Chapter

COENZYME Q_{10} AND UBIQUINOL FOR PHYSICAL PERFORMANCE

Stefan Siebrecht[1], Darren Yak Leong Chan[2], Franklin Rosenfeld[3] and Kenneth Weicong Lin[3]

[1]Consultant for Health Ingredients, Schwelm, Germany
[2]Department of Cardiothoracic Surgery, Alfred Hospital, Melbourne, Australia
[3]Monash University, Melbourne, Australia

ABSTRACT

The effect of coenzyme Q_{10} (CoQ_{10}) supplementation on physical performance has long been a controversial subject. There have been several studies that have demonstrated a beneficial effect of CoQ_{10} on sports performance whereas many others have been neutral. It has been difficult to interpret the multiple studies due to three main factors: the formulation of CoQ_{10} administered, its dosage and duration of administration; the wide variety of subjects enrolled in the studies ranging from untrained individuals to elite athletes including weight lifters and marathon runners; the wide variety of methods of assessing physical performance including work performed, either acute performance, endurance exercise or time to exhaustion. We have reviewed 28 studies ranging over a 25 year period. We have critically analysed the results and have reviewed the possible mechanisms of action. The results showed that the studies were more likely to show a beneficial effect if: the CoQ_{10} preparation was more readily bioavailable especially if it was

administered in the reduced form (ubiquinol) rather than oxidised form (ubiquinone); was given at high dosage 300 mg per day or more, for a period of two to three to months; where the exercise performed was peak performance such as sprinting or weight lifting and where the method of assessment of performance was physical work output rather than long lasting endurance exercise. We conclude that coenzyme Q_{10} and especially ubiquinol can have a beneficial effect on physical performance provided it is given in an appropriate form, adequate dosage and time of administration and where performance is assessed using a reliable and reproducible accurate measure of work output.

Keywords: coenzyme Q_{10}, ubiquinone, ubiquinol, dietary supplements, athletes, physical performance, exercise, physical exertion, muscle strength

INTRODUCTION

Coenzyme Q_{10} (CoQ_{10}) is a fat soluble antioxidant and a vital component of the mitochondrial respiratory chain for energy production. CoQ_{10} is the only lipid-soluble antioxidant that is synthesized in human cells [1]. CoQ_{10} can exist in an oxidised form (ubiquinone) or reduced form (ubiquinol). Virtually every cell in the body contains CoQ_{10} with the highest concentration in organs that have the highest energy requirements, such as heart, liver, kidney and muscles [2, 3, 4]. The daily human requirement of CoQ_{10} is covered by a mix of biosynthesis and dietary intake of which biosynthesis is more important [5]. A lower dietary intake of CoQ_{10}, as well as a decrease of biosynthesis due to a lower intake of nutrients essential for CoQ_{10} biosynthesis, or blocking of CoQ_{10} biosynthesis by statin therapy can lead to decreased CoQ_{10} plasma and tissue levels.

PHYSIOLOGICAL FUNCTIONS OF CoQ_{10}

The body contains around 2,000 mg of CoQ_{10} mainly located in mitochondria. CoQ_{10} is essential for energy production in the mitochondria but also functions as an antioxidant in cell membranes. CoQ_{10} plays an essential role in oxidative phosphorylation via the respiratory transport chain for mitochondrial ATP production. ATP is the energy molecule for all life processes, generating 96% of the total aerobically generated energy [5, 6].

During electron transport in the respiratory chain ubiquinol and ubiquinone are continuously converted into each other. Ubiquinone and ubiquinol work as catalysts and so are actually not consumed. Nevertheless, a small part of CoQ_{10} is destroyed and lost every day. Therefore, CoQ_{10} must be synthesized by the body or taken up from the daily diet. Body organs with a high energy turnover especially heart and skeletal muscles depend on an adequate supply of CoQ_{10}. If these organs become deficient in CoQ_{10} they generate less energy and power.

CoQ_{10} AND UBIQUINOL IN SPORT NUTRITION

Influence of Exercise and Diet on Plasma Levels in Athletes

The human body contains about 2,000 mg of CoQ_{10}. The normal CoQ_{10} plasma level of healthy people lies between 0.60 – 1 mg/l. The CoQ_{10} plasma levels are easy to measure but actually not a good guide to the overall CoQ_{10} status of the body. The CoQ_{10} levels in the blood can greatly fluctuate and often differ from the level in the tissues. Even if we find a normal CoQ_{10} level in the blood there can be a decreased level in the tissues. However, the CoQ_{10} level in the blood is easy to determine and a low level in the blood is at least an indication of a possible undersupply with CoQ_{10}. A total body deficiency of CoQ_{10} can show up as a decrease in the CoQ_{10} plasma level and give an indication that the tissue levels of CoQ_{10} may be decreased.

Increased oxidative stress can lead to a reduction of CoQ_{10} plasma levels. Hence people who are exposed to increased oxidative stress have lower CoQ_{10} plasma levels than healthy people [6]. In diseases such as diabetes or heart disease, the CoQ_{10} plasma levels can fall by 60% to 70% to a value of 0.3 – 0.4 mg/l [7, 8]. The CoQ_{10} plasma level depends on many factors and may vary greatly thus it would be useful for many people and especially athletes to determine their personal CoQ_{10} plasma levels.

Regular, medium intense exercise over some weeks leads to an increase of CoQ_{10} plasma levels in healthy humans as shown in a study with 28 male leisure-time cyclists, aged between 30-50 years (39.7±6.6), with normal body mass index (23.2±1.5) and good health. Their CoQ_{10} plasma levels were around 0.79 mg/l, which is normal. After 8 weeks of training the CoQ_{10} plasma level increased to 1.14 mg/l, an increase of +44%. It was found that supplementation with CoQ_{10} increased the CoQ_{10} plasma level from 0.78 mg/l

to 2.22 mg/l and a session of acute exercise further increased CoQ_{10} in the plasma to 2.38 mg/l (measured after exercise) [10].

On the other hand, excessive physical training and meatless diets can lower CoQ_{10} plasma levels in athletes. Studies have shown that hard physical training among athletes leads to a decrease of CoQ_{10} levels in the plasma [11,12]. Also, a vegetarian or vegan diet leads to a lowering of the CoQ_{10} levels in the blood. Vegan or vegetarian living triathletes had the lowest CoQ_{10} levels of all analysed athletes [12]. Thus athletes and especially endurance athletes should measure their plasma CoQ_{10} in the blood frequently. The CoQ_{10} plasma level is dependent on many factors and can vary greatly, due to:

- Dietary composition (low fat content reduces the CoQ_{10} intake)
- Nutritional behaviour (vegetarian etc. result in lower CoQ_{10} intake with food)
- Bad nutritional status (lack of selenium, B6, inhibits CoQ_{10} biosynthesis)
- High vitamin E supplements (inhibits CoQ_{10}-intake)
- Statin therapy for hypercholesterinaemia (inhibits CoQ_{10} biosynthesis)
- Older age (lowers CoQ_{10} biosynthesis)
- Illness (higher oxidative stress increases the use of CoQ_{10})
- Sustained physical endurance and training (increases the use of CoQ_{10})

PHYSICAL PERFORMANCE AND CoQ_{10} AND UBIQUINOL SUPPLEMENTATION

CoQ_{10} has been on the market for many years and is a popular dietary supplement. It has been used in the past in sports nutrition and tested in many clinical trials in athletes. Overall twenty eight studies of CoQ_{10} supplementation in sports have been published (Table 3). Of these, 26 studies used the oxidized form of CoQ_{10} and only two more recent studies have been conducted with the reduced form ubiquinol (QH). The athletes received dosages between 30 - 300 mg CoQ_{10} or QH per day for periods of time from 10 days to 6 weeks. These studies showed no consistent results, which is not surprising due to the many very different designs of the studies. Too low dosages, an insufficient period of supplementation and often small sample sizes are some of the reasons why some studies showed no effects and created

results conflicting with other studies that showed benefits. Furthermore, one of the most important variations in these studies was the method of measuring physical performance.

