

Effect of Coenzyme Q₁₀ supplementation on exercise-induced muscular injury of rats

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ABSTRACT

Aim: We aimed to examine the effect of Coenzyme Q₁₀ (CoQ₁₀) supplementation on the exhaustive exercise-induced injury and oxidative stress in skeletal muscle and liver.

Methods: Rats were divided into four groups: rest group [control (Con)-Rest; n = 6], exercise group (Con-Ex; n = 6), rest group with CoQ₁₀ supplement (CoQ₁₀-Rest; n = 6), and exercise group with CoQ₁₀ supplement (CoQ₁₀-Ex; n = 6). The exercise groups were run on a treadmill until exhaustion. The CoQ₁₀ supplemented groups received an oral administration of CoQ₁₀ (300 mg kg⁻¹, 4 weeks). After 4 weeks, total CoQ concentration, creatine kinase (CK), glutamic-oxaloacetic transaminase (GOT), malondialdehyde (MDA), scavenging activity against reactive oxygen species [ROS; superoxide anions (O₂⁻) and hydroxyl radicals (HO·)] were measured.

Results: Total CoQ concentration in plasma, slow-twitch muscles (soleus and gastrocnemius deep portion), and liver were significantly increased by CoQ₁₀ supplementation. Plasma CK was significantly higher in Con-Ex compared with Con-Rest, whereas there was no difference between CoQ₁₀-Rest and CoQ₁₀-Ex. There were no significant differences in muscle MDA in each group. Plasma GOT and liver MDA in exercise groups were significantly higher than that of rest

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groups, but not significantly different between CoQ₁₀ supplemented groups and control groups. CoQ₁₀ supplementation was not able to favorably influence ROS scavenging activity in skeletal muscle and liver.

Conclusions: These data indicated that CoQ₁₀ supplementation increased total CoQ concentration in the slow-twitch muscles, and was useful for reducing exhaustive exercise-induced muscular injury by enhancing stabilization of muscle cell membrane.

Key Words: Coenzyme Q₁₀, Intense exercise, Muscle damage, Oxidative stress

INTRODUCTION

In recent years, strenuous physical sports such as the ultra-marathon, cross-country running, and iron-man triathlon are becoming increasingly popular around the world (26, 48). The strenuous physical exercise is characterized by a 10- to 20-fold increase in whole body oxygen (O₂) consumption compared to rest (13, 38). The increase in O₂ uptake concomitant with physical exercise is related to a rise in the production of reactive oxygen species (ROS) by cells and tissues. ROS plays an important role in signal transduction and the regulation of a number of cellular function (12). However, the overproduction of ROS results in oxidative stress, an imbalance favoring pro-oxidants over antioxidants (39). Oxidative stress causes the damage of biological components, e.g. lipids, proteins and genetic material, and is associated with the appearance of many diseases (1, 10). Therefore, it is important to increase antioxidant capacity in tissues to scavenge ROS produced by strenuous exercise.

Recent research suggests that supplementation of certain antioxidants are practicable for physically active individuals to prevent exercise-induced tissue damage and recover from tiredness faster (3). Supplementation of exogenous antioxidants, such as vitamin C, vitamin E, carotenoids, and α -lipoic acid, has prevented strenuous exercise-induced oxidative injury in humans and rats (18, 23, 26, 29). The effect of coenzyme Q₁₀ (CoQ₁₀) supplementation on exercise-induced muscle damage and oxidative stress has been investigated in rats and in humans, however the existing data are sparse and inconsistent (16, 40). Furthermore, the effect of coenzyme Q₁₀ (CoQ₁₀) supplementation on strenuous exercise-induced oxidative stress in tissues has been unknown.

CoQ, which is also known as ubiquinone, is a lipid-soluble, vitamin-like substance presented in the hydrophobic interior of phospholipid bilayer of virtually all the cellular membranes. It consists of a quinone head attached to a chain of isoprene units numbering 9 or 10 in the various mammalian species (4). The most well-known function of CoQ is enhancement of mitochondrial activity related to the synthesis of adenosine triphosphate (ATP) (47). In addition, CoQ plays a role in inhibiting lipid peroxidation by either scavenging ROS directly or in conjunction with α -tocopherol (7, 8, 15, 25).

