Effect of Q10 Supplementation on Tissue Q10 Levels and Adenine Nucleotide Catabolism During High-Intensity Exercise

Michael Svensson, Christer Malm, Michail Tonkonogi, Björn Ekblom, Bertil Sjödin, and Kent Sahlin

The aim of the present study was to investigate the concentration of ubiquinone-10 (Q10), at rest, in human skeletal muscle and blood plasma before and after a period of high-intensity training with or without Q10 supplementation. Another aim was to explore whether adenine nucleotide catabolism, lipid peroxidation, and mitochondrial function were affected by Q10 treatment. Seventeen young healthy men were assigned to either a control (placebo) or a Q10-supplementation (120 mg/day) group. Q10 supplementation resulted in a significantly higher plasma Q10/total cholesterol level on Days 11 and 20 compared with Day 1. There was no significant change in the concentration of Q10 in skeletal muscle or in isolated skeletal muscle mitochondria in either group. Plasma hypoxanthine and uric acid concentrations increased markedly after each exercise test session in both groups. After the training period, the postexercise increase in plasma hypoxanthine was markedly reduced in both groups, but the response was partially reversed after the recovery period. It was concluded that Q10 supplementation increases the concentration of Q10 in plasma but not in skeletal muscle.

Key Words: ubiquinone-10, reactive oxygen species, antioxidants, training, mitochondria, skeletal muscle

Ubiquinone-10, also known as ubidecarenone, coenzyme Q10, or Q10, is a polyisoprenoid benzoquinone product of the mevalonate pathway (11). Q10 is available in animal products and is present at relatively low levels in vegetables (24). Since the discovery of ubiquinone as a component of the inner mitochondrial membrane, there has been growing interest in the antioxidant function of ubiquinone in its reduced form (ubiquinol). Coenzyme Q10 provides a “mobile link” between the nicotinamide adenine dinucleotide (NADH)-Q dehydrogenase, succinate-Q dehydrogenase, and cytochrome-b-c1 reductase complex of the electron transport chain. The functions of ubiquinone in nonmitochondrial fractions of the cell are less clear, but a growing body of evidence suggests that ubiquinol is an important ubiquitous

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antioxidant (11, 12, 40, 44, 45). It has also been proposed that coenzyme Q10 has a role in controlling plasma membrane tyrosine kinase and signal transduction (9). In addition, Q10 has been implicated in both the mitochondrial antioxidative defense (12, 38, 40) and in the production of reactive oxygen species (ROS) by mitochondria (6, 7, 43). It has been suggested that various diseases such as congestive heart failure and some neuromuscular disorders are associated with tissue ubiquinone deficiency (13, 15, 29). Furthermore, it has been shown that patients with ischemic heart disease have lower plasma Q10 and higher plasma low-density lipoprotein (LDL) levels than control subjects (16). There have been speculations that strenuous endurance exercise could reduce Q10 in tissue, as a consequence of increased peripheral antioxidant turnover (26), due to elevated formation of ROS (25). To our knowledge, no one has studied skeletal muscle and isolated skeletal mitochondria Q10 concentrations in healthy humans during physical training.

High-intensity intermittent exercise, according to the present protocol, is characterized by extended catabolism of skeletal muscle adenosine triphosphate (ATP) with subsequent elevated plasma hypoxanthine (HX) and uric acid (UA) (20). This model may increase the generation of ROS, through mitochondrial respiration (34) and/or by xanthine dehydrogenase/oxidase-catalyzed reduction of molecular oxygen (30, 39). Increased generation of ROS may damage mitochondrial lipids, including Q10, and proteins (14). Consequently, oxidative stress on the mitochondrial membrane could decrease the mitochondrial Q10 content and subsequently impair oxidative phosphorylation.

The present report is part of a large study investigating the effect of Q10 supplementation on training response, plasma creatine kinase levels, and biochemical parameters. The training response and creatine kinase levels have been reported elsewhere (35, 36). The present paper includes data on Q10 distribution between tissues as well as the effects of Q10 and training on biochemical parameters such as plasma markers of adenine nucleotide degradation and mitochondrial function. There is no overlap between these papers, and the present results have not been reported previously.