POTENTIAL REASONS FOR INCONCLUSIVE STUDY RESULTS

Wrong Study Designs: General Remarks

We clearly have to state that is easier to design nutritional supplementation studies that generate no results at all than to design a study that creates positive results. There are many different parameters that determine the outcome of such studies and one or more parameters that are wrongly chosen can cause the failure of the whole study. Some of these important parameters are: the chosen participants, age, sex, physical training status; dosage of supplement; duration of the supplementation; chosen measurement parameters; compliance of the patients; performance measurement protocol; general diet and health status; chosen dosage form; bioavailability of the nutrients e.t.c., and many more. In the case that the study generates no results at all, this does not mean that the supplement is inefficient. It just means in the first line, that the design of the study was unable to show a benefit and or as another possibility, that the nutritional supplement is potentially inefficient at all. Some scientist wait before they give advice, until there are many studies published showing all consistent positive result which is almost impossible, and doesn`t happen in reality. In most cases, some studies show benefits and other studies do not. But: “No observed effects” in a study are not the opposite of “positive observed effects”! Nutritional supplements that have shown positive results in some studies, demonstrate that the ingredient has the potential to be effective under certain circumstances and that the design of the study is important to create positive results. The term “mixed results” is often used when some nutritional studies showed positive effects while others do not show any positive or negative effects. In such cases a nutritional supplement has the potential to be effective, depending on the chosen design. So in this case there is a possibility of a positive benefit for people who consume the nutritional supplement. In this case, the positive advice for trying the supplement might already be available to consumers who want to investigate the benefits of the supplement. Some of

the potential reasons that caused problems in showing clinical evidence for CoQ_{10} in sport nutrition are:

Poor Absorption of Ubiquinone

A possible explanation for the failure of many studies in the field of athletic performance and CoQ_{10} is that traditional CoQ_{10} is poorly absorbed after oral ingestion [13]. This fact requires the use of higher dosages is required for athletes to achieve the desired physiological effects. CoQ_{10} is absorbed at a constant rate of 100 mg per 6.2 hours in the gastrointestinal tract. In a study by Mohr et al single oral doses of 100 and 200 mg of CoQ_{10} supplement resulted in an increase of the total plasma CoQ_{10} levels of 80% and 150%, respectively, within 6 hours. Long term supplementation with 300 mg CoQ_{10} per day for 11 days resulted in plasma levels of the CoQ_{10}3-5 fold higher than before [14]. QH as a supplement has been newly developed (Kaneka QH,) and has shown an advantage of a greatly improved bioavailability. Hosoe et al. showed that after a single oral dose of 300mg of QH a 4.7-times increase in the QH plasma levels was achieved [15]. After regular daily administration of 300 mg QH for 28 days, a 10-fold increase in plasma levels was achieved. Such an increase of plasma QH levels is far greater after using QH, than was ever observed after supplementation with the traditional CoQ_{10}. So far QH has been used only in 2 of 29 studies in athletes.

Too Low Dosages of CoQ_{10}

In most published studies the conventional poorly absorbed CoQ_{10} was given at quite low dosages: 15 studies used 100mg or even less per day, 7 studies used dosages of 120 - 200 mg CoQ_{10} per day and 5 studies were using either 300 mg CoQ_{10} or 300 mg ubiquinol (Table 3).

In the past the maximum daily dosage of CoQ_{10} in dietary supplements in Europe and Germany was limited by regulation to 30 mg daily. Today in many countries of the EU CoQ_{10} dosages of 100-200 mg per day have been approved for dietary supplements for normal people. It is known from studies of other nutrients that athletes often require higher dosages than normal people due to a higher bodyweight and/or due to more intense training and performance. This means that we do not know yet the optimal dosage for ubiquinol for athletes. So far the maximum dosage used in athletes was 300

mg ubiquinol, whether this is already the optimal dosage or if some athletes need and benefit from higher dosages than 300 mg ubiquinol is not known yet and has to be evaluated by further studies. Especially as new studies with higher doses of CoQ_{10} and ubiquinol show better effects in athletes.

Ubiquinol is an extremely potent antioxidant and the oxygen in the air will quickly oxidise it. This was the main reason why it has not been possible to produce QH and use it in a stable form in dietary and sports supplements.

Since the Japanese company Kaneka has succeeded in establishing a process to produce QH in a stabilized form, ubiquinol is now available on the market and can be used in the new studies in athletes. The increased use of CoQ_{10} and QH in sport nutrition will depend on the number of new studies that are done with the correct dosage and will hopefully show consistent results in performance enhancement. In fact, so far all studies where athletes were given higher dosages of 300 mg CoQ_{10} or QH per day show better results on performance than lower dosages [16, 17, 18, 19] (Table 3). Incidentally, the highest plasma CoQ_{10} concentration ever reported in the literature thus far is 10.7µmol/l (=9.23 mg/l). This was achieved using CoQ_{10} in the form of QH [20]. Whether this represents a value close to a ceiling for plasma CoQ_{10} needs to be established. Furthermore, it would be important to determine whether such high plasma concentrations afford maximum therapeutic benefit [21]. The highest net increase in plasma CoQ_{10} concentration and also the highest increase per 100 mg CoQ_{10} ingested was observed using solubilized CoQ_{10} as QH at a dose of 600 mg and these values are higher than those obtained with much larger doses of CoQ_{10} (up to 3,000 mg; [20]).

Too Low CoQ_{10} Plasma Level and Too Short Duration of Supplementation

To compensate for a CoQ_{10} deficiency in the plasma and to bring levels back to normal (0.8 - 1.0 mg/l) only small amounts of CoQ_{10} are needed. On the other hand to achieve clinical effects, to enhance physical performance or to treat a systemic tissue CoQ_{10} deficiency the CoQ_{10} plasma levels must be greatly increased for a longer period of time so that the organs will have sufficient time to replenish their CoQ_{10} pools and this happens quite slowly. The target therapeutic CoQ_{10} plasma levels have been raised by experts over the last 30 years. In the 1980s the target CoQ_{10} plasma level was around 1.5 mg/l and was increased in the 1990's to 2.5 mg/l [22]. Today the recommended value of the plasma CoQ_{10} level is > 3.5mg/l or higher [22]. Studies in the past

linked the effectiveness of the CoQ_{10} supplementation principally to the CoQ_{10} plasma levels: the higher the plasma level, the better the effects. At this point the bioavailability of the CoQ_{10} became the main barrier to increasing CoQ_{10} plasma levels to a maximum value. As a response to this, great strides were made in improving the bioavailability of CoQ_{10} especially the development of the much more bioavailable QH.