Shimomura *et al.* (1991) have reported that intravenous CoQ₁₀ supplementation diminished increased muscle damage markers (creatine kinase: CK and lactate dehydrogenase: LDH) in rats following downhill running. In addition, Okamoto *et al.* (1995) have showed that CoQ₁₀ protected cultured skeletal muscle

cells from electrical stimulation-induced LDH release. Furthermore, exogenous administration of CoQ₁₀ suppressed hepatic oxidative damage after reperfusion following ischemia (37). From these findings, CoQ₁₀ supplementation has the potential to reduce strenuous exercise-induced tissue injury and oxidative stress.

The purpose of this study, therefore, was to determine the effect of CoQ₁₀ supplementation on the exhaustive exercise-induced injury and oxidative stress in rat skeletal muscle and liver. Such knowledge might prove useful in reducing strenuous exercise-induced tissue injury and oxidative stress of athletes and recreational athletes.

METHODS

Animals.

Eight-week-old male Sprague-Dawley rats ($n = 24$) (Charles River Laboratories, Yokohama, Japan) were housed in a temperature-controlled room (25 °C) with a 12:12-h light-dark cycle (8:00-20:00 hours light; 20:00-8:00 hours dark) and were allowed food (control AIN-93G, Oriental Yeast Co., Ltd., Tokyo, Japan) and water *ad libitum* throughout the study period.

All animal protocols were reviewed and approved by the Animal Subjects Committee of the University of Tsukuba, Japan.

Treatment.

All rats were randomly assigned to four groups: rest group [control (Con)-Rest; $n = 6$], exercise group (Con-Ex; $n = 6$), rest group with CoQ₁₀ supplement (CoQ₁₀-Rest; $n = 6$), and exercise group with CoQ₁₀ supplement (CoQ₁₀-Ex; $n = 6$). The CoQ₁₀ supplemented groups (CoQ₁₀-Rest and CoQ₁₀-Ex) received an oral administration of CoQ₁₀ at doses of 300 mg kg⁻¹ of body weight per day dissolved in rape oil for 4 weeks. The control groups (Con-Rest and Con-Ex) received an oral administration of rape oil for the same duration.

Exercise protocol.

The exercise protocol described by Kimura *et al.* (2007) was used in the present study. All rats were familiarized with treadmill running at 0 to 15 m.min⁻¹ for 10 to 15 min.day⁻¹ over a period of 5 days (Natsume Seisakusyo Co, Tokyo, Japan). In the experimental session, the exercise groups (Con-Ex and CoQ₁₀-Ex) ran at 15 m.min⁻¹ for first 30 min. The treadmill speed was then gradually increased until the rats refused to run despite being physically prodded (i.e., until they reached exhaustion). The point of exhaustion was determined by the loss of righting reflex when being physically prodded. Electrical shocks were not used as negative reinforcement.

Sample preparation.

The rats in the exercise groups were killed immediately after exhaustive exercise. The rest groups (Con-Rest and CoQ₁₀-Rest) were anesthetized with diethyl ether and killed after 2 h fasting without exercise. Heparinised blood samples were collected from the heart in all groups. The blood was centrifuged (3000 rpm, 4 °C, 10 min) to isolate plasma. The plasma sample was frozen at -40 °C until analysis.

Soleus (Sol), gastronemius [deep/surface portions (GasD/GasS)] muscles, and liver were carefully isolated in all groups. Isolated muscles specimens were frozen with liquid nitrogen, and stored at -80 °C until analysis.

Biochemical analysis.

Creatine kinase (CK) activity in plasma was measured by using a commercial kit (Kanto Chemical Co., Tokyo, Japan). Plasma glutamic-oxaloacetic transaminase (GOT) activity was determined by using a commercial kit (Shino-Test Co., Tokyo, Japan). Quantification of CoQ in plasma and tissues were performed by HPLC (11).

Lipid peroxidation in skeletal muscle tissues and liver.

Muscles and liver were homogenized in 0.2 mM phosphate buffer (pH 7.4) containing 5 mM butylated hydroxytoluene. Insoluble material was removed by centrifugation (10000 rpm for 15 min at 4 °C). Protein concentrations of homogenates were determined by using the method of Lowry *et al.* (1951). Malondialdehyde (MDA) concentrations of tissue samples were assessed by using a commercial kit (BIOXYTECH MDA 586; Oxis International Inc., USA.) and adjusted by total protein concentration.

