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REVIEW ARTICLE

Recovery response of coenzyme Q_{10} to exercise-related physiological muscle damage, inflammation and oxidative stress: A systematic review

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Abstract

This systematic review aims to demonstrate that coenzyme Q_{10} (CoQ_{10}) supplementation may be an effective molecule in improving exercise performance and recovering muscle damage, improving antioxidant capacity, and suppressing inflammatory processes. The study covers the literature in PubMed, Google Scholar, Web of Science and Scopus databases from 2011 to 2023. The final review was conducted on June 6. In the literature analysis, eight keywords (exercise, oxidative stress, CoQ_{10}, muscle damage, inflammation, skeletal muscle, heart muscle, and performance) were employed to investigate the publications. The full texts of 362 full texts of articles were included in this study. These were analyzed according to the PRISMA reporting criteria. In the analysis, one study was conducted with experimental animals, two studies were conducted with male and female participants, and 12 studies were conducted with only male participants. Participants in twelve studies were well-trained. However, two studies were conducted with a sedentary group. In addition, CoQ_{10} supplementation was present in all studies. CoQ_{10} supplementation was between 5-60 mg/kg in 4 studies and 100 mg/kg and above in the remaining 10 studies. Antioxidant capacities and inflammation markers were among the parameters of most interest. There were fewer studies on skeletal and cardiac muscle damage and performance markers. CoQ_{10} supplementation during intense exercise elevates plasma CoQ_{10} and antioxidant levels while reducing inflammation markers. Additionally, it enhances contractile function in sarcomeres and cardiomyocytes. Nevertheless, additional studies are necessary to comprehensively as certain CoQ_{10} impact on athletic performance.

Introduction

Exercise represents a major challenge to whole-body homeostasis, triggering acute and adaptive responses at cellular and systemic levels. This challenge causes some physiological changes by modulating various signaling pathways (Bouviere et al., 2021). The state induced by exercise promotes oxidative stress in skeletal muscle by heightening the generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) (Di Meo et al., 2019). While aerobic organisms possess an efficient antioxidant defense system to counteract the oxidative impact of these reactive metabolites, an imbalance occurs when their production surpasses cellular antioxidant capabilities, leading to heightened oxidative stress. This elevation contributes to structural and functional alterations within cells, triggering the onset of various pathological conditions (Di Meo et al., 2019). Specifically, a single session of intense or prolonged exercise generates elevated ROS levels, which can result in tissue damage, dysfunction, and compromised contractility (Di Meo et al., 2019). Excessive ROS elevation leads to modifications in cellular proteins, lipids, and DNA, culminating in cellular damage (Nordberg & Arnér 2001; Patwell et al., 2004; Gomez et al., 2015). ROS are also associated with prolonged muscle contraction and early muscle fatigue during exercise (Lamb & Westerblad, 2011). Antioxidant responses are required to eliminate or reduce the negative effects of ROS on performance, fatigue, and muscle damage (Vincent et al., 2000; McArdle et al., 2001). Typically, both acute and chronic exercise boosts the expression and activity of internal antioxidant enzymes within skeletal muscle, aiming to counteract the adverse impact of ROS (Braun et al., 2009). Nevertheless, athletes often turn to external antioxidant