BIOAVAILABILITY OF UBIQUINOL AND UBIQUINONE

CoQ_{10} is fat soluble and as a result has first of all to be emulsified in the watery medium of the intestine before being absorbed into the body. So its bioavailability depends on the CoQ_{10} formulation and the method of uptake. Fats, oils and emulsifying agents like lecithin increase the bioavailability of CoQ_{10}. CoQ10 is a crystalline powder that is insoluble in water. Absorption follows the same process as that of lipids and the uptake mechanism appears to be similar to that of vitamin E, another lipid-soluble nutrient. This means that if taking high dosages the Vitamin E (for example 1000 mg) competes versus CoQ_{10} for the absorption and this can decrease the absorption of CoQ_{10}. [72]. The absorption process in the human body involves the secretion into the small intestines of pancreatic enzymes and bile that facilitate emulsification and micelle formation that is required for the absorption of lipophilic substances [73]. Food intake (and the presence of lipids) stimulates bodily biliary excretion of bile acids and greatly enhances the absorption of CoQ10. Exogenous CoQ10 is absorbed from the small intestinal tract and is best absorbed if it is taken with a meal. Serum concentration of CoQ10 in fed condition is higher than in fasting conditions [74].

It has been clearly demonstrated that there is an almost linear relationship between the CoQ_{10} plasma level and dosage up to around 200 - 300 mg a day [23, 17] where it reaches a plateau. Humans appear to have a limited capacity to absorb CoQ_{10}. In studies with people suffering from Parkinson's disease, it was only possible to achieve a plasma level of 6 mg/l with a 2,400-3,000 mg dose [24]. Studies have shown QH is 2-4- times more bioavailable than the conventional CoQ_{10}. An oral dosage of 300 mg conventional CoQ_{10} achieves plasma CoQ_{10} levels of around 3 mg/l [25] whereas the similar plasma levels can already be achieved with 90 mg of QH [15] (Figure 1). Plasma levels of 6-8 mg/l can be achieved in humans with 300 mg QH [17] (Figure 1). With 450 – 600 mg QH, CoQ_{10} plasma levels of 6-8 mg/l can be achieved [26].

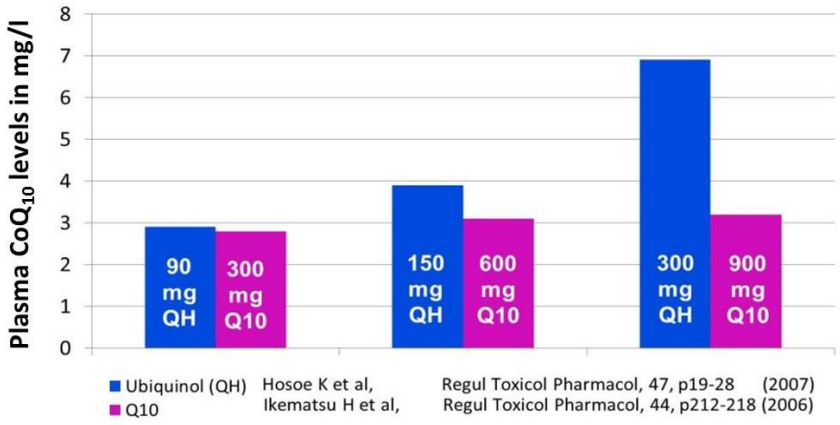

Figure 1. Comparison of human CoQ_{10} plasma levels after supplementation with ubiquinol (QH) or conventional ubiquinone (Q10).

The mechanism behind the higher bioavailability of QH versus the traditional CoQ_{10} has not yet completely determined. Most probably, it is because conventional oxidized CoQ_{10} must first react with the CoQ_{10}-reductase enzyme, where it is then reduced to ubiquinol, before it is incorporated into lipoproteins, which are then released into the blood. QH as a reduced form of CoQ_{10} is independent of this enzyme and can be immediately incorporated into the lipoproteins and therefore quickly enter the bloodstream.

CoQ_{10} Plasma Levels in Humans and Athletes

QH is the preferred form of CoQ_{10} for transport in the blood plasma: 95% of the CoQ_{10} transported in the plasma is in the reduced form. That might be another reason for the better bioavailability of QH. So when we talk about CoQ_{10} plasma levels we mostly talk about QH plasma levels. The optimal plasma level of CoQ_{10} for athletes has yet to be elucidated and many questions remain. Should athletes take CoQ_{10} supplements and what should their plasma CoQ_{10} value be? Do athletes need more CoQ_{10} due to their higher physical exertion? Is a normal, "healthy" plasma level of 1mg/l enough for athletes or should athletes aim for the highest possible value of >3.5mg/l, for example?

Although CoQ_{10} actually acts a catalyst and is theoretically always regenerated, it appears that a certain proportion of CoQ_{10} is lost during sustained exertion, for example such as sports training [11]. Trained athletes

often have lower CoQ_{10} plasma levels than untrained people [11, 12]. The most likely reason for this is that athletes appear to have a greater requirement for CoQ_{10} due to a higher CoQ_{10} consumption which is not fully covered by normal food intake and biosynthesis in the body [27]. Highly trained athletes can therefore have lower CoQ_{10} levels in tissue and blood [28] and this can limit their performance. So it is especially important for athletes to monitor their CoQ_{10} plasma level and to supplement their CoQ_{10} levels as necessary. There is as yet no recommended CoQ_{10} plasma level for athletes. But the latest studies show a link between the CoQ_{10} plasma level and performance capacity: the higher the CoQ_{10} plasma level, the higher the performance capacity [17].

A Possible CoQ_{10} deficiency in athletes can be triggered by:

- Increased consumption/losses of CoQ_{10} due to increased oxidative stress during physical exercise
- Reduced CoQ_{10} uptake due to vegetarian or vegan diet
- Limited CoQ_{10} biosynthesis due to nutrient deficiencies such as selenium, vitamin B6, magnesium etc.
- Intake of high doses of vitamin E inhibiting CoQ_{10} uptake from food and lowering CoQ_{10} plasma level
- Statin therapies limiting CoQ_{10} biosynthesis and lowering the CoQ_{10} plasma level

Dosages of CoQ_{10} and Ubiquinol for Athletes

Lowered CoQ_{10} plasma values can be normalized by supplementing with small dosages of CoQ_{10} or QH (30 -100 mg per day). In contrast, it appears that a dosage of 100 mg CoQ_{10} a day for athletes is too low to create a performance-enhancing effect. It should also be pointed out that a few earlier studies were unsuccessful because the CoQ_{10} plasma level could not be increased sufficiently despite supplementation with 100 mg CoQ_{10} per day. In an early Italian study, a dosage of 100 mg CoQ_{10} per day increased the plasma level to a value of only 1.34 mg/l [29], which is too low to achieve any effect for athletes.

In a later Italian study, it was possible to raise the CoQ_{10} plasma level to 2.23 mg/l using an improved CoQ_{10} formulation with the same dosage of 100 mg per day. After 2 months of CoQ_{10} supplements, muscles achieved greater exertion before exhaustion and overall performance improved [30]. In a dose finding study, a dose of 100 mg CoQ_{10} showed no effects, but a 300 mg

dosage of CoQ_{10} and a CoQ_{10} plasma level of 3.29 mg/l significantly increased endurance and exhaustion improved in a maximum speed test on the ergometer [16].