Electron spin resonance protocol in skeletal muscle tissues and liver.

Muscles and liver were homogenized with 1.15 % KCl homogenate buffer at a factor of 10. The homogenates were diluted in 0.2 mM phosphate buffer (pH 7.4). Protein concentrations of homogenates were determined by using the method of Lowry *et al.* (1951). Scavenging activities against superoxide anions (O₂⁻) and hydroxyl radicals (HO·) were measured using the method described by Tanabe *et al.* (2006) and adjusted by total protein concentration.

Statistical analysis.

Data were analyzed using StatView software (Hulinks, Tokyo, Japan), and values were expressed as means ± SD. An unpaired t-test was used to compare between rest groups (Con-Rest and CoQ₁₀-Rest). The effects of CoQ₁₀ supplementation as well as exhaustive exercise were tested by two-way ANOVA. If significance was observed in the interactions in the two-way ANOVA, one-way ANOVA was used to assess the difference between rest and exercise in each group (CoQ₁₀ supplemented and control) and unpaired t-test was used to compare the difference between exercise groups (Con-Ex and CoQ₁₀-Ex). Differences were considered statistically significant when $P < 0.05$.

RESULTS

Body weight and endurance time.

At the end of 4 weeks, body weight in the Con-Rest, Con-Ex, CoQ₁₀-Rest, and CoQ₁₀-Ex groups were 346 ± 7, 353 ± 9, 351 ± 7, and 355 ± 11 g, respectively. There was no significant difference in body weight between groups. The mean running time of Con-Ex and CoQ₁₀-Ex groups was 72 ± 3 and 76 ± 3 min, respectively; there was no significant difference between groups.

Total CoQ (CoQ₉₊₁₀) concentration in plasma, skeletal muscles, and liver.

Table 1 shows total CoQ concentration in plasma, skeletal muscles, and liver. Total CoQ concentration in plasma was significantly higher by 236 % in the CoQ₁₀-Rest compared with the Con-Rest ($P < 0.05$). Total CoQ concentration in

Table 1. Effects of CoQ₁₀ supplementation on CoQ₉, CoQ₁₀ and CoQ₉₊₁₀ concentrations of plasma, soleus (Sol), deep portion of gastrocnemius (GasD), surface portion of gastrocnemius (GasS), and liver after exhaustive exercise.

	Con-Rest	CoQ ₁₀ -Rest	Con-Ex	CoQ ₁₀ -Ex
CoQ₉				
Plasma (µg/ml)	0.28 ± 0.08	0.12 ± 0.03 * #	0.17 ± 0.04	0.13 ± 0.05 #
Sol (µg/g)	5.93 ± 3.53	10.64 ± 2.71 *	12.49 ± 6.47 †	11.81 ± 3.50 †
GasD (µg/g)	10.84 ± 9.57	23.18 ± 4.16 *	8.38 ± 7.07	5.08 ± 6.04 ‡
GasS (µg/g)	2.07 ± 1.42	3.11 ± 1.70	4.12 ± 1.74	1.54 ± 0.59
Liver (µg/g)	38.52 ± 12.24	27.57 ± 8.64 #	42.88 ± 6.85	26.25 ± 8.54 #
CoQ₁₀				
Plasma (µg/ml)	0.16 ± 0.09	1.37 ± 0.39 * #	0.04 ± 0.01	0.84 ± 0.57 #
Sol (µg/g)	0.73 ± 0.35	1.19 ± 0.38	1.33 ± 0.65	1.41 ± 0.46
GasD (µg/g)	3.46 ± 6.28	1.87 ± 0.45	0.94 ± 0.43	0.64 ± 0.48
GasS (µg/g)	0.43 ± 0.18	0.41 ± 0.19	0.49 ± 0.09	0.30 ± 0.11
Liver (µg/g)	8.54 ± 6.29	86.58 ± 31.61 * #	5.49 ± 1.79	76.35 ± 39.39 #
CoQ₉₊₁₀				
Plasma (µg/ml)	0.44 ± 0.17	1.48 ± 0.40 * #	0.21 ± 0.05 †	0.97 ± 0.58 ‡ #
Sol (µg/g)	6.66 ± 3.87	11.83 ± 3.08 *	13.81 ± 7.12 †	13.23 ± 3.89 †
GasD (µg/g)	14.30 ± 13.63	25.05 ± 4.52 *	9.33 ± 7.42 †	5.72 ± 6.51 †
GasS (µg/g)	2.50 ± 1.49	3.52 ± 1.87	4.61 ± 1.77	1.84 ± 0.66
Liver (µg/g)	47.06 ± 17.89	114.15 ± 29.48 * #	48.37 ± 8.57	102.60 ± 44.69 #

