

Effect of coenzyme Q10 supplementation on exercise-induced response of inflammatory indicators and blood lactate in male runners

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Abstract

Background: Heavy exercise cause muscle damage associated with production of inflammatory agents. The purpose of present study was to determine the effect of acute and 14-day Coenzyme Q10 supplementation on inflammatory, blood lactate and muscle damage in male middle-distance runners.

Methods: Eighteen male middle-distance runners in a randomized and quasi experimental study were allocated into two equal groups: supplement group (n=9, Coenzyme Q10: 5mg/kg/day) and placebo group (n= 9, Dextrose: 5mg/kg/day). After acute (1day) and 14-day supplementation, all subjects were participated in a training like running (competitive 3000 meters). Blood samples were obtained in the four phases: one hour before and 18-24 hours after two running protocols. Lactate, serum interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-alpha), C-reactive protein (CRP) and creatine kinase (CK) were analyzed. Repeated ANOVA and Bonferuni as a post hoc tests were used to determine the changes in four stages. Differences between groups were determined by t-test.

Results: The results showed that acute and short-term Coenzyme Q10 supplementation had not significant effect on basal parameters. The acute coenzyme Q10 supplementation attenuated only the exercise-induced increase in response of the plasma CRP. The short-term (14-day) coenzyme Q10 supplementation attenuated the exercise-induced increase in response of the lactate, serum interleukin-6, tumor necrosis factor-alpha, and CRP in male middle-distance runners. However, the acute and short-term coenzyme Q10 supplementation had not any significant effect on the exercise-induced increase response of total serum creatine kinase.

Conclusion: Based on the present results, it can be concluded that the 14-day coenzyme Q10 supplementation (5mg.kg-1.day-1) is more effective than the acute supplementation to overcome the exercise-induced adverse responses in some oxidative, inflammatory and biochemical parameters. Therefore, short-term coenzyme Q10 supplementation is recommended to reduce exercise-induced adverse consequences.

Keywords: Runners, Coenzyme Q10, Inflammatory, Lactate, Muscle damage.

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Introduction

The health benefits of systematic and regular exercise training in reducing the risk of some diseases such as cancer, diabetes, obesity, hypertension, and sudden death, is well established (1). Yet, exhaustive exercise training especially in non-

professional and untrained athletes cause oxidative stress associated with inflammatory response s, which is the cause for the muscle cell membrane damage observed in this sort of high-intensity and exhaustive activity and exercise (2, 3). It is well known that exhaustive exercise result membrane

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cell damage to or inflammatory responses into the muscle cells (2, 4). The strenuous and exhaustive activity-induced muscular injury and damage has been related with oxidative stress, inflammation and an increase in the pro-inflammatory mediators (3, 4-6). This increase in oxidative stress related with strenuous exercise increases inflammatory cytokines and marker include hs-CRP, IL-6, and TNF-alpha, among others (2, 5).

Oral intake of compounds capable to decrease these components will reduce the muscle damage and thus they will be beneficial for these athletes. The coenzyme Q10 (CoQ10) is a such compound due to its well-known antioxidant and anti-inflammatory effects (6, 7). Therefore, muscle damage might be prevented by optimizing nutrition, especially via increasing the nutritional content of dietary antioxidants (8).

Mechanical and metabolic stresses caused by vigorous training and competitive long-distance running and swimming endurance may result to fatigue (increased lactate) and change in some biochemical indicators include enzymes (e.g., creatine kinase) to the serum (9).

Given the significance of oxidative stress, inflammation, and muscular damage related with high-intensity exercise, it would be interesting to evaluate the influence of oral supplementation with an antioxidant substance able of diminishing muscular damage, free radicals production, and inflammatory signaling associated with this performance. CoQ10, an indispensable part of the mitochondrial electron transport chain is necessary for ATP production, especially in muscle cells with high metabolic requirement including muscle cells over high-intensity and intensive exercise. CoQ10 acts as a redox electron carrier and transporter into the mitochondria (6). For many years, CoQ10 has been used as a dietary supplement intended to promote optimal health by trapping free radicals and the interest for this molecule obtained from the fact of this role as a redox link in the mito-

