



Review

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Effect of high-dose vitamin C and E supplementation on muscle recovery and training adaptation: a mini review

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INTRODUCTION

Nutrition is a critical factor in the optimization of post-exercise muscle recovery and training adaptation. Therefore, those engaged in regular exercise have used supplementation as part of their training routine¹. Among nutritional methods, antioxidant supplementation is the most popular in the general population and athletes to reduce oxidative stress during exercise². **Oxidative stress is defined as an imbalance between reactive oxygen species (ROS) and antioxidant defense**³. Exercise-induced oxidative stress may enhance the natural, endogenous antioxidant defense systems as well as lead to muscle damage and fatigue, which can cause reduced performance^{4,5}. Among the tissues in the human body, skeletal muscles are highly correlated with athletic performance. Thus, the oxidative stress response and control of the skeletal muscles are important in training adaptation.

Antioxidant supplementation is essential to reducing exercise-induced oxidative stress, and the most frequently consumed supplements are vitamins C and E⁴. In a previous study, over 60% of athletes were found to take vitamin supplements, of which vitamins C and E accounted for 97.5% and 78.3%, respectively⁶. Studies have also reported that antioxidant supplementation could effectively reduce oxidative stress and muscle damage during exercise⁷. On the other hand, there other studies reported contrasting results that suggest vitamins C and E supplementation do not contribute to reduced oxidative stress, muscle damage, and performance^{8,9}.

The negative effects of vitamins C and E supplementation at high doses were reported to reduce performance and hypertrophy by impairing skeletal muscle adaptation, while highlighting the indispensable role of oxidative stress in the cellular adaptation process exhibited by skeletal muscles^{4,5,10}. Recently, Dutra et al.¹¹ suggested that most current scientific evidence indicates that **vitamins C and E supplementation could weaken muscle hypertrophy over time** without facilitating muscle growth, as supplementation had no effect on muscle force production following chronic strength training. Despite the concerns raised by such diverse findings, many people still take vitamin C or E supplements at rest or after exercise, and the consumption of antioxidant supplements has substantially increased in both professional and amateur athletes⁴. This study aimed to present a specific set of data on how to view vitamin C and E supplementation in the exercise field by analyzing previous studies on the effects of

[Purpose] This review aimed to investigate the effects of high-dose vitamins C and E supplementation combined with acute or chronic exercise on muscle recovery and training adaptation.

[Methods] We used PubMed, Web of Science, and Wiley Online Library databases to perform a literature search based on the keywords 'vitamin C, vitamin E, antioxidants, muscle recovery, training adaptation, and oxidative stress'.

[Results] Vitamin C or E supplementation has been reported to contribute to a reduction in oxidative stress and muscle damage; however, there is currently inadequate evidence of their positive effects on muscle recovery. Long-term vitamin C or E supplementation can have negative effects on physiological phenomena required for training adaptation, such as strength, muscle hypertrophy, and endurance. Numerous studies emphasized that an adequate diet consisting of fruits and vegetables is a more appropriate way of consuming antioxidants than supplementation.

[Conclusion] The effects of high-dose vitamin C and E supplementation on post-exercise muscle recovery remain unclear and ambiguous, although there is evidence of potential negative effects on training adaptation.

[Keywords] antioxidants, athletes, muscle recovery, training adaptation, vitamin C, vitamin E

high-dose vitamin C and E supplementation combined with acute or chronic exercise on muscle recovery and training adaptation.

HIGH-DOSE VITAMIN C AND E SUPPLEMENTATION AND MUSCLE RECOVERY

In general, high-intensity or prolonged exercise causes muscle damage, which is accompanied by increased oxidative stress and inflammation¹². Antioxidant supplementation not only lowers the ratio of glutathione to oxidized glutathione that is produced during exercise, but also suppresses oxidative stress characterized by increased levels of lipid peroxidation markers, malondialdehyde, and total lipid peroxidation¹³. While vitamin C or E supplementation has been used after high-intensity exercise to reduce oxidative stress and facilitate muscle recovery, its effects remain unclear.