Values are means ± SD. * $P < 0.05$ compared to Con-Rest. ‡ $P < 0.05$ compared to CoQ₁₀-Rest. † $P < 0.05$ compared to rest groups (Con-Rest and CoQ₁₀-Rest). # $P < 0.05$ compared to control groups (Con-Rest and Con-Ex).

exercise groups was 39 % lower than that of rest groups ($P < 0.05$). These results indicated that total CoQ concentration in the plasma was changed by exhaustive exercise and CoQ₁₀ supplementation.

Total CoQ concentration was significantly higher by 77 % and 75 % in the CoQ₁₀-Rest compared with the Con-Rest in Sol and GasD, respectively ($P < 0.05$). In addition, exhaustive exercise significantly increased by 46 % total CoQ concentration in Sol and decreased by 62 % that of GasD ($P < 0.05$). In contrast, exhaustive exercise and CoQ₁₀ supplementation did not influence the total CoQ concentration in GasS. These results suggested that total CoQ concentration in slow-twitch muscles (Sol and GasD) was significantly increased by CoQ₁₀ supplementation and changed by exhaustive exercise.

The concentration of total CoQ was higher by 143 % in CoQ₁₀-Rest compared with Con-Rest in the liver ($P < 0.05$). This data indicated that CoQ₁₀ supplementation significantly increased total CoQ concentration in the liver.

Plasma CK and GOT activities.

Figure 1A showed plasma CK activity. Compared with Con-Rest, plasma CK

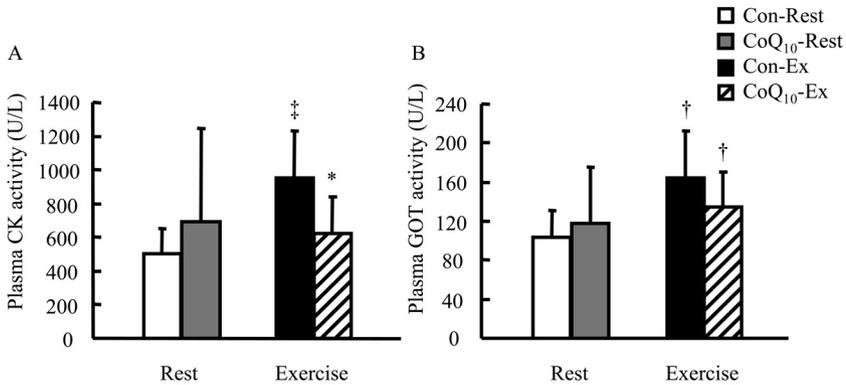


Figure 1. Effects of CoQ₁₀ supplementation on plasma creatine kinase (CK) (A) and glutamic oxaloacetic transaminase (GOT) (B) activities after exhaustive exercise. Values are mean ± SD. ‡ *P* < 0.05 compared to Con-rest group. * *P* < 0.05 compared to Con-Ex group. † *P* < 0.05 compared to rest groups (Con-rest and CoQ₁₀-rest).

activity was significantly higher by 88 % in Con-Ex (*P* < 0.05). In contrast, there was no difference between CoQ₁₀-Rest and CoQ₁₀-Ex. In addition, plasma CK activity in CoQ₁₀-Ex was significantly lower than that of Con-Ex (*P* < 0.05). These results suggested that supplementation of CoQ₁₀ reduced exhaustive exercise-induced muscular injury.

Figure 1B showed plasma GOT activity. Plasma GOT activity in exercise groups was 35 % higher than that of rest groups (*P* < 0.05), whereas there was no difference between CoQ₁₀ supplemented groups and control groups.

Lipid peroxidation in the skeletal muscle and liver tissues.