chondrial electron transport chain, where also has important antioxidant characteristics under lipophilic conditions (7). The data available have provided a direct relationship between exercise performance and blood and muscle tissue and CoQ10 levels (9). However, most of studies are focused largely in the exercise performance and radical-scavenging activity of CoQ10 during low-intensity exercise (9), being scarce the studies about the influence of CoQ10 supplementation during the performance of high-intensity strenuous exercise and inflammatory signaling. Therefore, the purpose of the present study was to determine the effect of acute (one day) and short-term (14day) CoQ10 (5mg/kg body weight/day) supplementation (10) in response to exercise muscle damage, inflammation and fatigue, inflammatory markers in men runners in the middle-distance (following a competition run 3000 meters) in form of a two-group design. A double-blind repeated measures was performed.

Methods

Data

Eighteen male middle-distance runners (mean \pm SD age of 19.9 ± 2.64 years; mean \pm SD height of 177.6 ± 2.3 cm; mean \pm SD of VO_2 max 60.6 ± 3.9) in a randomized and quasi experimental study were allocated in two equal Q10 supplement and placebo group. All subjects eligible to participate in the study completed a familiarization session where they were provided information regarding the study design, testing and supplementation protocols. None of the subjects had ingested CoQ10, or any other dietary supplements before initiation of the study. In addition, they had no past history of heart or kidney diseases, diabetes or any physical damage and problems. Study was approved by the Research Ethics Committee of Tabriz University of Medical Sciences. Sample size for each of the two groups with regard to study design and results of previous studies, was estimated as seven (11, 12). However, in order to prevent possible losses during the pro-

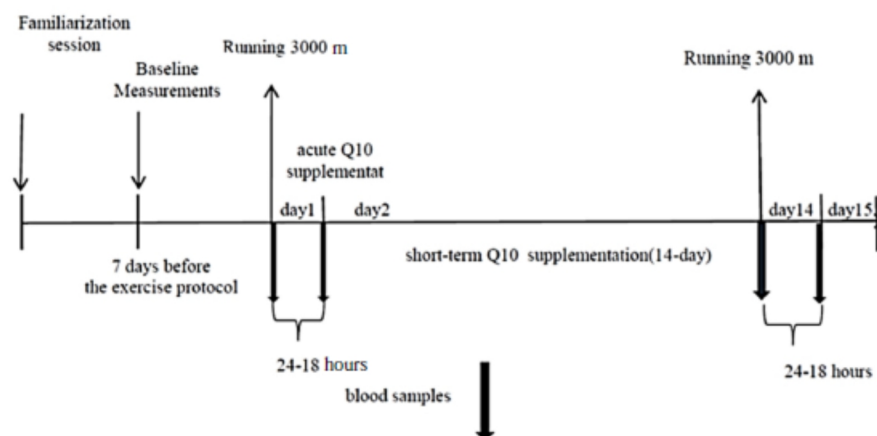


Fig.1.Training protocol and supplementation of CoQ10

cess of research subjects and the anthropometric indices and aerobic power, sample size for each group increased to 9.

Finally, with regard to maximal oxygen consumption test (Bruce), percentage of body fat and some blood parameters (hemoglobin and hematocrit), subjects were divided into nine groups matched in homogenized supplement.

The subjects were randomly assigned to either the CoQ10 (5 mg per kg per day Q10) or placebo (5 mg per kg per day dextrose). Both treatments were effervescent capsules, pre-packaged to be identical in taste and appearance. Each group ingested one capsule three times per day at regular interval (breakfast, lunch and dinner) for one day and 14days. (9) The CoQ10 dosage was based on previous studies and least amount of CoQ10 plasma levels required for promotion or deal with the loss of a relatively intense aerobic activity (11, 13).

An outline of the study design is shown in Fig. 1. After acute (1day) and 14-day supplementation periods, all subjects were participated in a training like running (competitive 3000 meters). A three thousand competitive running was performed after a general warm-up. In addition, it was assumed that running the 3000 meters running competition with relatively high intensity and hard work as a fuel pressure should cause significant changes in markers of inflammation in the male distance runners (14).