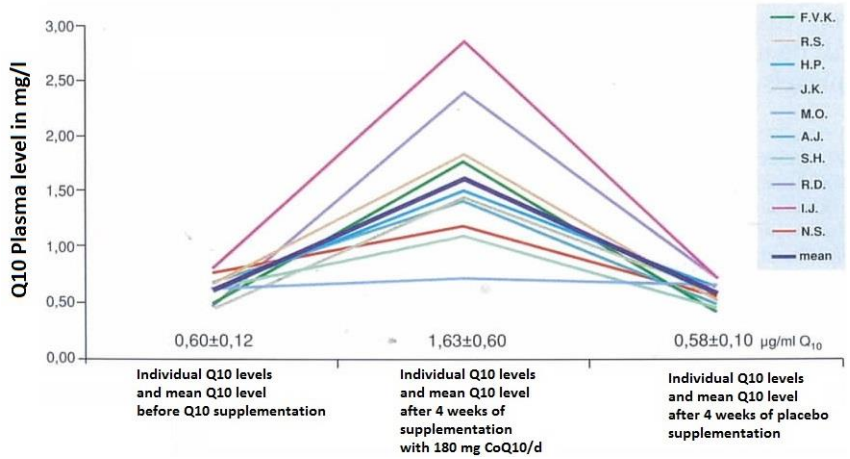

Figure 2. CoQ_{10} plasma levels in 10 Triathletes before and after supplementation with 180 mg CoQ_{10} for 4 weeks in mg/l.

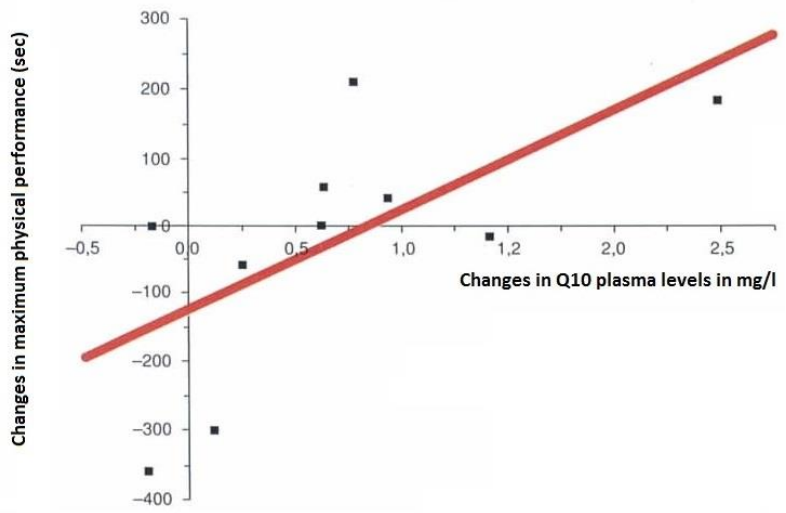

Figure 3. Correlation of the plasma CoQ_{10} level changes with the change on physical performance (sec) in 10 German professional triathletes.

Today, we must conclude that the CoQ_{10} dosages used in the earlier athlete studies were generally too low to achieve any significant positive results. Clinical studies with athletes are increasingly showing positive effects for a dosage of 300 mg CoQ_{10} or CoQ_{10} plasma levels >3.3 mg/l (Table 3). With a dosage of QH even higher CoQ_{10} plasma levels can be achieved with smaller dosages.

From previous studies we also know that athletes react extremely differently to supplementation with CoQ_{10}. In a double blind, placebo controlled, crossover study, Geiß gave 180 mg of CoQ_{10} per day for 10 days to 10 triathletes, measured plasma CoQ_{10} levels and measured physical performance as time to fatigue in a treadmill running test [12].

The major outcomes from the study from Geiß (1994) [12] were:

1. The tested triathletes had on average a lower CoQ_{10} plasma levels than normal people. The average plasma CoQ_{10} level in the beginning was 0.63 mg/l which fell to 0.58 mg/l after the placebo phase. Average CoQ_{10} plasma levels in healthy people are normally higher (around 0.83 to 1.0 mg/l): meaning that prolonged extreme endurance exercise can lead to reduced CoQ_{10} plasma levels.Among these athletes the vegetarian and vegan triathletes had the lowest CoQ_{10} plasma levels of all (around 0.4 mg/l which were 33% lower than the average of all triathletes and more than 50% below normal values: This means that a vegetarian and a vegan diet further decreases plasma CoQ_{10} levels over and above prolonged extreme endurance exercise
2. All 10 athletes reacted with very different increases in CoQ_{10} plasma levels (Figure 2). Some athletes responded very well to CoQ_{10} supplementation and achieved plasma levels of above 2.5 mg/l with the dosage of 180 mg of traditional CoQ_{10}. Other triathletes that were not included in the study had increases of CoQ_{10} levels up to 3.42 mg/l and also showed increases in physical performance. Some of the triathletes were non-responders because their plasma CoQ_{10} levels did not increase and or stayed almost at their starting values of around 0.6 - 1.0 mg/l although they had taken the same dosage of CoQ_{10}. This means: From the given dosage of CoQ_{10} and QH it is almost impossible to predict the plasma CoQ_{10} level. Thus CoQ_{10} levels should always be measured to identify the responders that are characterized by greatly increased CoQ_{10} plasma levels after CoQ_{10} or

QH supplementation and the non-responders who react with low CoQ_{10} plasma level increases.

3. The best effects on performance enhancement were found the people with the highest CoQ_{10} plasma levels and who achieved the highest increase in CoQ_{10} plasma levels.A positive correlation of plasma CoQ_{10} levels with physical performance was found (Figure 3).

These data suggest that there is a threshold increase in CoQ_{10} plasma level that must be reached to enhance performance. In the treatment of heart failure a similar threshold was found which is at least above 2.5 mg/l or maybe even higher (above 3.5mg/l) [26]. With QH supplementation plasma levels of around 6 - 8 mg/l can be reached.

Studies measuring CoQ_{10} plasma levels and performance after CoQ_{10} supplementation in athletes and healthy people:

Author	Dosage and Form of CoQ_{10}	Plasma level	Effects
Zuliani 1989[29]	100 mg traditional CoQ_{10}	1.34 mg/l	No effects
Amadio 1991[31]	100 mg traditional CoQ_{10}	1.85 mg/l	Some performance enhancement
Geiß 2004[12]	180 mg traditional CoQ_{10}	1.63 mg/l	Performance enhancement at levels >2.5mg/l
Zeppili 1991[30]	100 mg traditional CoQ_{10}*	2.23 mg/l	Some Performance enhancement
Mizuno 2008[16]	100 mg traditional CoQ_{10}	1.94 mg/l	No effects
Mizuno 2008[16]	300 mg traditional CoQ_{10}	3.29 mg/l	Performance enhancement
Kon 2008[17]	300 mg Ubiquinol (QH)	3.29 mg/l	Performance enhancement
Hosoe 2007[15]	300 mg Ubiquinol (QH)	6.80 mg/l	Not Measured
Bloomer 2012[19]	300 mg of Ubiquinol (QH)**	2.13 mg/l	Some performance enhancement
Alf 2013[18]	300 mg of Ubiquinol (QH)	Not measured	Performance enhancement

*Bioavailability enhanced CoQ_{10} formula

**found quite low CoQ_{10} plasma levels. Hosoe 2007 reached much higher CoQ_{10} plasma levels with the same ubiquinol dosage. Explanation is missing.

MEASURING PHYSICAL PERFORMANCE

Measuring human physical performance is difficult. To measure an increase in performance, it is important to establish reliable measurement parameters and also the test the configuration and range of test groups. Performance can be measured in 5 different levels:

1. Increased performance in animals (rats)
2. Increase in true performance parameters in untrained individuals or older athletes

3. Increased endurance (time to exhaustion) and reduced clinical parameters
4. Enhanced performance and recovery with intermittent exertion for athletes
5. Enhanced true performance parameters for trained athletes

Level 1. The first indications of whether a substance can have performance enhancing effect are usually obtained in animals (usually rats).

Level 2. The enhanced performance in untrained or older people is a low level indication of a substance's potential to improve physical performance. But training can have a confounding influence here and the effect of the substance must be clearly differentiated from the effect of training.

