cancer and skin aging,^{33,58} guarding against prostate and breast cancers,^{29,36,64,92} supporting healthy blood sugar levels in diabetics,^{4,5} and averting endothelial dysfunction.⁹³



Scientists also report additional novel uses of CoQ10, such as helping to slow the progression of Parkinson's disease,^{47,94,95} preventing crippling migraine headaches,^{96,97} supporting immune health,⁹⁸⁻¹⁰⁰ guarding against periodontal disease,^{34,38} preserving healthy vision,^{28,101} and boosting male fertility.¹⁰²

In what may be one of the most dramatic anti-aging discoveries to date, scientists have demonstrated that the ubiquinol form of CoQ10 provides anti-aging effects that are far superior to those associated with the conventional ubiquinone form used by millions of Americans each day.

Figure 6. As humans age, coenzyme Q10 levels in various tissues decline dramatically.

For the first time, ubiquinol is available as a stabilized dietary supplement that provides more activated coenzyme Q10 to the body—at a lower cost—than any other form of CoQ10.

HAS YOUR COENZYME Q10 BECOME OBSOLETE?

What You Need to Know

- Coenzyme Q10 may protect against many age-related disorders, including cancer, heart disease, diabetes, and various neurological disorders.
- Nutritional scientists have recently developed a method to deliver the highest concentrations of the biologically active (ubiquinol) form of CoQ10 into the bloodstream.
- Ubiquinol is absorbed up to eight times better than standard CoQ10 formulations, which contain only ubiquinone. Additionally, ubiquinol maintains higher CoQ10 blood levels longer than ubiquinone.
- Higher blood levels of active (ubiquinol) CoQ10 provide superior health benefits.
- Large amounts of ubiquinone must be ingested to achieve high blood levels of CoQ10. By consuming CoQ10 in its active (ubiquinol) form, one can achieve higher blood CoQ10 levels using far lower doses.
- Senescence-accelerated mice that consumed ubiquinol displayed slower rates of aging, degenerative decline, energy depletion, and physical decay compared to animals that consumed ubiquinone or placebo.
- People seeking to protect their whole-body health should consider supplementing with 100-150 mg of ubiquinol daily. Those seeking to capture the documented anti-aging benefits of ubiquinol should consider consuming 200-300 mg daily.

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