Plasma lactate were obtained in the two phases: before and immediately after two running protocols. Blood samples were obtained in the four phases: one hour before and 18-24 hours after two running protocols. Blood samples were obtained from subject's antecubital vein using venipuncture (5 ml; made by SUHA Co) before and 24-18 hours after acute (one day) and short-term (14day) supplementation protocol. All were measured during 12-9pm, the temperature of 28-23°C, humidity 65-50%, and identical ventilation and lighting. In addition, subjects performed 24hours before the test, avoided doing any heavy physical activity with similar meal (breakfast) before the test. In addition, prior to the second blood sampling, subjects' diet was controlled using 24hour dietary recalls (11).

Statistical Analysis

The normality assumption for variables was tested by the Kolmogorov-Smirnov test. Descriptive statistics were expressed as mean \pm SD. Repeated ANOVA and Bonferroni as a post hoc test were used to determine the changes in four stages. Differences between groups were determined by t-test. All statistical analyses were performed using SPSS 18. The significance level was considered at less than 0.05.

Results

The mean and standard deviation of in-

Table 1. Descriptive statistics of physical characteristics of the Q10 and Placebo group

Variable	CoQ10, n=9 (Mean±SD)	Placebo, n=9 (Mean±SD)
Age (years)	19.4±2.35	19.9±2.64
Height (cm)	175.6±5.61	177.8±6.12
Weight (kg)	68.4±6.38	68.6±6.54
BMI (kg.m ⁻²)	22.1±1.51	21.6±2.18
Body fat (%)	8.9±1.89	8.9±1.26
VO _{2max} (ml/kg ⁻¹ /min ⁻¹)	61.6±3.92	60.1±4.20
HR (beats min ⁻¹)	70.8±2.58	71.4 ±2.14
SBP (mmHg)	114.2±12.15	112.2±14.10
DBP (mmHg)	72.1±5.10	73.42±5.80

BMI, Body Mass Index; HR , Heart Rate; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure

Table 2. Inflammatory and blood lactate of exercise-trained middle distance runner before (pre) and after (post) first and second running 3000 meters like-competitive, following acute and short term treatment with CoQ10 or placebo

Variable	Group	Baseline (Mean±SD)	24 h after first test (Mean±SD)	post-supplementation and before test (Mean±SD)	24 h after second test (Mean±SD)
Lactate (mmol / L ⁻¹)	Q10	2.4±0.50	12.8±1.41	2.28±0.34	8.4±0.91
	Placebo	2.5±0.62	11.8±2.12	2.1±0.70	13.9±1.17
CK (IU / L)	Q10	164.6±15.70	276.8±25.55	164.6±13.34	250.1±35.71
	Placebo	160.7±15.72	282.5±19.32	156.1±25.57	274.5±12.78
TNF-α (pg/ml)	Q10	21.4±2.61	28.1±3.70	22.6±3.14	25.4±4.14
	Placebo	20.1±2.39	28.8±4.18	22.6±3.13	29.1±1.43
IL-6 (pg/mL)	Q10	3.56±0.29	7.1±1.22	3.47±0.48	3.9±1.81
	Placebo	3.44±0.75	7.4±1.41	3.51±0.43	7.6±1.86
hs-CRP	Q10	1.24±0.54	4.71±0.92	1.14±0.27	4.24±0.82
	Placebo	1.18±0.45	5.11±1.1	1.63±0.35	4.97±0.97
Hemoglobin (g.dL ⁻¹)	Q10	15.8±1.24	15.3±0.70	15.6±0.93	15.8±0.75
	Placebo	15.2±1.22	15.3±1.17	15.4±0.64	15.4±0.5

hs-CRP, high sensitivity CRP; TNF-α, Tumor necrosis factor-α; IL-6, interleukin 6; CK, creatine kinase.