The present study had four aims. The first was to assess whether Q10 concentrations in plasma, skeletal muscle, and isolated mitochondria, at rest, changed following short periods of Q10 supplementation and either ordinary living or high-intensity training. The second purpose was to investigate whether Q10 supplementation and high-intensity training influenced plasma HX and UA (markers of adenine nucleotide catabolism) after high-intensity intermittent exercise. The third purpose was to evaluate whether the ATP synthesis rate of isolated mitochondria from skeletal muscle, at rest, was affected by a short training period, with and without Q10 supplementation. The fourth purpose was to assess whether concentration of lipid peroxidation products in plasma, measured as plasma malondialdehyde-thiobarbituric acid (MDA-TBA) complex, was affected.

**Materials and Methods**

Seventeen healthy, well-trained male subjects, age 20–34 years (Table 1), volunteered to participate and were assigned to either a placebo (n = 8) or a Q10-supplementation (n = 9) group. The subjects were informed of the nature of the study and possible risks involved, and they signed an informed consent form. The study was approved by the Ethics Committee at the Karolinska Institute.
Table 1  Subject Data

<table>
<thead>
<tr>
<th>Group</th>
<th>Age</th>
<th>Body weight</th>
<th>VO_{peak} (ml \cdot kg^{-1} \cdot min^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
</tr>
<tr>
<td>Q10-supplemented</td>
<td>27.8</td>
<td>4.8</td>
<td>79.6</td>
</tr>
<tr>
<td>Placebo</td>
<td>22.8*</td>
<td>2.0</td>
<td>76.5</td>
</tr>
</tbody>
</table>

Note. Age, total body weight, and peak oxygen uptake (VO_{peak}) were determined during running (treadmill) and cycling (cycle ergometer) before Day 1.

*Significant difference (unpaired t test, \( p < .01 \)) compared with the Q10-supplemented group.

After the exercise test on Day 1, subjects were supplemented orally, twice daily, in a double-blind fashion, with either 60 mg Q10 (totally 120 mg Q10 per day) (Marinyl®, Mölnlycke, Sweden) or a placebo equivalent. Subjects were instructed to ingest the tablets together with breakfast and dinner. The purity of the Q10 supplement was tested with high-pressure liquid chromatography (HPLC) as described subsequently. The subjects were assigned to either the placebo or the Q10-supplementation group after the VO_{peak} pretests (cycle ergometer and treadmill) in order to match two equal groups according to maximal oxygen uptake per kilogram total body weight.

A high-intensity intermittent ergometer cycling test was performed in the mornings of Days 1, 11, 15, and 20 (Figure 1). The test consisted of a 30-s all-out cycling period followed by 5 min rest, and ten 10-s all-out cycling periods with 50 s rest between each bout. Following the test on Day 1, subjects were not allowed to participate in any strenuous exercise until the test on the morning of Day 11. One training session was performed in the afternoon on Day 11, consisting of fifteen 10-s all-out cycling periods with 50 s rest. On Days 12, 13, and 14, this exercise model was repeated twice daily. The test on Day 15 was followed by a recovery period without strenuous exercise until the test on Day 20. Materials, methods, and results from the physical performance tests are described in detail elsewhere (35).

On Days 1, 11, 15, and 20, blood samples were collected in the nonfasting state at rest (before warm-up) approximately 1 hr after breakfast and immediately after, 20 min after, and 50 min after completion of the high-intensity intermittent ergometer cycling test. Blood was drawn from a polyethylene catheter inserted into a superficial vein of the forearm. Heparinized EDTA-containing tubes were used to collect blood samples for analysis of Q10 (rest state), plasma purines, and MDA (at rest and immediately after, 20 min after, and 50 min after the cycling tests). Additionally, blood samples were taken in the mornings of Days 12 and 16 for MDA analysis. The blood samples were centrifuged immediately at +4 °C, 1,500 \( \times \) g for 8 min, and the plasma was frozen within 30 s and stored at -70 °C until analysis. Preparation and analysis of purines (HX and UA) in blood plasma are described in detail elsewhere (19). HX and UA concentrations were adjusted for the acute plasma
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Figure 1 — Time schedule. The study was divided into three periods: Days 1–10, ordinary living with normal physical activity; Days 11–15, controlled exercise (tests and training); and Days 16–19, ordinary living with normal physical activity (recovery period). An all-out cycling test was performed in the mornings of Days 1, 11, 15, and 20. Treatment (Q10 or placebo equivalent) started at Day 1, after the all-out cycling test, and continued to Day 20.

volume changes, during and following high-intensity intermittent ergometer cycling tests. We matched values by using the preexercise test hematocrit (Hct) on each test day as a reference base.