Chou et al.¹⁴ investigated the effects of vitamin C (2000 mg) and E (1400 IU) supplementation on muscle damage and inflammation in elite athletes after simulated Taekwondo matches and reported that compared to the placebo group, the vitamin groups showed lower levels of creatine kinase (CK) and myoglobin (Mb), which were used as indicators of muscle cell membrane damage. Gabriel et al.¹⁵ examined the effect of consuming 500 mg vitamin C capsules after breakfast for 90 days in male adolescents who participated in recreational activities and reported that the plasma levels of CK, lactate dehydrogenase (LDH), malondialdehyde (MDA), urea, uric acid, and C-reactive protein (CRP) were significantly reduced after vitamin C intake. Righi et al.¹⁶ explored the role of vitamin C in acute exercise by conducting a meta-analysis and reported that vitamin C reduced oxidative stress and inflammatory responses after acute exercise.

In contrast, there are reports that vitamin C or E supplementation does not affect skeletal muscle recovery. Dawson et al.¹⁷ investigated the effect of daily supplementation with vitamin C (500 mg or 1000 mg) and vitamin E (500 IU or 1000 IU) for four weeks on muscle damage indicators in 15 male long-distance runners after a 21 km run. The results showed that CK, Mb, and malondialdehyde levels did not vary significantly between the vitamin supplementation and placebo groups. Bailey et al.¹⁸ conducted a study in which healthy young men were administered vitamin C and E supplements for six weeks, after which they were instructed to perform intermittent shuttle running. Vitamin C and E supplementation following the muscle damage caused by exercise did not affect oxidative stress and inflammation indicators or the recovery of muscle function. Additionally, professional soccer players administered vitamin C (500 mg) and E (400 IU) supplementation before performing plyometric jumping and strength resistance training did not show changed in the levels of CK or delayed onset muscle soreness (DOMS) during recovery, and muscle function remained unimproved, indicating a lack of any effect on muscle recovery¹³.

Martínez-Ferrán et al.⁹ also conducted a study on runners who participated in resistance training and reported that vitamin C (1000 mg) and E (235 mg) supplementation did not significantly affect any of the tested indicators, including post-exercise CK; rather, the results indicated that antioxidants could prevent or delay post-exercise recovery. Teixeira et al.¹⁹ administered antioxidant supplementation with tocopherol (272 mg) and vitamin C (400 mg) for four weeks to kayakers who were then instructed to perform a 1000 m kayak race and no effects on indicators such as interleukin-6 (IL-6) and thiobarbituric reactive acid substances (TBARS). Instead, they reported that the CK level was reduced to a far greater degree in the placebo group than in the antioxidant supplementation group. Thus, Teixeira et al.¹⁹ suggested that antioxidant supplementation is not recommended for an already well-trained individual to ameliorate exercise-induced oxidative stress or muscle damage. Hence, while the ROS generated during exercise could be a protective mechanism that limits additional muscle damage, such protection would be inhibited by antioxidant supplementation and lead to a greater level of muscle damage that could delay recovery^{19,20}.

A recent study by Martínez-Ferrán et al.²¹ on exercise-induced muscle damage highlighted that currently available evidence for the protective effect of vitamins C and E is not definitive. The authors also pointed out that not all studies report clear benefits of vitamins C or E. Similarly, in a meta-analysis conducted by Torre et al.²² also concluded that current evidence is inadequate for verifying the effect of antioxidants such as vitamins C or E in minimizing post-exercise DOMS, despite the positive effect reported in certain studies.

HIGH-DOSE VITAMIN C AND E SUPPLEMENTATION AND TRAINING ADAPTATION

Performance (i.e., strength or endurance) or muscle hypertrophy can be improved by long-term exercise. Training adaptation is the basis of such improvements and an essential part of successfully attaining exercise goals²³. However, high-dose vitamin C and E supplementation has been reported to disturb physiological phenomena required for training adaptation, and potentially weaken strength or muscle hypertrophy in the long run^{10,24}. A recent meta-analysis also showed that vitamin C and E supplementation had no positive effect on strength and did not facilitate muscle hypertrophy, although it may also have had negative effects¹¹.