Level 3. Endurance (time to exhaustion) is easy to measure and can provide high values (10-30%) of performance Improvement. On the other hand, time to exhaustion is not a true performance parameter and values are generally higher than true performance enhancements usually by a factor of around 10 times. Time to exhaustion does give a general indication of a substance's potential to enhance performance.

Level 4. Enhanced performance for intermittent exertion is a true parameter of enhanced performance, which is based on protecting the muscles and improving recovery after exercise.

Level 5. The most difficult measurement to make but the most important is to measure enhanced performance in trained athletes as changes are in the order of only 1-3% (Alf 2013[18]). If a substance has shown positive effects in the lower test stages, this is a good indication that enhanced performance might also be found in trained athletes. But if a substance does not show any effects in the initial test levels, it can be concluded that this substance would not be effective in trained athletes.

CoQ_{10} supplements have been shown to increase physical performance parameters in a few studies:

- Level 1: In animals (rats) [32, 33]
- Level 2: In untrained athletes or older people [30, 34, 35]
- Level 3: In endurance athletes as time to exhaustion [16, 23, 36]
- Level 4: Enhanced performance in athletes for intermittent exertion [18]

But CoQ_{10} can act, above all, as an indirect tool to enhance performance. As CoQ_{10} reduces damage to cell membranes induced by exertion, recovery

time is shorter and higher exertion/performance can be achieved during further exertion.

Physical Performance with Ubiquinol and Ubiquinone Supplementation

As CoQ_{10} and QH are located in the mitochondria it would be expected that the benefits would be stronger on the aerobic type 1 (slow twitch) muscles that have a high content of mitochondria and are responsible for endurance performance rather than in anaerobic type 2 (fast twitch) muscles that are involved in sprinting and weightlifting. However, so far studies especially using high dosages of QH supplementation have shown benefits in maximum power output, maximum workload or maximum velocity, which is probably mostly due to type-2 muscles that have far fewer mitochondria, and therefore should be less dependent on CoQ_{10} because the muscles produce energy via anaerobic metabolism [10, 18, 19, 35]. Thus it is a surprise that CoQ_{10} supplementation shows benefits more in the Type-II muscle performance than in the aerobic Type-I muscle performance. The mechanism for the effects of CoQ_{10} on Type II muscles is still unknown and speculative.

On the other hand if CoQ_{10} should work in the aerobic type 1 muscle it is obvious that the concentration of CoQ_{10} within the mitochondria should be higher so as to cause an increased and prolonged production of ATP preferably from fatty acids via the ß-oxidation which could then lead to an enhancement of aerobic endurance performance. In one study, muscular exhaustion was reached at significantly higher workloads after CoQ_{10} treatment of 28 male cyclists with 100 mg CoQ_{10} for 8 weeks. There was a statistically significant difference of +4% between the, CoQ_{10} treatment and the placebo group (These results could not be explained by a placebo effect, because in the placebo group, there was no difference in maximal workload before and after treatment [10]. These data are also confirmed by other studies [30, 34, 37].

Potential Mechanisms of Action for Ubiquinol and Ubiquinone in Athletes

There are several potential mechanisms as to how ubiquinol and ubiquinone could work in athletes to improve physical performance.

Increase of Creatine Phosphate Production

The administration of 100 mg of CoQ_{10} over a period of six months significantly increased creatine phosphate production after exercise in post-polio patients [38]. Whether this could be a potential mechanism in healthy athletes is not yet known.

Increasing Muscle Content of CoQ_{10}

CoQ_{10} and QH work in the mitochondria of muscles.Type-1 muscle fibers work mainly aerobically and therefore have many mitochondria in their cells. In mitochondria, CoQ_{10}/QH contributes to the electron transport of the respiratory chain, which facilitates the production of ATP in muscle. Now the question arises, can an increase of the CoQ_{10}/QH content in the type 1 muscle fibers increase the ATP production in the muscle, and thus lead to an increase in the physical performance of the muscle. This would be the case if CoQ_{10}/QH production were involved at the rate limiting step of the respiratory chain for ATP production. The question is whether it is possible to increase the CoQ_{10} levels in the muscles through oral supplementation with CoQ_{10} and if the CoQ_{10} that reaches the muscle is in fact really entering the mitochondrial membrane and if this results in activation and an increase in the mitochondrial metabolism and consequently ATP production. The uptake of CoQ_{10} into the mitochondrial membrane is very strictly regulated and some scientists have doubts that the mitochondrial CoQ_{10} can be increased by supplementation in humans.

However, in animal models it was shown that chronic ingestion of relatively large doses of CoQ_{10} in the diet was able to increase the CoQ_{10} concentrations especially in the mitochondrial fractions of heart and brain in rodent models. This indicates that the dosage and the duration of oral CoQ_{10} administration are important key factors that influence the uptake by the mitochondria in heart and the brain and possibly also muscle and other tissue mitochondria [69, 70].

Lenaz has already claimed in 1987 that CoQ_{10} saturation of the mitochondria is not reached under normal conditions and that slight changes in the mitochondrial Q10/QH content cause greater changes in mitochondrial energy production [39] (Figure 4). This would indicate that there is still a capacity for the mitochondria to absorb more CoQ_{10} and to therefore increase its metabolism.

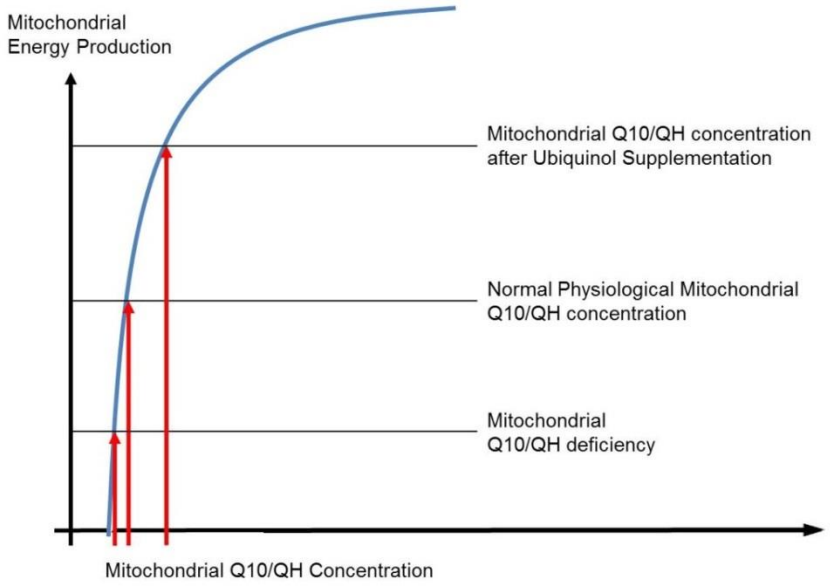

Figure 4. Mitochondrial energy production as function of their CoQ_{10}/ubiquinol content (schematic) (Lenaz 1991).

Kon showed that the CoQ_{10} content increased in the aerobic working type 1 (slow-twitch) muscles in rats after oral administration with CoQ_{10} [40]. Another effect was the reduction of the exercise-induced increase of the muscle enzyme creatine kinase (CK) in the plasma thus CoQ_{10} promotes better function and protection of cell membranes, and also causes a reduction in stress-induced muscle damage. This study showed that the CoQ_{10} levels in the type 1 (slow twitch) muscles can be increased by CoQ_{10} supplementation at least in animal models. Similar evidence that the CoQ_{10} content in healthy young human muscles can be increased by CoQ_{10} or QH supplementation is still missing. However, in humans Rosenfeldt et al. showed that the CoQ_{10} content in the heart muscle of cardiac surgery patients could be elevated by CoQ_{10} supplementation and that this resulted in increased efficiency of ATP production [41]. Whether a similar effect in the muscles of healthy athletes occurs has not yet been shown.