After injection of local anaesthesia (2 ml of Carbocain [20 mg/ml], Astra) preexercise muscle samples (40–80 mg) were taken from the lateral portion of the quadriceps femoris muscle (vastus lateralis) on Days 1, 11, 15, and 20 with the needle biopsy technique (4). One portion of the sample (10–15 mg) was rapidly frozen in liquid nitrogen, freeze dried, and stored at −70 °C. Samples were trimmed free from visible blood and connective tissue, powdered, and homogenized (12.5 mg·ml⁻¹) in ice-cold 50 mM KH₂PO₄ buffer (pH 7.5) containing 0.05% Triton X-100 (v/v) and EDTA (1 mM). The homogenates were stored at −70 °C until determination of Q10 content and citrate synthase (CS) activity. CS activity was assayed spectrophotometrically at 30 °C according to Alp et al. (2). A remaining portion of each muscle sample was used to isolate skeletal muscle mitochondria by the method of Tonkonogi and Sahlin (46). The Q10 concentration and CS activity in the mitochondrial suspension were measured after disruption of mitochondrial integrity by freeze-thawing and dilution (5- and 10-fold, respectively) in the buffer described previously. Since a large fraction of muscle Q10 is located in the mitochondria, Q10 was expressed in relation both to muscle weight and to CS activity. Skeletal muscle Q10 concentration and CS activity were calculated and expressed per kilogram wet weight (kg/ww). We converted the values from dry to wet weight, assuming that the muscle water content was 77% (4). Q10 in the mitochondria fraction was related to CS activity in the same fraction.

Analysis

To assess the Q10 and vitamin E concentration in plasma in the resting state, and the Q10 content of skeletal muscle and isolated mitochondria, suspensions (150 μl) from each were extracted three times with a solution consisting of 60% methanol and 40% petroleum. The organic phase was evaporated at +37 °C in a nitrogen atmosphere, and the dry residue was dissolved in isopropanol (150 μl). We determined total Q10 and vitamin E concentrations using reversed-phase HPLC, slightly
modified from Åberg et al. (1). The analyses were performed with Waters HPLC instruments (WISP Model 712, Model 510 HPLC pump, and 486 tunable absorbance detector), with separation achieved on a Bondapak C-18, 10 µm analytical column (3.9 × 300 mm, Supelco) equipped with a Bondapak C-18 Guard-Pak (Waters). The ultraviolet detector was set at 275 nm. External standards were used as a reference. The mobile phase consisted of 96.6% ethanol with a flow rate of 1.2 ml per minute. Plasma Q10 coefficient of variability between double samples was 6%. Plasma total cholesterol concentration was determined with a Reflectron® spectrophotometer (Boehringer Mannheim, Mannheim, Germany). The hematocrit was determined by high-speed centrifugation.

Fresh muscle specimens from 4 subjects on Days 1, 11, and 15 were analyzed for mitochondrial ATP production, using a standard chemiluminescence assay (49). The results from these 4 subjects indicated no consistent change from Day 1 to Days 11 and 15, with or without Q10 supplementation. Since determining mitochondrial ATP production rate requires relatively large muscle samples (>80 mg) and is time consuming, we decided to exclude this analysis from the remaining subjects. MDA was assessed by derivatization with TBA and subsequent HPLC separation of MDA-TBA complex as described elsewhere (41). Samples with visible hemolysis were excluded (3%).

Statistics

Values are presented as means ± SD. We conducted analysis of variance (ANOVA) repeated measures with one independent factor, Treatment (Q10 or placebo), and one dependent factor, Time (time points on Days 1, 11, 15, and 20). Post hoc comparisons were made with Fisher’s post hoc test if significance was found with the ANOVA. Unpaired t test was used where applicable. We evaluated regression analysis assuming a linear relationship. For all tests, p < .05 was accepted as the significant level.