Paulsen et al.¹⁰ conducted a study on recreationally strength-trained men and women who were administered vitamins C (1000 mg) and E (235 mg) for 10 weeks. The authors reported that the post-exercise phosphorylation of p38 mitogen-activated protein kinase (MAPK), extracellular signal-regulated protein kinases 1 and 2, and 70-kDa ribosomal protein S6 kinase (p70S6K) was reduced, while strength increase was hampered. In Bjørnsen et al.²⁴, elderly men participated in a 12-week strength training program

that included vitamin C (500 mg) or vitamin E (117.5 mg) administration before and after the training. The results showed that the total lean mass increased more in the placebo group than in the vitamin C and E groups, while the thickness of the rectus femoris muscle also increased more in the placebo group than in the vitamin C and E groups. Thus, the authors suggested that training adaptation in the elderly is impaired by high-dose vitamin C and E supplementation. Similarly, in a recent study by Martínez-Ferrán et al.²⁵, upper body strength and hypertrophic adaptation in men decreased after 10 weeks of strength training with vitamins C and E supplementation. Dutra et al.²⁶ conducted a 10-week strength training program with vitamin C (1,000 mg) and vitamin E (235 mg) supplementation that showed that post-exercise peak torque and total work in the vitamin C and E groups were not different than those of the placebo group of adult females. However, when the two groups were compared with the control, the peak torque and total work were higher in the placebo group, indicating that athletic performance could be reduced by chronic antioxidant supplementation.

High-dose vitamin C and E supplementation was also shown to have similar effects on endurance training. Young men and women who participated in endurance training and were administered a daily supplement of vitamin C (1000 mg), vitamin E (235 mg), or a placebo for 11 weeks showed that in the vitamin C and E groups, the levels of the mitochondrial biosynthesis markers, cytochrome c oxidase subunit IV (COX4) and cytosolic peroxisome proliferator-activated receptor- γ coactivator 1 α (PGC-1 α), were lower compared to the placebo group, which indicated that cellular adaptations could be impaired by vitamins C and E²⁷. Morrison et al.²⁸ also reported that when healthy young men were administered vitamins C (1000 mg) and E (400 mg) for four weeks followed by four weeks of endurance

training, the mitochondrial transcription factor A (TFAM) was reduced when compared with placebo group. PGC-1 α is a member of a family of transcription factors that play a key role in regulating cellular energy metabolism. During chronic endurance training, PGC-1 α stimulates mitochondrial biogenesis to create a more oxidative metabolic environment²⁹. However, Yada and Matoba³⁰ showed that PGC-1 α levels after training were not affected by high-dosage vitamin C supplementation, which also did not interfere with mitochondrial biogenesis, but it should be noted that the study conducted using an animal model.

The potential mechanism of the effect of high-dose vitamins C and E supplementation on training adaptation could be explained by some studies in the field (Figure 1). Some studies have suggested that antioxidant supplementation could reduce normal redox signaling in the muscle and have a negative effect on training adaptation^{31,32}. High doses of antioxidants from supplementation reduced the induction of favorable redox signaling associated with exercise, assuming that the redox status of the body fell within the normal range³². Gomez-Cabrera³¹ also hypothesized that redox signaling could be key to normal molecular and cellular reactions induced by exercise; whereas, certain ROS and reactive nitrogen species (RNS) generated in the body serve as important signaling molecules. In a recent study, supplementation with antioxidants such as vitamins C and E was reported to potentially disturb the optimal cellular redox status, which could have a positive effect on strength and muscle hypertrophy responses²⁶. In fact, high-dose vitamin C and E supplementation was shown to reduce hypertrophic signaling¹⁰. Moreover, redox signaling was reported to play a key role in mitochondrial biogenesis in skeletal muscles, and chronic endurance training could reduce the negative consequences of oxidative stress by increasing the expression and activity of endogenous antioxidant enzymes².