One study in humans a dosage of 120 mg CoQ_{10} given to athletes for 20 days was unable to increase the muscle CoQ_{10} content [42]. To increase the human muscle CoQ_{10} content it seems to be necessary to maintain the plasma CoQ_{10} levels as high as possible over a longer period of time, so that the

muscle tissues have sufficient time to absorb the CoQ_{10} from the plasma. Higher dosages of 200 - 300 mg CoQ_{10} per a day or preferably the better bioavailable QH should be taken for a longer period of at least 4-12 weeks or maybe even longer to increase muscle CoQ_{10} content. Whether it is possible to increase the muscular CoQ_{10} content significantly by such CoQ_{10} or QH supplementation and if this has any impact on physical performance is not yet known and must be established by clinical trials.

In athletes, Cooke showed in 2008 that after 14 days of administration of 200 mg CoQ_{10} levels in muscle tended to increase. On the other hand an acute CoQ_{10} dose increased muscular CoQ_{10} from 1.2µg/mg to 1.6µg/mg where the placebo group showed a decrease in the muscular CoQ_{10} content, from 1.6µg/mg to 1.5µg/mg [23]. This could mean that acute exercise triggers the uptake of CoQ_{10} into the muscle maybe due to an increased uptake of fats and lipoproteins that also transport CoQ_{10}. After exercise the muscular CoQ_{10} level decreased again.

This could be an argument for a supplementation of QH and CoQ_{10} to raise the QH plasma level as high as possible before the exercise to enable the body to absorb more QH into the muscle. To raise the total muscle CoQ_{10} content it seems that doses of CoQ_{10} higher than 200 mg per day or for a longer period than 14 days are necessary.

Changing of Muscle Composition

Clinical trials have shown an effect of CoQ_{10} administration on skeletal muscles (vastus lateralis part of quadriceps) of aged individuals [43]. After supplementation of 300mg CoQ_{10} per day for four weeks prior to hip replacement surgery, muscle samples were analysed for changes in gene and protein expression and muscle fiber type composition. In the CoQ_{10}-treated subjects, 47 genes were up-regulated and 68 down-regulated in comparison with placebo-treated subjects. The expression of 174 proteins was induced by CoQ_{10} while 77 proteins were repressed by CoQ_{10} supplementation. Muscle fibers types were also affected by CoQ_{10} treatment; CoQ_{10}-treated individual showed a lower proportion of type I (slow twitch) fibers and a higher proportion of type IIb (fast twitch) fibers, compared to age-matched placebo-treated subjects [43]. Type II fast twitch muscles are important for strength development. Elderly people especially lose Type II muscles during aging, and hence could profit from CoQ_{10} supplementation.

Such an effect of CoQ_{10} and QH would also be interesting for strength development in athletes such as weight lifters to accelerate muscle remodelling towards a greater increase in muscle strength. It seems that CoQ_{10} and QH stimulate the creation of fast twitch Type-2 muscle fibers which are needed for fast developing muscle force and muscle strength. That would at least explain why CoQ_{10} and QH supplementation has been shown to be effective in disciplines such as maximum power output and strength (Type-2 muscle fiber action) and not in endurance performance (Type-1 muscle fiber action).

Changing of Gene Expression by Ubiquinone and Ubiquinol Supplementation

CoQ_{10} and QH supplementation have been shown to change the expression of some genes that could be of great importance for athletes:

Up-Regulation

- Glutamate receptor protein GluR5, which has a function in neuronal transmission and synapse development [44]
- Guanylyl cyclase, which is the receptor for nitric oxide signalling [45] and which is redox sensitive [46]
- Fibroblast growth factor receptor N-SAM is essential for muscle growth and development
- Activation of Lipolysis
- A number of protein kinases that are involved in cell cycle control and cell signalling

Down-regulation

- TTF-1 interacting peptide 20, which is important in transcription termination
- TR3 orphan receptor, which is a steroid hormone receptor involved in apoptosis(Uemura 1998[47], Li 2000[48])
- Gene regulator hZFH helicase [49] is the major group Rhinovirus receptor, which is an adhesion molecule essential for cold virus infection [50]

Other Potential Positive Effects of CoQ_{10} and Ubiquinol Supplementation for Athletes

Stabilizing Red Blood Cells

CoQ_{10} is also important in the red blood cell membranes. CoQ_{10} supplementation can increase the CoQ_{10} content in red blood cells and make the membrane more flexible and more resistant to oxidative stress [51].

This is important for athletes because the red blood cells are important for the oxygen transport and a functioning membrane is needed for optimal transfer of oxygen.

Increasing Blood Flow to the Working Muscles

It is known that CoQ_{10} supplementation improves endothelial function and increases blood flow [8].

If similar mechanisms occur in athletes during exercise then an increased blood flow to the working muscle would be beneficial to support aerobic metabolism, to decrease formation of reactive oxygen radicals, decrease formation of lactate and could reduce exercise-induced muscle damage.

Increasing Immune Function

CoQ_{10} has shown in animals and cells in vitro to enhance the activity of immune cells and the cellular response to vaccines. An increased immune function would be beneficial for athletes to reduce “open window” upper respiratory tract infections) of athletes that often happen after strenuous exercise

Antioxidant Action

High level physical activity increases production of oxygen free radicals especially in untrained individuals [52]. High levels of oxygen free radicals can impair cellular function [53]. Thus by building up antioxidant levels CoQ_{10} could decrease the exercise-induced oxidative stress and thus improve performance.

UBIQUINOL AND UBIQUINONE DOSAGES FOR ATHLETES

In studies to date similar dosages have been used in athletes as in non-athletes. QH and CoQ_{10} are metabolically active ingredients that work especially in the muscles and other tissues but little is known yet about the actual need and demand for ubiquinol and ubiquinone in highly trained intensive performing athletes. The same dosage of QH taken orally by athletes with different bodyweights, leads to a different uptakes of QH per kg body weight. So the CoQ_{10}/QH dosage should be adapted to the body weight or the weight of the muscles in the subject.

Table 1. Ubiquinol/Q10 dosage of 100 mg as function of bodyweight

Body weight	Ubiquinol /Q10 dosage in mg per day	Ubiquinol/Q10 dosage in mg/kg bodyweight
70 kg	100 mg	1,43
80 kg	100 mg	1,25
90 kg	100 mg	1,11
100 kg	100 mg	1,00
110 kg	100 mg	0,91
120 kg	100 mg	0,83
150 kg	100 mg	0,67

Dosages of 300 mg QH have shown to enhance physical performance in German Olympic athletes [18]. These athletes were lean with a body weight between 70-80 kg and they took 300 mg QH per day, which is around 4 mg per kg body weight. The same dosage consumed by a heavy strength athlete of 150 kg body weight would result in a dosage of only 2 mg per kg body weight (see Table 1).

To achieve a constant and comparable QH dosage in all athletes with different bodyweights of for example 4 mg QH per kg bodyweight a heavy strength athlete with a weight of 150 kg would have to take 600 mg of QH. In the future we expect that the optimal dosage for CoQ_{10} and QH supplementation in athletes should be around the area of 4 - 6 mg CoQ_{10} or QH per kg bodyweight which means that the supplemented QH dosages should be adjusted by body weight (see Table 2).