Results

Plasma Q10 Concentration

Plasma Q10 levels on Day 1 (before Q10 treatment) were positively correlated with plasma vitamin E (n = 17, r = .66, p < .005) as well with plasma total cholesterol concentration (n = 17, r = .58, p < .05) when both groups were analyzed together. There was no significant difference in plasma Q10 concentration or plasma Q10/cholesterol ratio on Day 1 between the two groups. The plasma Q10 concentration and plasma Q10/cholesterol ratio of the placebo group did not change from Day 1 to Day 20, but treatment with Q10 significantly increased the plasma concentrations of Q10, from 0.74 ± 0.1 µg · ml⁻¹ on Day 1 to 1.23 ± 0.16 on Day 20 (p < .05, ANOVA, Fisher’s protected least significant difference (PLSD) post hoc test, Figure 2a), respectively. A large interindividual variation in plasma Q10 concentration on Day 1 was observed (range 0.32–1.10 µg · ml⁻¹, n = 17). The variation was even greater within the Q10-supplemented group on Day 20 (range 0.64–2.63 µg · ml⁻¹).

The increase in plasma Q10 from Day 1 to Day 20 (Figure 2) was not correlated with the initial levels (Day 1) of total cholesterol or Q10. The vitamin E concentration in plasma, before Q10 treatment, on Day 1 was 18.2 ± 4.5 µg · ml⁻¹...
Figure 2 — Plasma Q10 ($n = 17$) on Days 1, 11, 15, and 20, in the placebo and Q10-supplemented groups. Values (means $\pm SD$) of plasma Q10 are expressed (a) as $\text{mg} \cdot \text{ml}^{-1}$ plasma and (b) in relation to total cholesterol concentration ($\text{mg} \cdot \text{mg}^{-1}$). Significant differences from Day 1 are indicated (ANOVA, Fisher's PLSD post hoc test).
Table 2  Q10 Concentration, Citrate Synthase (CS) Activity, and Q10 Related to CS Activity in Skeletal Muscle and Mitochondrial Fraction

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 11</th>
<th>Day 15</th>
<th>Day 20</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>Range</td>
<td>M</td>
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<tr>
<td>Placebo (n = 6)</td>
<td></td>
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<tr>
<td>Mu Q10</td>
<td>48.2</td>
<td>7.2</td>
<td>36.9-55.1</td>
<td>48.2</td>
</tr>
<tr>
<td>Mu CS</td>
<td>22.9</td>
<td>5.0</td>
<td>16.3-30.4</td>
<td>23.6</td>
</tr>
<tr>
<td>Mu Q10/CS</td>
<td>2.23</td>
<td>0.75</td>
<td>1.48-3.36</td>
<td>2.19</td>
</tr>
<tr>
<td>Mi Q10/CS</td>
<td>1.59</td>
<td>0.30</td>
<td>1.04-1.91</td>
<td>1.47</td>
</tr>
<tr>
<td>Q10-supplemented (n = 7)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mu Q10</td>
<td>40.8</td>
<td>12.4</td>
<td>28.6-57.3</td>
<td>38.9</td>
</tr>
<tr>
<td>Mu CS</td>
<td>23.8</td>
<td>6.0</td>
<td>16.9-33.6</td>
<td>21.9</td>
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<tr>
<td>Mu Q10/CS</td>
<td>1.75</td>
<td>0.48</td>
<td>1.22-2.56</td>
<td>1.78</td>
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<tr>
<td>Mi Q10/CS</td>
<td>1.26</td>
<td>0.59</td>
<td>0.64-2.39</td>
<td>1.37</td>
</tr>
</tbody>
</table>