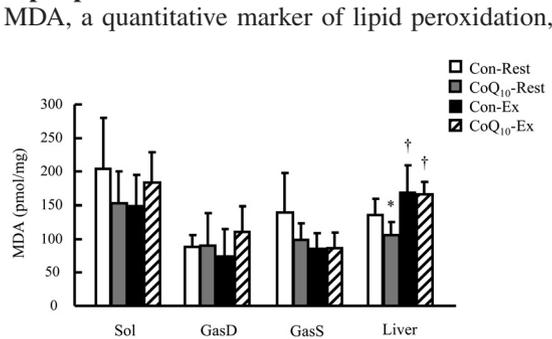


Figure 2. Effects of CoQ₁₀ supplementation on malondialdehyde (MDA) concentrations in soleus (Sol), deep portion of gastrocnemius (GasD), surface portion of gastrocnemius (GasS), and liver after exhaustive exercise. Values are means ± SD. * *P* < 0.05 compared to Con-rest group. † *P* < 0.05 compared to rest groups (Con-rest and CoQ₁₀-rest).

MDA, a quantitative marker of lipid peroxidation, was measured in the skeletal muscle and liver tissues as shown in Figure 2. In Sol, GasD, and GasS, there were no significant differences in MDA level in each group. Therefore, CoQ₁₀ supplementation and exhaustive exercise did not influence the level of MDA in the skeletal muscle tissues. The liver MDA level in exercise groups was 22 % lower than that of rest groups (*P* < 0.05). In addition, the liver MDA level was lower by 38 % in CoQ₁₀-Rest compared with Con-Rest (*P* < 0.05). These data suggested that

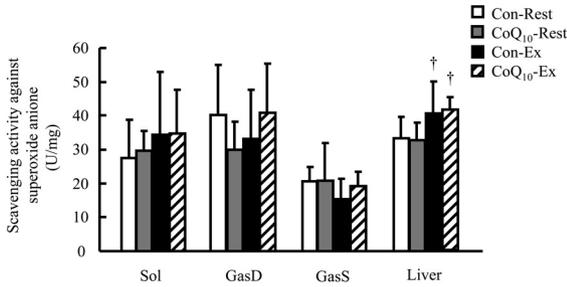


Figure 3. Effects of CoQ₁₀ supplementation on scavenging activity against superoxide anion in soleus (Sol), deep portion of gastrocnemius (GasD), surface portion of gastrocnemius (GasS), and liver after exhaustive exercise. Values are means \pm SD. † $P < 0.05$ compared to rest groups (Con-rest and CoQ₁₀-rest).

ference between each group in three skeletal muscle tissues level of scavenging activity against O₂⁻. In contrast, O₂⁻ scavenging activity in the liver in exercise groups was 24 % higher than that of rest groups ($P < 0.05$). These findings indicated that CoQ₁₀ supplementation had no influence on O₂⁻ scavenging activity in the liver, and that the effect of CoQ₁₀ supplementation on O₂⁻ scavenging activity in the skeletal muscle tissues was not clarified.

Scavenging activity against hydroxyl radical in the skeletal muscle and liver tissues.

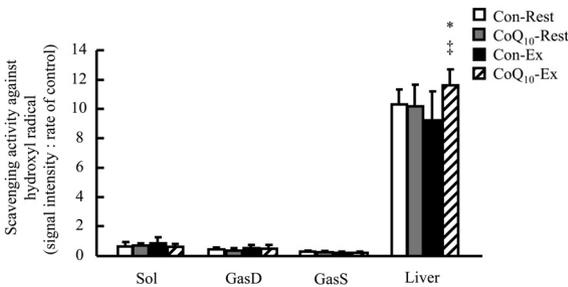


Figure 4. Effects of CoQ₁₀ supplementation on scavenging activity against hydroxyl radical in soleus (Sol), deep portion of gastrocnemius (GasD), surface portion of gastrocnemius (GasS), and liver after exhaustive exercise. Values are means \pm SD. ‡ $P < 0.05$ compared to CoQ₁₀-rest group. * $P < 0.05$ compared to Con-Ex group.

supplementation increased HO \cdot scavenging activity in exercise.

supplementation of CoQ₁₀ reduced lipid peroxidation in the liver at rest, although it did not reduce exhaustive exercise-induced lipid peroxidation.