dividual characteristics and hemodynamic parameters in both groups before the exercise protocol are shown in Table 1. All subjects reported adherence to the experimental protocol and complete ingestion of the supplement. There were no differences among groups at the beginning of the study for physical characteristics (Table 1) and biochemical and hemodynamic variables (Table 2) ($p>0.05$). Acute and short-term supplementation had no significant effect on the variables in baseline levels ($p>0.05$). Acute supplementation had no significant effect on variables changes ranges after exercise protocol ($p>0.05$). Also, lactate, IL-6, tumor necrosis factor-alpha, and CRP ($p= 0.112$; $p= 0.21$; $p= 0.614$; $p= 0.12$; $p= 0.51$, respectively) were not significantly increased following the short-term supplementation (Table 2 and Fig. 2). In other word, compared with the placebo group, inflammatory markers were significantly

lower in the group of CoQ10. In contrast, levels of serum CK in CoQ10 group was significantly increased following the short-term supplementation and running 3000 meters like-competitive (Table 2) ($p=0.073$).

Discussion

Acute CoQ10 supplementation increased lactate, IL-6, TNF-alpha, CRP and creatine kinase in male middle-distance runners after the race, but did not prevent running 3000 meters. However, CoQ10 supplementation could prevent increase inflammatory markers and lactate after running 3000 meters competition. However, total serum creatine kinase response was not affected after the 3000 meter race running in acute and short-term supplementation of CoQ10.

Robust evidence exists to demonstrate that exhaustive and high intensity exercise result oxidative stress and muscle cells