Note: Skeletal muscle (Mu) Q10 concentration (mg·kg⁻¹ wet muscle) and citrate synthase (CS) activity (mmol·min⁻¹·kg⁻¹ wet muscle), skeletal muscle Q10 content (µg) related to muscle CS activity (U), and isolated mitochondrial (Mi) Q10 content (µg) related to CS activity (U) in isolated mitochondrial fraction.
(n = 17) and there was no change over time within each group. The total plasma cholesterol concentration was unchanged over the treatment period in both groups. However, the Q10 treatment significantly increased the plasma Q10/cholesterol ratio on Day 11 (0.76 ± 0.42 μg · mg⁻¹, p < .01, ANOVA, Fisher's PLSD post hoc test) and on Day 20 (0.76 ± 0.30 μg · mg⁻¹, p < .01, ANOVA, Fisher's PLSD post hoc test) as compared to Day 1 (0.39 ± 0.11 μg · mg⁻¹). During the training period (Days 11–15), plasma Q10 concentration in the Q10 treatment group tended to be decreased, when expressed both as plasma concentration (Figure 2a) and in relation to cholesterol (Figure 2b).

**Skeletal Muscle and Isolated Skeletal Muscle Mitochondrial Q10 and CS**

The concentration of Q10 in muscle and in the mitochondrial fraction of skeletal muscle was affected neither by Q10 treatment nor by time. Skeletal muscle CS activity did not change significantly in either the supplemented or the control group over the experimental period (Table 2).

Skeletal muscle Q10 was not related to plasma Q10 concentration, peak oxygen uptake, or muscle CS activity at any point during the experimental period. Similarly, plasma Q10 was not correlated with aerobic training status (peak oxygen uptake or muscle CS activity). Further, there was no correlation between skeletal muscle Q10 concentration and subjects' work performance in either group, at any time.

**Isolated Skeletal Muscle Mitochondrial ATP Production**

The ATP synthesis rate of isolated skeletal muscle mitochondria was only determined in samples from 4 subjects (2 Q10-supplemented and 2 placebo). The ATP synthesis rate was 0.30 ± 0.08 μmol · min⁻¹ · U⁻¹ CS, 0.27 ± 0.05 μmol · min⁻¹ · U⁻¹ CS, and 0.31 ± 0.07 μmol · min⁻¹ · U⁻¹ CS on Days 1, 11, and 15, respectively. Since we found no consistent change in mitochondrial ATP synthesis rate in these subjects and no differences between the two groups, we did not analyze this parameter on the remaining subjects.

**Plasma Hypoxanthine, Uric Acid, and Malondialdehyde**

Since we found no interaction effect between Treatment (Q10 or placebo) and Time (Days 1, 11, 15, and 20 and time points on each test day) on HX and UA (ANOVA, repeated measures), data of both groups are presented together. A significant increase of HX and UA was found following the exercise test on Days 1, 11, 15, and 20 (Figure 3). For example, on Day 11, the mean HX concentration in plasma 20 min after the exercise test was 912% of the mean preexercise-test value. The plasma HX concentration after the exercise test was markedly reduced and significantly different on Day 15 as compared with same time point on Days 1, 11, and 20 (all p < .0001, ANOVA post hoc test, Figure 3). On Day 20, the HX level at the 20-min time point was partially returned to the level at same time point on Days 1 and 11 (Figure 3). Similarly, peak UA (50 min after the exercise test) decreased after the training period (Day 15), but the response was partially restored after 5 days of rest (Day 20).
Figure 3 — Plasma purines. Plasma (a) hypoxanthine (HX) and (b) uric acid (UA) concentration (mM) before the exercise test (black bars) and 0 min (white bars), 20 min (gray bars), and 50 min (hatched bars) after the exercise test on Days 1, 11, 15, and 20 (n = 17). Results are presented as means ± SD.

*Significant differences (p < .05, ANOVA, Fisher’s PLSD post hoc test) between Day 11 and the same time points on Day 15 or 20. **Significant difference between Day 15 and the same time points on Day 20.
Plasma MDA level was not significantly affected by Treatment or Time (data not shown); large interindividual differences in plasma MDA existed at all times. Preexercise-test plasma MDA concentrations, for both treatment groups together, were 0.48 ± 0.75, 0.45 ± 0.12, 0.55 ± 0.14, 0.46 ± 0.13, 0.62 ± 1.0, and 0.42 ± 1.0 μmol·L⁻¹ on Days 1, 11, 12, 15, 16, and 20, respectively.