Table 2. Different ubiquinol/Q10 dosages as function of bodyweight

Body weight	Ubiquinol/Q10 dosage in mg per day	Ubiquinol dosage in mg/kg bodyweight
70 kg	300 mg	4,30
80 kg	300 mg	3,75
90 kg	450 mg	5,00
100 kg	600 mg	6,00
110 kg	600 mg	5,46
120 kg	800 mg	6,67
150 kg	900 mg	6,00

CONCLUSION

Overall we conclude that for athletes the CoQ_{10} dosages used in earlier studies were simply too low to achieve consistently positive results. Clinical studies on athletes show increasingly positive effects at a dosage of 300 mg of CoQ_{10} and QH. It seems that there is a correlation between the CoQ_{10} plasma levels > 3.3 mg/l and physical performance.

By QH, adequate plasma levels can be achieved with lower dosages than with the CoQ_{10}. In contrast, by using higher dosages of QH much higher plasma CoQ_{10} levels can be achieved that are relevant for athletes in several ways: to increase the muscular CoQ_{10} content and to induce performance enhancing effects. Performance enhancing effects a have been shown after supplementation of higher dosages of CoQ_{10} and or QH of 300 mg per day over 4-6 weeks.

In the future the individual CoQ_{10} plasma levels should be measured and individual dosages of 4-6 mg CoQ_{10}/QH per kg bodyweight should be used by athletes to achieve CoQ_{10} plasma levels higher than 2.5 mg/l (better higher than 3.3 mg/l) for optimal performance.

Table 3. Studies of CoQ_{10} and ubiquinol (QH) supplementation in physical exercise

	Author Year	Year	Subjects	Q10/Ubiquinol (QH) Dosage	Protocol	Performance Benefits	Summary
1.	Alf et al. (2012) [18]	2012	100 male and female young top trained, German Olympic athletes, Double blind placebo controlled study	300 mg QH / day 6 weeks	Cycling to maximum power output till they reached the 4 mmol lactate threshold	Yes	Maximum Power Output (+2,5%)⇑ (+11% QH Group vs +8,5% Placebo)
2.	Amadio et al. (1991) [31]	1991	10 Male professional basketball players (5 Verum, 5 control)	100 mg Q10 / day 40 days	Astrand-Rhyming test used for the indirect calculation of the V02max	Yes	VO2 max (+18%)⇑ Plasma Q10 (0,85 to 1,85 mg/l) ⇑ Cardiac performance parameters⇑
3.	Bloomer et al (2012) [19]	2012	15 trained man and women (10 men and 5 women; 30–65 years	300 mg QH / day 4 weeks	Graded exercise treadmill test and a repeated cycle sprint test were performed (separated by 48 hours)	Trend	Trend to increased maximum work load (P=0,06009), moderate to strong correlation with higher Q10 Plasma levels
4.	Bonetti et al. (2000) [10]	2000	28 Male cyclists, single blind, placebo controlled	100 mg Q10 / day 8 weeks	Cycling Incremental test with increase of 50 W/minutes until exhaustion	Yes, in some parameters	Plasma Q10 levels⇑ Aerobic power⇔ Maximum Workload (+4%, significant)⇑ Improved tolerance of higher workloads

Table 3. (Continued)

	Author Year	Year	Subjects	Q10/Ubiquinol (QH) Dosage	Protocol	Performance Benefits	Summary
5.	Braun et al. (1991)54	1991*	10 male cyclists Parallel group design	100 mg Q10 / day 8 weeks	Cycling Incremental test to exhaustion	No	Oxygen Consumption (+4%, NS) Performance increased equally in both groups from pre- to post-supplementation. Q10 had no effect on cycling performance or any measured parameters. Malondialdehyde concentrations reduced in both groups after training.
6.	Cerioli et al. (1991)55	1991	13 Male young healthy untrained	100 mg Q10 / day 30 days	Ergometer bicycle test for 60 min at 50% VO2Max and followed by increases of 25 watts every 2 minutes till exhaustion	Yes	Blood free fatty acid concentration⇓ Fat metabolism (Conclusion)⇑ Aerobic exercise capacity (Concl.)⇑
7.	Cooke et al. (2008)23	2008	22 trained and untrained athletes	200 mg Q10 / day 14 days	Isokinetic knee extension endurance test, a 30-second Wingate anaerobic capacity test, and a maximal cardiopulmonary graded exercise test interspersed with 30-minutes of recovery	Yes (Trend)	Muscle CoQ10 concentration⇑ Serum SOD oxidative stress⇓ Plasma CoQ10 concentrations⇑ Time to exhaustion (tendency)⇑

	Author Year	Year	Subjects	Q10/Ubiquinol (QH) Dosage	Protocol	Performance Benefits	Summary
8.	Fiorella et al. (1991) [36]	1991	11 Highly trained runners	100 mg Q10 / day 40 days	Running test	Yes	Longer distance (+12,9%)⇑ Time to exhaustion (+7,9%) ⇑ Exercise capacity (+13%)⇑
9.	Geiß et al. (2004) [12]	1994	10 trained endurance athletes Placebo controlled double blind study	180 mg Q10 / per day 4 weeks	30 min cycling (submaximal) 50 levels increasing power to maximum power output	Yes	Increase in Blood Q10 ⇑
10	Gökbel et al. (2010) [35]	2010	15 healthy sedentary men	100 mg Q10 / day 8 weeks	Five Wingate tests with 75g/kg body weight load with 2-minute intervals between tests 3 times at baseline, after Q10, or placebo supplementation	Yes	Mean Power output ⇑ Fatigue index⇓
11	Guerra et al. (1987) [56]	1987	Professional Cyclists				Cyclists had decreased plasma levels of Q10 after several races and at the end of the cycling season
12	Kaikkonen et al. (1998) [57]	1998	37 moderately trained marathon runners	90 mg Q10 / day / 3 weeks (+13.5 mg Vit E)	Marathon run	Not measured	No Change in Plasma Q10 Levels!!! No Change in Plasma of any other parameter!

Table 3. (Continued)

	Author Year	Year	Subjects	Q10/Ubiquinol (QH) Dosage	Protocol	Performance Benefits	Summary
13	Kon et al. (2008) [17]	2008	18 Male professional Kendo athletes	300 mg Q10 / day 20 days	Practicing Kendo for 5,5 h per d for 6 d	Yes	Plasma Creatin Phosphinase release ⇓ Plasma Myoglobin Release ⇓ CoQ10 may prevent muscle damage during sustained exercise.
14	Laaksonen et al. (1995) [58]	1995*	11 young and 8 older trained males Crossover design	120 mg Q10 / day 6 weeks	Cycling Prolonged endurance test to exhaustion	No—in fact, performance impairment	No change in muscle coenzyme Q10 concentrations or plasma malondialdehyde as a result of coenzyme Q10 supplementation. Negative effect on time to exhaustion (placebo had greater endurance, -6%).
15	Leelarungrayub (2010) [59]	2010	16 young swimmers (7 males and 9 females, 15.13±0.96 years)	300 mg Q10 / day 12 days	Exhaustive exercise time was evaluated before (days 1 and 9) and after-supplementation (day 22) on a mechanical treadmill using a modified Bruce protocol. Swimming speeds for 100 and 800 meters were recorded	Yes	Plasma CoQ10 (2.34±0.78 mg/l) ⇑ Erythrocyte GSH increased ($p<0.05$)⇑ Maximal treadmill time ($p<0.05$) ⇑ 100m swimming time decreased ($p<0.05$) ⇓ 800m swimming times ($p>0.05$). ⇔