Scavenging activity against superoxide anion in the skeletal muscle and liver tissues.

Scavenging activity against O₂⁻ in the skeletal muscle and liver tissues were shown in Figure 3. There was no difference

As shown in Figure 4, there was no significant difference between the four groups in scavenging activity against HO \cdot in each of the three skeletal muscle tissues. In contrast, the scavenging activity against HO \cdot was higher by 14 % in CoQ₁₀-Ex compared with CoQ₁₀-Rest in the liver ($P < 0.05$). Also, HO \cdot scavenging activity was higher by 26 % in CoQ₁₀-Ex compared with Con-Ex in the liver ($P < 0.05$). These data suggested that CoQ₁₀

in the liver after exhaustive

DISCUSSION

Our study had 3 main findings in skeletal muscle and liver, respectively: In the skeletal muscle, CoQ₁₀ supplementation 1) increased total CoQ concentration in the slow-twitch fiber dominant type muscle (Sol and GasD), 2) suppressed the muscular injury induced by exhaustive exercise, and 3) did not influence oxidative stress. In the liver, CoQ₁₀ supplementation 1) increased total CoQ concentration, 2) did not reduce hepatic injury caused by exhaustive exercise, 3) did not decrease the oxidative stress caused by exhaustive exercise.

CoQ plays several crucial roles in the body, acting as a redox electron carrier in the mitochondria related to the synthesis of ATP, acting as an essential antioxidant, influencing the stability of membranes (6, 14, 32). In the present study, plasma total CoQ concentration at rest was increased 236 % by administering CoQ₁₀ (see Table 1). This result was consistent with that of a previous study (24). In addition, exhaustive exercise significantly decreased total CoQ concentration in plasma (see Table 1). Exhaustive exercise increases energy demand manifold and oxidative stress in tissues, and induces tissue damage. Therefore, CoQ in plasma may be distributed to various tissues during exhaustive exercise.

Results from previous animal studies have reported that CoQ₁₀ supplementation increased total CoQ level in various tissues including skeletal muscle in rats (24, 42). In the present study, CoQ₁₀ supplementation increased total CoQ concentration in the slow-twitch fiber dominant type muscles (Sol and GasD), but not in fast-twitch fiber dominant type muscle (GasS) (see Table 1). The highest amounts of CoQ are found in the outer and inner mitochondrial membranes (47). The slow-twitch muscles are thought to have substantially higher mitochondrial volume densities than the fast-twitch muscle. Thus, it is possible that the increase of total CoQ concentration was specific to the slow-twitch dominant fibers of the skeletal muscle.

Many researches have indicated that exercise increases plasma CK activity, which is the most commonly used marker of skeletal muscle damage induced by exercise (22, 34). In the present research, plasma CK activity in Con-Ex significantly increased about 1.9-fold compared with Con-Rest (see Figure 1A). This result indicated that muscle damage was induced by exhaustive exercise. However, there was no difference between CoQ₁₀-Rest and CoQ₁₀-Ex groups in the plasma CK activity. Furthermore, plasma CK activity was significantly lower in CoQ₁₀-Ex group compared with Con-Ex group. Thus, CoQ₁₀ supplementation provided protection against strenuous exercise-induced muscular injury. In the previous studies, it has been reported that CoQ₁₀ had a structural stabilizing effect on cell membrane phospholipids (17, 31). Therefore, it is quite likely that CoQ₁₀ supplementation increases CoQ concentration in muscle cell membranes and reduces strenuous exercise-induced muscular injury by enhancing cell membrane stabilization.

There is growing evidence that ROS are involved in the skeletal muscle damage observed following strenuous exercise (18, 21, 26). In response to exercise, O₂ consumption increases 100- to 200-fold at the level of the skeletal muscle, resulting in an increase in the production of ROS (i.e., O₂⁻, hydrogen peroxide (H₂O₂), and HO⁻) in the skeletal muscle (41). However, in the present study, exhaustive exercise did not induce the increase of lipid peroxidation (see Figure