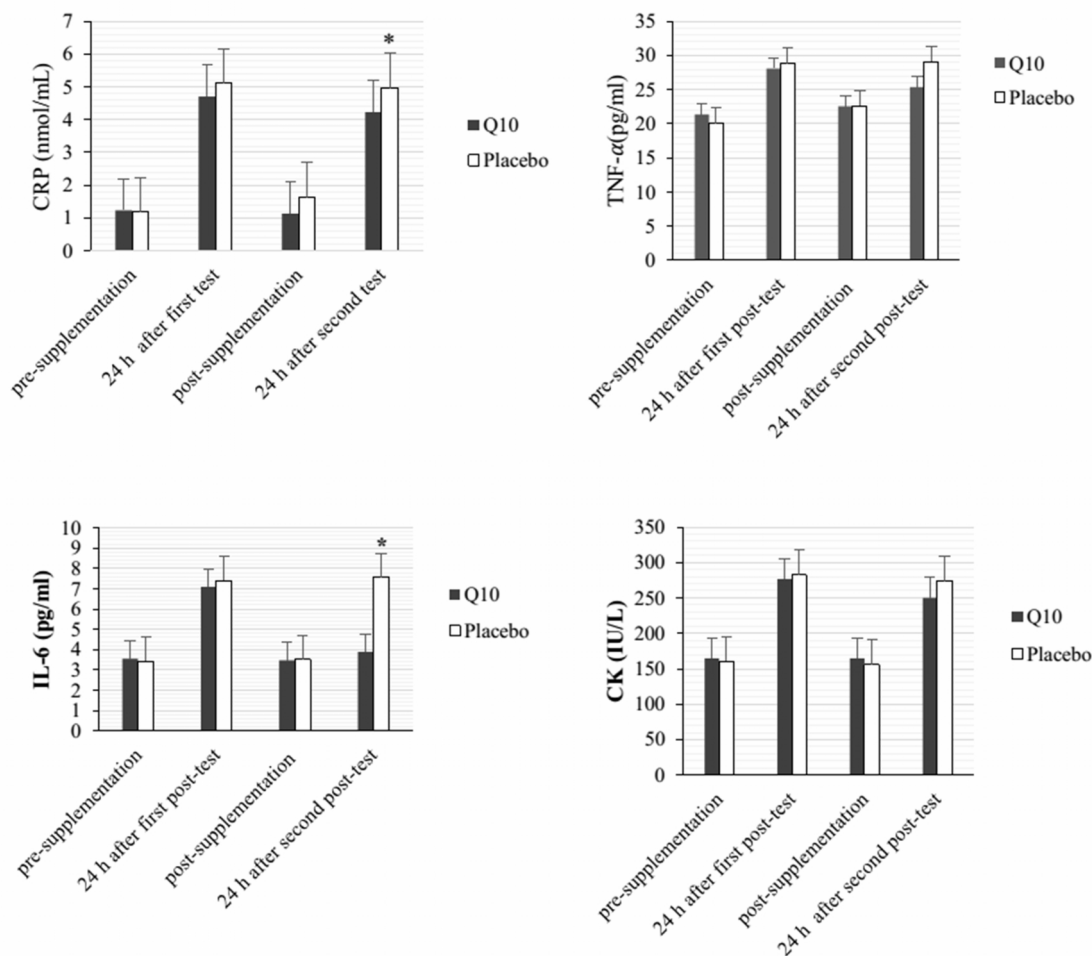


Fig. 2. Effects of CoQ10 supplementation on inflammatory indexes in exercise-trained middle distance runner before (pre) and after (post) first and second running 3000 meters like-competitive, following acute (1 day) and short term (14 days) treatment with CoQ10 or placebo.

damage as evidenced by an increase in the plasma levels of enzymes. (15) The significance of inflammation in the muscle to increase muscle generation after skeletal muscle damage or exercise (16) and limited oxidative stress might in the long run be beneficial for optimal skeletal muscle function. The use of anti-inflammatory dietary supplements or drugs after exercise and the use of antioxidant dietary supplements before moderate or vigorous exercise have therefore been questioned (16, 17). Moreover, it has been suggested that CoQ10 may act not only as an antioxidant but also may have a pro-oxidant function (19). This could be an alternative mechanism by which CoQ10 supplementation in theory could improve exercise capacity.

Elevated levels of CK acts as an indicator

of skeletal muscle damage. There was a muscular effect of the exhaustive tests measured as an increased CK concentration on day 2 of each test period. However, there was no difference between the intervention and placebo groups. In fact, the increase over time in CK was lower in the CoQ10 group, although the statistical test for difference was not significant.

Doses as high as 3000 mg have been used to safe the tissue uptake of CoQ10. (18) The present study was designed to represent the dosage commonly used and recommended by the CoQ10 manufacturer. In adaption, 90 mg of CoQ10 has been shown to be sufficient to increase plasma concentrations (18, 19).

Research have shown that CoQ10 supplementation in situations such as heavy or

exhaustive exercise may increase the plasma levels of CoQ10 oxidative phosphorylation, accelerates the electron transfer (adenosine triphosphate production), increases availability to another sources of carbohydrates, increases fatty acid metabolism (less reliant anaerobic pathways) and lower subsequent accumulation of plasma lactate (20, 21).

This result can be due to two reasons: firstly, the main content of this antioxidant in these membranes as a consequence of the supplementation as it has been observed in other studies (7) and would explain also the lower antioxidant production before the physical test, because this would act as an essential antioxidant and assisting in the regeneration of other antioxidants (7). On the other hand, there would be a lower free radicals production during the run in the CoQ10 supplemented group (22).

As it has been mentioned above, acute exercise causes oxidative stress, particularly when the exercise is intense and vigorous; the fact that can be related with the increase of inflammatory cytokines include IL-12 and IL-6, TNF- α , and CRP (5). It has been demonstrated that exogenous and oral intake of CoQ10 leads to a substantial decline in oxidative stress because of its ability to scavenge hydroxyl radicals and pro-inflammatory cytokines (23). According to this, our results showed a reduction in inflammatory parameters and a modulation of inflammatory signaling.

Plasma IL-6 increases in a progressively fashion with exhaustive activity and is associated to exercise intensity, duration, mass of muscle involved, and muscular endurance capacity (24). This study has shown that a significant increase in IL-6 concentrations cytokine related with physical activity in both groups. CoQ10 supplementation was able to decrease the levels of IL-6 after the run. This effect on IL-6 levels is in accordance with that found for other authors after supplementation with CoQ10 but in different conditions (25, 26).