Discussion

**Plasma, Skeletal Muscle, and Mitochondrial Q10**

In the present study, dietary supplementation with Q10 produced a highly pronounced elevation of plasma Q10 concentration (Figure 2), a finding in accordance with earlier reports (8, 34, 37, 47, 48). However, the elevation in plasma Q10 concentration was quite modest considering the amount of Q10 intake. In one pharmacokinetic study, about 62% of the orally supplemented Q10 was recovered in the human feces (34). Thus, with an assumed uptake of 38% and a distribution within the vascular compartment (5.5 L calculated), the supplemented Q10 in the present study would correspond to an increase of 8.3 μg·ml⁻¹ plasma per day. However, the mean increase in plasma Q10 from Day 1 to 11 was only 0.49 μg·ml⁻¹. This indicates that plasma Q10 concentration is affected by a number of factors other than intake, such as absorption from the small intestine; distribution of Q10 in plasma lipoproteins, blood cells, and peripheral tissues; rate of degradation; and rate of Q10 biosynthesis in and release from the liver.

The plasma Q10 level before supplementation on Day 1 was closely related to plasma total cholesterol concentration, which is consistent with previous findings (10, 23, 42). Earlier reports demonstrated that plasma Q10 concentrations were lower in endurance athletes and higher in hypercholesterolemic patients when compared to healthy control subjects (16, 33). This could be a consequence of variations in the concentration of LDLs in the plasma, since it is known that LDLs contain high amounts of Q10 and cholesterol (21). The lower plasma Q10 concentration in endurance-trained subjects may, therefore, be due to a decline in LDLs in plasma, caused by regular endurance physical training. An alternative explanation suggested by Karlsson et al. (26) is that the lower plasma Q10 concentration in endurance-trained athletes is a consequence of elevated Q10 consumption, due to increased "oxidative stress" in tissues. A tendency toward decreased plasma Q10 per total cholesterol in plasma was found in the Q10-supplemented group, from Day 11 to Day 15 (Figure 2b). This could be due to either an increased uptake of the plasma Q10 by different tissues or a decreased absorption of Q10 from the small intestine during training.

The observed Q10 concentration of skeletal muscle in the present study is in agreement with earlier data from human skeletal muscle Q10 (25, 33). It has been shown that both young and old endurance-trained subjects have higher skeletal muscle Q10 concentrations than other healthy subjects (33). This is probably explained by higher mitochondrial density in the endurance-trained individuals. In rats, endurance training leads to an adaptive increase in skeletal muscle Q9 content simultaneous with increased succinate cytochrome c reductase activity (5, 26). Studies in humans have shown that skeletal muscle Q10 is positively correlated with skeletal muscle CS activity (25), a finding not confirmed in the present study. The absence of a correlation could be due to the similar training status of the subjects
(Table 1), with narrow ranges of CS activity and peak VO$_2$. An important finding of the present study was that neither the Q10 concentration in skeletal muscle nor the ratio between Q10 and CS in isolated skeletal muscle mitochondria changed over the three test periods, in either the placebo or in the Q10-supplemented group.

In agreement with Laaksonen et al. (33), we found no correlation between plasma and skeletal muscle Q10 in the present study. This result suggests that muscle Q10 concentration is determined by factors other than plasma Q10 concentration, for example, endogenous Q10 synthesis rate within skeletal muscle. The independent relationship between plasma and muscle Q10 concentration is further supported by the finding that treatment of hypercholesterolemia with simvastatin, a liver 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitor drug, reduces serum Q10 and total cholesterol concentration in humans without changing skeletal muscle Q10 content (32). Q10 supplementation in humans, during strenuous endurance training, has been studied in two controlled, double-blind studies (8, 48). Braun et al. (8) reported no effect of Q10 supplementation on respiratory parameters, heart rate, total work performance, or plasma concentration of MDA. Further, the increase in serum MDA after the exercise test was attenuated after the training period in both groups. These changes were considered to be adaptive responses to a long period of metabolic stress related to the physical training (8). Weston et al. (48) reported that Q10 supplementation had no effect on peak oxygen uptake or on blood lactate kinetics. In the present study, we found no significant effect with Q10-supplementation on plasma MDA before or after the training period with high-intensity exercise, which is consistent with the findings of Braun et al. (8).