2) and the change in scavenging activities against O₂⁻ and HO· in the three muscle tissues (see Figure 3 and 4). This result suggested that ROS were not involved in the muscular injury immediately after exhaustive exercise, and the effect of CoQ₁₀ supplementation on exercise-induced oxidative stress in skeletal muscle was unclear. When muscular damage is induced by strenuous exercise, inflammatory cells (i.e., neutrophil and macrophage etc.) infiltrate into the site of injury. Neutrophils and macrophages produce ROS and remove damaged cells in skeletal muscle (30, 36). Following muscle damage, the infiltration of neutrophils reaches a peak within 12 hours (28, 45) and that of macrophages peaks between 1 and 3 days (9, 35, 36, 46). Therefore, future studies are necessary to measure oxidative stress at later time points after strenuous exercise to clarify the effect of CoQ₁₀ supplementation on exercise-induced oxidative stress in skeletal muscle.

Total CoQ concentration in the liver in CoQ₁₀-Rest was increased by administering CoQ₁₀ for 4 weeks, reaching levels 2.6-fold higher than the value for Con-Rest (see Table 1). This finding was consistent with that of previous animal researches (24, 42). In addition, there was no significant difference between exercise and rest groups in total CoQ concentration of the liver (see Table 1). This result showed that exhaustive exercise did not affect the total CoQ concentration in the liver.

Previous studies indicated that exhaustive exercise increased GOT activity and resulted in acute liver damage, including necrosis of the central veins of hepatic lobules, a reduction in hepatocyte numbers in the microvillus, and a decrease in the endothelium of hepatic veins (5). In this study, an increase in GOT activity in plasma was induced by exhaustive exercise (see Figure 1B). However, CoQ₁₀ supplementation did not suppress the elevation of GOT activity in plasma (see Figure 1B). Therefore, the present study showed that supplementation with CoQ₁₀ did not provide protection against liver injury caused by exhaustive exercise.

Kim *et al.* (2002) suggested that liver injury was associated with an increase in liver ROS generation. In the present study, MDA concentration in the liver in exercise groups were significantly higher compared with rest groups (see Figure 2). In addition, the ROS scavenging activity in exercise groups was significantly higher than that of rest groups in the liver (see Figure 3 and 4). These results suggested that exhaustive exercise significantly increased oxidative stress in the liver, and ROS were related to the liver injury immediately after exhaustive exercise. Previous studies have reported that pretreatment with CoQ₁₀ reduced ochratoxin A or acetaminophen-induced lipid peroxidation in the liver (2, 43). However, the present study showed that CoQ₁₀ supplementation was not able to reduce the increase in lipid peroxidation in the liver immediately after exhaustive exercise, although the supplement of CoQ₁₀ decreased the lipid peroxidation in the liver at rest (see Figure 2). Thus, CoQ₁₀ supplementation did not inhibit oxidative damage in the liver caused by exhaustive exercise in the present study.

In conclusion, we investigated the effect of CoQ₁₀ supplementation on the exhaustive exercise-induced injury and oxidative stress in skeletal muscle and liver. The study revealed that CoQ₁₀ supplementation increased total CoQ concentration in the slow-twitch fiber dominant type muscle, and reduced exhaustive exercise-induced muscular injury. On the other hand, CoQ₁₀ supplementation was not able to reduce liver injury and oxidative stress in the liver, although total CoQ

concentration in the liver was increased by administering CoQ₁₀. Thus, our results support the notion that CoQ₁₀ is useful for reducing exhaustive exercise-induced muscular injury. Further studies are required to determine the mechanism of reducing exhaustive exercise-induced muscular injury through supplementation of CoQ₁₀.

ACKNOWLEDGMENTS

We thank Kaneka Corp. for the generous gift of CoQ₁₀. "This study was partly supported by a Grant-in-Aid for Science Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan (18680047 to T. A.) and was supported by "Establishment of Consolidated Research Institute for Advanced Science and Medical Care", Encouraging Development Strategic Research Centers Program, the Special Coordination Funds for Promoting Science and Technology, Ministry of Education, Culture, Sports, Science and Technology, Japan."

NOTES

MK, FK, and TA were responsible for the study concept and design, acquisition of data, analysis and interpretation of data, and preparation of manuscript. KT, YM, and SI were responsible for the acquisition of data and analysis and interpretation of data. IK was responsible for the acquisition of subjects and data, for obtaining funding, and for supervision. None of the authors had a conflict of interest.

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