Generally, the supplementation effects on the TNF- α pathway. We found a significant

increase in the pro-inflammatory cytokine TNF- α , after high-intensity exercise in both groups (Table 2), which is in line with previous findings (2). Yet, CoQ10 supplement significantly attenuated this over-generation of TNF- α in the runner after the high-intensity running compared with the placebo group. TNF- α seems to have a biphasic effect on muscle: high levels of the cytokine promote muscle catabolism, probably by a NF- κ B-mediated effect, whereas low levels of TNF- α , which do not induce NF- κ B, stimulate myogenesis (27). Thus, TNF- α can be associated with muscle regeneration, (28) normally produced by muscle cells, or inhibits myogenesis by activating NF- κ B. In addition, this cytokine is known to inhibit contractile function of skeletal muscle, and it may be related to NO production (29) and increased mitochondrial production of ROS that in turn regulate TNF- α / NF- κ B signaling (28).

Conclusion

CoQ10 short-term supplementation at a dose of 5 mg/kg/d (14-day) can decrease inflammation (TNF- α , CRP and IL-6) in male middle-distance runners. However, acute and short-term supplementation cannot decrease CK after the high-intensity exercise compared with the placebo group. We believe a higher dose of CoQ10 supplements (>5mg/kg/d) might provide sustainable anti-inflammatory in middle-distance runners. However, further study is needed to demonstrate whether a high dose of CoQ10 correlates with health benefits.

References

1. Siddiqui N, Nessa A, Hossain M. Regular physical exercise: way to healthy life. *Mymensingh Medical Journal* 2010;19(1):154.
2. Suzuki K, Yamada M, Kurakake S, Okamura N, Yamaya K, Liu Q, et al. Circulating cytokines and hormones with immunosuppressive but neutrophil-priming potentials rise after endurance exercise in humans. *European Journal of Applied Physiology*. 2000;81(4):281-7.
3. Powers SK, Jackson MJ. Exercise-induced oxidative stress: cellular mechanisms and impact on muscle force production. *Physiological Reviews*.

2008;88(4):1243-76.

4. Gomez-Cabrera MC, Borrás C, Pallardó FV, Sastre J, Ji LL, Viña J. Decreasing xanthine oxidase-mediated oxidative stress prevents useful cellular adaptations to exercise in rats. *The Journal of Physiology*. 2005;567(1):113-20.

5. Kasapis C, Thompson PD. The Effects of Physical Activity on Serum C-Reactive Protein and Inflammatory Markers: A Systematic Review. *Journal of the American College of Cardiology*. 2005; 45(10):1563-9.

6. Zhou S, Zhang Y, Davie AJ, Marshall-Gradisnik SM, Hu H, Wang J, et al. Muscle and plasma coenzyme Q10 concentration, aerobic power and exercise economy of healthy men in response to four weeks of supplementation. *The Journal of Sports Medicine and Physical Fitness*. 2005;45(3):337-46.

7. Ochoa JJ, Quiles JL, Huertas JR, Mataix J. Coenzyme Q10 protects from aging-related oxidative stress and improves mitochondrial function in heart of rats fed a polyunsaturated fatty acid (PUFA)-rich diet. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*. 2005;60(8):970-5.

8. Vinña J, Gomez-Cabrera MC, Lloret A, Marquez R, Miñana JB, Pallardó FV, et al. Free radicals in exhaustive physical exercise: mechanism of production, and protection by antioxidants. *IUBMB Life*. 2000;50(4-5):271-7.

9. Cooke M, Iosia M, Buford T, Shelmadine B, Hudson G, Kerkick C, et al. Effects of acute and 14-day coenzyme Q10 supplementation on exercise performance in both trained and untrained individuals. *Journal of the International Society of Sports Nutrition*. 2008;5(1):1-14.

10. Kaikkonen J, Tuomainen T-P, Nyssönen K, Salonen JT. Coenzyme Q10: absorption, antioxidative properties, determinants, and plasma levels. *Free Radical Research*. 2002;36(4):389-97.

11. Gibson RS. Principles of nutritional assessment: Oxford University Press; 2005.

12. Medicine ACoS. ACSM's health-related physical fitness assessment manual: Lippincott Williams & Wilkins; 2013.

13. Leelarungrayub D, Rawattikanon A, Klaphajone J, Pothongsunan P, Bloomer RJ. Coenzyme Q10 supplementation decreases oxidative stress and improves physical performance in young swimmers; a pilot study. *The Open Sports Med J*. 2010;4:1-8.