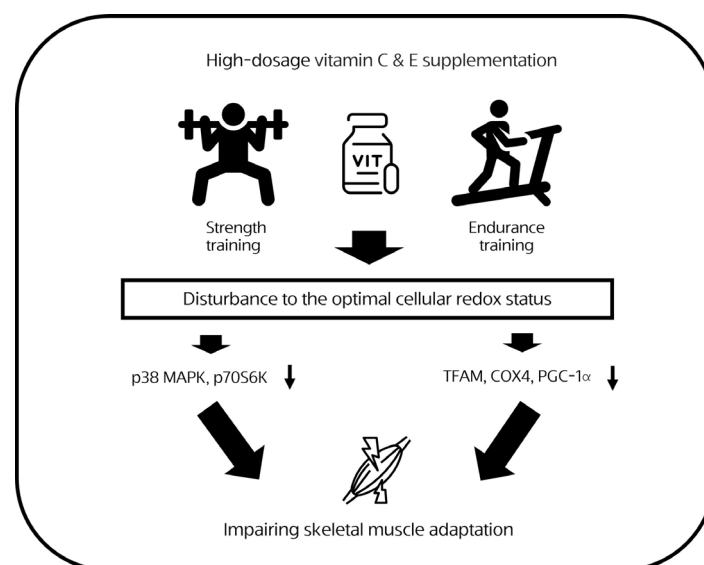


Figure 1. Potential mechanism of high-dosage vitamin C and E supplementation on training adaptation. COX4: cytochrome c oxidase subunit IV; MAPK: mitogen-activated protein kinases; p70S6K: 70-kDa ribosomal protein S6 kinase; PGC-1 α : peroxisome proliferator-activated receptor- γ coactivator 1 α ; TFAM: mitochondrial transcription factor A.

THE USE OF VITAMIN C AND E SUPPLEMENTATION IN THE EXERCISE FIELD

These recent studies highlight that exercise-induced oxidative stress plays an important role in regulating intracellular mechanisms and markedly contributes to the diversity of cell signaling associated with training adaptation. These studies also reported that cellular exposure to high levels of antioxidants may reduce or block cell signaling pathways to reduce the physiological adaptation of cells^{4,5}. High-dose vitamin C and E supplementation was also reported contradictory evidence of the effects on performance and redox homeostasis; therefore, permanent intake of non-physiological doses of vitamins C and E was not recommended for healthy individuals engaged in regular exercise³³. These reports suggest that care should be taken when administering vitamin C and E supplementation in the general population and in athletes because of their potential negative effects on regular training.

Several studies have recommended whole-food intake rather than supplementation as a suitable method for antioxidant delivery. The intake of vitamins through a balanced and well-diversified diet has been suggested as the best way to promote optimal antioxidant status^{1,4,34}. In Antonioni et al.³⁵, the antioxidant requirement during sports training was reported to be either equivalent to or covered at a dose close to the recommended dietary allowance (RDA), and that antioxidants were provided by a balanced and well-diversified diet. In a recent study by Higgins et al.⁴, no additional benefit was ensured by vitamin C or E supplementation, except in special circumstances like altitude training. The study also emphasized that athletes should focus on the intake of fruits, vegetables, and other plant-based foods enriched with antioxidants. In addition, Higgins et al.⁴ suggested that if the priority is to reduce oxidative stress and inflammation, a balanced diet consisting of a mixture of fruits, vegetables, and berries is recommended, and supplementation with antioxidant-enriched beverages may be necessary.

Vitamin C or E supplementation should not be entirely excluded from the exercise field because it could be valuable in certain circumstances^{1,4,36,37} where 1) rapid muscle recovery is needed within a short recovery time, such as in a tournament; 2) an athlete is engaged in altitude training; 3) supplementation has been recommended by a doctor or sports dietitian due to nutritional deficiency; 4) energy intake is being controlled or restricted for weight loss; 5) rehabilitation is ongoing after a tendon or ligament injury; and 6) antioxidants cannot be adequately acquired through food intake. Under these circumstances, supplementation may be a valid option.

The effects of high-dose vitamin C and E supplementation on post-exercise muscle recovery are unclear and ambiguous, although there is evidence that it may have negative effects on training adaptation. Although it is difficult to draw a definite conclusion about the effects of vitamin C and E supplementation due to differences in the characteristics of participants, experimental methods, and supple-

mentation protocols used in each study, the current evidence suggests that acquiring antioxidants through a balanced and well-diversified diet is generally better than taking vitamin supplements.

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