The results from analysis of plasma MDA in present study could not confirm the presence of oxidative stress following exercise. However, we previously showed that plasma creatine kinase (CK), an indirect marker of cellular damage, was significantly increased in the Q10-supplemented group following the cycling test (36). In a pilot study (2 control and 2 Q10-supplemented individuals) we observed, in all subjects, a decrease in the reduced form of glutathione (GSH) and an increase in the oxidized form (GSSG) in blood samples taken, at rest, after the training period (Day 15) versus before the training period (Day 11). This indicates that the training period induced oxidative stress, which we need to confirm in a larger group of subjects.

The attenuated training response in the Q10-supplemented group on work performance (35) is an interesting finding, but the mechanism of this attenuation is unclear. It has been suggested that the incorporation of plasma Q10 in plasma membranes affects plasma membrane electron transport as well as signal transduction on tyrosine kinase–linked growth factor receptors (9). In the reduced state, plasma membrane Q10 inhibits the tyrosine kinase activity and thereby inhibits cellular proliferation and growth (9). Furthermore, incorporation of plasma Q10 in leukocytes may also affect the interaction between skeletal muscle and the immune system, by disturbing cytokine production and release. Therefore, we can speculate that the attenuated training response is a result of altered signal transduction in skeletal muscle, due to "reductive stress" of the increased plasma Q10 combined with the high-intensity exercise.

**Purine Catabolism and Exercise**

High-intensity exercise, as performed in the present study, decreases ATP concentration in the exercised skeletal muscle (3, 21, 22, 27). Both HX and UA are catabolites of the adenine-nucleotides, and increased concentrations of HX and UA in
plasma can be used as markers of adenine-nucleotide catabolism and increased activity in a catabolic pathway with capacity to produce ROS following exercise. In the present study, plasma HX and UA increased markedly in both groups after all exercise-test sessions, and the increases were similar between the two groups. This indicates an extensive catabolism of the intracellular adenine nucleotide pool (ATP, adenosine diphosphate [ADP], adenosine monophosphate [AMP] and thus a high metabolic stress during high-intensity exercise. The increase in plasma HX and UA, postexercise, was markedly reduced on Day 15 as compared to Day 11 (Figure 3), although more work was performed on Day 15 (35).

The attenuation of HX (and UA) response to acute exercise was not related to Q10 supplementation and plasma Q10 levels. Previous studies have shown that 6 weeks of high-intensity training reduces the increase in plasma HX following a 30-s Wingate test (20). The same authors also reported that the total skeletal muscle ATP concentration and total adenine pool (TAN) decreased by more than 20% after 1 week of high-intensity training, without a negative effect on work performance. It is possible that this decrease in plasma purine accumulation is related to reduced intramuscular levels of adenine nucleotides and/or an increased salvage of HX, by increased activity of muscle HX phosphoribosyl transferase (rephosphorylate HX to inosine monophosphate, IMP) (18). The partial reversal of the response in plasma HX on Day 20 as compared to Day 15 may be related to restoration of adenine nucleotide pool content as well as to a reversal of HX phosphoribosyl transferase and AMP deaminase activities to their former levels.

Summary

In the present study, the acute increase in plasma HX and UA following high-intensity exercise was (in both groups) reduced after 4 days of training but was partially restored after 5 days of recovery. Treatment with Q10 had no significant effect on purine catabolism or plasma MDA level. Dietary Q10 supplementation markedly increased plasma Q10 concentration without affecting Q10 concentration in skeletal muscle and isolated mitochondria of exercising individuals. In the placebo group, plasma, skeletal muscle, and mitochondrial Q10 concentration remained unchanged and the individual plasma Q10 concentration (both groups) was not related to skeletal muscle Q10 concentration at any point. The practical implication of the present data together with previously presented data (35, 36) is that supplementation with high amounts of Q10 during high-intensity exercise may attenuate training-induced increases in physical performance.

We suggest that the combined effect of increased plasma Q10 and high intracellular proton concentration alters the signal transduction in skeletal muscle due to "reductive stress" induced by increased plasma Q10 levels combined with high-intensity exercise.

References


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