14. Thompson WR, Gordon NF, Pescatello LS. ACSM's guidelines for exercise testing and prescription: Hubsta Ltd; 2009.

15. Armstrong R. Mechanisms of exercise-induced delayed onset muscular soreness: a brief review. *Medicine and Science in Sports and Exercise*. 1984;16(6):529-38.

16. Ambrosio F, Kadi F, Lexell J, Fitzgerald GK,

Boninger ML, Huard J. The effect of muscle loading on skeletal muscle regenerative potential: an update of current research findings relating to aging and neuromuscular pathology. *American Journal of Physical Medicine & Rehabilitation*. 2009; 88(2):145-55.

17. Gomez-Cabrera M-C, Domenech E, Viña J. Moderate exercise is an antioxidant: upregulation of antioxidant genes by training. *Free Radical Biology and Medicine*. 2008;44(2):126-31.

18. Bhagavan HN, Chopra RK. Plasma coenzyme Q10 response to oral ingestion of coenzyme Q10 formulations. *Mitochondrion*. 2007;7:S78-S88.

19. Malm C, Svensson M, Ekblom B, Sjödin B. Effects of ubiquinone-10 supplementation and high intensity training on physical performance in humans. *Acta Physiologica Scandinavica*. 1997; 161(3):379-84.

20. Kon M, Kimura F, Akimoto T, Tanabe K, Murase Y, Ikemune S, et al. Effect of Coenzyme Q10 supplementation on exercise-induced muscular injury of rats. *Exerc Immunol Rev*. 2007;13:76-88.

21. Littarru GP, Tiano L. Bioenergetic and antioxidant properties of coenzyme Q10: recent developments. *Molecular Biotechnology*. 2007;37(1):31-7.

22. Sohet FM, Neyrinck AM, Pachikian BD, de Backer FC, Bindels LB, Niklowitz P, et al. Coenzyme Q10 supplementation lowers hepatic oxidative stress and inflammation associated with diet-induced obesity in mice. *Biochemical Pharmacology*. 2009;78(11):1391-400.

23. Tsuneki H, Sekizaki N, Suzuki T, Kobayashi S, Wada T, Okamoto T, et al. Coenzyme Q₁₀ prevents high glucose-induced oxidative stress in human umbilical vein endothelial cells. *European Journal of Pharmacology*. 2007;566(1):1-10.

24. Pedersen B, Steensberg A, Fischer C, Keller C, Keller P, Plomgaard P, et al. The metabolic role of IL-6 produced during exercise: is IL-6 an exercise factor? *Proceedings of the Nutrition Society*. 2004; 63(02):263-7.

25. Gökbel H, Gergerlioğlu HS, Okudan N, Gül İ, Büyükbay S, Belviranlı M. Effects of Coenzyme Q10 supplementation on plasma adiponectin, interleukin-6, and tumor necrosis factor- α levels in men. *Journal of Medicinal Food*. 2010;13(1):216-8.

26. Bessler H, Bergman M, Blumberger N, Djaldetti M, Salman H. Coenzyme Q10 Decreases TNF- α and IL-2 Secretion by Human Peripheral Blood Mononuclear Cells. *Journal of Nutritional Science and Vitaminology*. 2010; 56(1):77-81.

27. Reid M, Li YP. Cytokines and oxidative signalling in skeletal muscle. *Acta physiologica scandinavica*. 2001;171(3):225-32.

28. Kuru S, Inukai A, Kato T, Liang Y, Kimura S, Sobue G. Expression of tumor necrosis factor- α in regenerating muscle fibers in inflammatory and non-

-
- inflammatory myopathies. *Acta Neuropathologica*. 2003; 105(3):217-24.
29. Glass DJ. Skeletal muscle hypertrophy and atrophy signaling pathways. *The International Journal of Biochemistry & Cell Biology*. 2005; 37(10): 1974-84.