	Author Year	Year	Subjects	Q10/Ubiquinol (QH) Dosage	Protocol	Performance Benefits	Summary
16	Malm et al. (1996) [60]	1996*	15 active males Parallel group design	120 mg Q10 / day 20 days Days 2–10: usual activity Days 11–15: 2/d anaerobic training Days 16–20: recovery	Cycling Days 1, 11, 15 and 20 30-second Wingate cycle + 5-minute recovery + 10 × 10-second sprints	No—in fact, impairment	Placebo group improved anaerobic work capacity at day 15 or 20—training effect. However, Q10 group did achieve this training effect. CK levels maintained during placebo trial but were increased at various time points in Q10 group.
17	Malm et al. (1997) [61]	1997*	18 males Parallel group design	120 mg Q10 / day 22 days Days 2–9: usual activity Days 11–14: 2/d anaerobic training Days 15–22: recovery	Cycling anaerobic test (days 1, 11, 15 and 20) 30-second Wingate cycle + 5-minute recovery + 10 × 10-second sprints Aerobic test (pre-trial and day 18) Cycling VO2 max Aerobic test (pre-trial and day 22) Running VO2 max	No—in fact, impairment No No	Placebo and Q10 group both improved performance of repeated sprint test after training, however, only placebo group maintained this improvement during recovery to day 20. Placebo group achieved higher average power, and greater improvement in latter intervals during anaerobic training sessions. No change in VO2 max outcomes in either group over time or in oxygen use during submaximal cycling.

Table 3. (Continued)

18	Author Year	Year	Subjects	Q10/Ubiquinol (QH) Dosage	Protocol	Performance Benefits	Summary
19	Mizuno et al. (2008) [16]	2008	17 healthy volunteers, double-blinded, placebo-controlled, three crossover design	100mg Q10 / day 300mg Q10 / day 8 days	Workload trials on a bicycle ergometer at fixed workloads twice for 2 h and then rested for 4 h. During the physical tasks, subjects performed non-workload trials with maximum velocity for 10 s at 30 min (30-rnin trial) after the start of physical tasks and 30 min before the end of the tasks (210-rnin trial).	Yes	Maximum velocity ⇑ Subjective fatigue sensation ⇓ (both effects only in the 300 mg group)
20	Nielsen et al. (1999) [62]	1999*	7 well-trained male triathletes Crossover design	100 mg Q10 / day 6 weeks (+ vitamin E + vitamin C)	Cycling Incremental VO2 max test to exhaustion	No	No effect on maximal oxygen uptake or muscle energy metabolism (determined by nuclear magnetic resonance spectroscopy).
21	Porter et al. (1995) [63]	1995	15 middle-aged men (44,7 y) (44.7 + 2.0 years) Placebo controlled	150 mg Q10 / day 2 months	Cycling Ergometer test		blood levels of CoQ10 ⇑ subjective perceived level of vigor ⇑ Lactate release (Tendency) ⇓ Aerobic capacity ⇔ firearm exercise metabolism ⇔

	Author Year	Year	Subjects	Q10/Ubiquinol (QH) Dosage	Protocol	Performance Benefits	Summary
22	Snider et al. (1992) [64]	1992*	11 highly trained triathletes Crossover design	100 mg Q10 / day 4 weeks + vitamin E, inosine, Cytochrome C	Cycling and running 90 minutes on treadmill at 70% VO2 max + cycling at 70% VO2 max to exhaustion	No	Time to exhaustion (+4%, P=0,57) No differences in blood metabolites or RPE. High dose Vitamin E blocks absorption of Q10!
23	Vanfraechem et al. (1981) [37]	1981	6 inactive young men	60 mg Q10 / day 4 to 8 weeks	Maximal aerobic test on an electromagnetic bicycle ergometer (Löde)	Yes	Exercise performance ⇑
24	Weston et al. (1997) [65]	1997*	18 trained male cyclists and triathletes Parallel group design	1 mg/kg Q10 / day for 28 days	Cycling Incremental test to exhaustion	No	Test undertaken pre- and post 28 days of training; coenzyme Q10 did not enhance performance compared with placebo group.
25	Wyss et al. (1990) [11]	1990	18 healthy young untrained male athletes double-blinded placebo-controlled crossover study	100 mg Q10 / day 30 days	strenuous exercise test with increasing work load, tests to measure vo2max of each athlete	Yes	Total oxygen uptake after maximum intensity exercise (+9%) ⇑ Oxygen equivalence of lactic acid⇑ Total oxygen metabolism ⇑ Maximum oxygen uptake ⇑ Maximum work capacity (+33%) ⇑ Total work volume ⇑

Table 3. (Continued)

	Author Year	Year	Subjects	Q10/Ubiquinol (QH) Dosage	Protocol	Performance Benefits	Summary
26	Yamabe et al. (1991) [34]	1991	Subjects with decreased work ability absent from disease Middle aged housekeepers with sedentary lives	90 mg Q10 / day 6 months	Treadmill exercise test. 1 min incremental Test which was appropriate to detect the anaerobic threshold. Subjects underwent the symptomatic maximal load	Yes	Physical ability ⇑ Exercise aerobic function⇑ Increase in exercise time⇑ Peak VO2 ⇑ Anaerobic threshold ⇑ Severity of symptoms of physical inability ⇓
27	Ylikoski et al. (1997) [66]	1997	25 Finnish top-level cross-country skiers double-blind cross-over study Parallel Group design	90 mg Q10 / day 6 weeks	Cross-country skiing Treadmill pole-walking to exhaustion	Yes	VO2Max (+3%)⇑ Exercise capacity (+5%)⇑ Improved performance and recovery time in 94% Q10 period vs 33% in placebo period. Improved VO2 max with coenzyme Q10 supplementation. Increase in aerobic and anaerobic thresholds. No control of exercise during supplementation periods.

28	Author Year	Year	Subjects	Q10/Ubiquinol (QH) Dosage	Protocol	Performance Benefits	Summary
29	Zeppili et al. (1991) [30]	1991	9 Volleyball athletes and inactive adults	100 mg Q10 / day 30 days	Maximal graded supine bicycle exercise test (30 watt increase every 4 min)	Yes	Total work capacity (+10%)⇑ Maximum oxygen uptake (+11%)⇑ Plasma Q10 concentration⇑
30	Zhou et al (2005) [67]	2005	6 healthy volunteers Single blind study	mg Q10 / day 4 x 2-week phases, Placebo run-in CoQ10 (150 mg/d) CoQ10 (150 mg/d) + Vit E (1,000 IU) Placebo wash-out	Three-stage cycle economy test (4 minutes at each of 50, 100, and 150 watts), followed by a VO2max test (25 watts increment every minute till exhaustion), were performed prior to the supplementation and at the end of each phase. (Comment: High dose Vitamin E blocks the absorption of Q10!)	No, Yes, in some subjective parameters	Plasma CoQ10 ($P<0.05$)⇑ Muscle CoQ10 concentration⇔ VO2max ventilatory threshold⇔ Exercise economy⇔ Oxygen deficit⇔
31	Zuliani et al. (1989) [29]	1989	12 healthy untrained subjects	100 mg Q10 / day 28 days	Exhaustive cycling exercise test		Free Fatty Acid levels⇓

*Adapted from a table of chapter 16. Supplements and sports foods, Burke and Deakin (eds). Clinical Sports Nutrition, 4th ED, McGraw Hill, Sydney 2010 (Version December 2011) [68].

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