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supplements regularly to enhance the skeletal muscle's capability to neutralize ROS generated during exercise (Petróczi et al., 2008). Antioxidant supplements contribute to the improvement of cellular redox status or the reduction of oxidative modifications in DNA, lipids and proteins (Jäger et al., 2019). There is evidence suggesting that antioxidants might facilitate the recovery from muscle damage post-intense exercise (Jäger et al., 2019). Presently, endurance athletes commonly use antioxidant supplements to reduce exercise-induced oxidative stress, expedite recovery, and potentially enhance performance (Mason et al., 2020). Among the favored antioxidant supplements is coenzyme Q10 (Drobnic et al., 2022). After CoQ_{10} was discovered in the 1970s and its association with exercise was established, its bioenergetics role in muscle contraction, its muscle-protective effect, and its role in inflammatory processes were examined (Drobnic et al., 2022). CoQ_{10} is believed to play a crucial role in hindering peroxidative damage to membranes and combating oxidation induced by free radicals (Gutierrez et al., 2020). Its contribution to energy production, particularly through its function as an electron carrier in mitochondrial biogenesis, underscores its significance as a supplement (Lenaz et al., 1999). Apart from its primary role in mitochondria, CoQ_{10} serves various other functions. These include its involvement in signal generation through oxidant action, regulation of cellular redox status, contribution to proton gradient formation in the endomembrane and plasma membrane, and its role in modulating membrane structure and phospholipid status (Gutierrez et al., 2020). The most prominent and relevant function of CoQ_{10}, which has attracted attention since its first discovery, is its effect on antioxidant capacity (Gutierrez et al., 2020). Hence, CoQ_{10} plays a vital role in energy production and serves as a preventive measure against peroxidative damage and oxidation induced by free radicals on membrane phospholipids (Sarmiento et al., 2016). However, although the popularity of CoQ_{10} and its dramatic responses to exercise-induced metabolic changes, there has not yet been a comprehensive overview of the use and effects of CoQ_{10} in exercise conditions. This approach has the potential to be a practical reference source in determining the direction of future research. Therefore, the research has been based on the hypothesis that CoQ_{10} may have important functions on exercise-induced metabolic changes and aimed to evaluate the level of response of CoQ_{10} supplementation to exercise-induced metabolic stress through metabolic parameters.

Methods

Study Design

This systematic review was conducted following the guidelines set forth by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Page et al. 2021). For the data to be eligible for inclusion, subjects had to be healthy and exposed to the exercise intervention and CoQ_{10} supplementation. Therefore, we excluded studies that did not include these three keywords as an established exclusion criterion. In this context, the research focused on antioxidants, CoQ_{10}, exercise, muscle damage, sports performance and inflammation. The research conducted was analysed by YY, BY and MEY and was independently cross-examined to generate findings. In case of any disagreement, the fourth and fifth authors, ÖS and VC, were consulted. The "Cochrane risk of bias" tool was used to assess the risk of bias (Higgis et al., 2008).

The articles published in PubMed, Web of Science, Scopus and Google Scholar databases using the keywords "antioxidant, CoQ_{10}, exercise performance, inflammation, cardioskeletal muscle damage, oxidative stress" until 6 June 2023 were included in the research. A total of 4485 researches were obtained by using the mentioned keywords. Then, three authors (YY, BY and MEY) independently reviewed the titles and abstracts of these articles and identified 362 studies for eligibility assessment. Out of these, 348 studies were excluded for various reasons, including those inaccessible in full text pilot studies, systematic/meta-analyzed reviews, congress abstracts, case reports, duplications across databases, and those not published in English, were excluded. Eventually, 14 studies met the criteria and were included in the review. The search strategy encompassed three sets of keywords: one for study design, another for participant groups, and a third focused on dietary supplements. The full texts of the studies that were deemed to meet the inclusion criteria were evaluated separately by two independent, blind researchers, and the studies that both researchers deemed appropriate were included in the study.

Results

In the initial literature review across databases, a total of 4,485 results were obtained. Upon evaluating the titles and abstracts, 362 articles were selected for full-text assessment. Ultimately, only 14 papers met the eligibility criteria for inclusion in this review. Figure 1

depicts the PRISMA flow diagram illustrating the selection process for the studies included in this review.

It is seen that 2 of the 14 included articles were conducted with sedentary individuals, while the participants in 12 articles were well-trained. In general, CoQ_{10} supplementation in the articles was from 5 mg to 300 mg, but in 9 studies this was at a dose of 100 mg and over. In addition, a placebo-controlled design is seen in all studies. The research includes both genders, but the proportion of male participants is higher. The research analyzed in this review includes experimental animal and human studies. Table 1 outlines authors/years, study design, participant, gender, exercise history, CoQ_{10} dose/duration, exercise type-duration and results.

Discussion

The Relationship between Exercise, CoQ_{10} Supplementation and Plasma Levels

An exercise load of more than six metabolic equivalents (METs) per minute can have detrimental effects on the organism by inducing a feeling of exhaustion. Additionally, this load, which negatively affects cells, can cause muscle damage and hematologic changes by stimulating the high production of pro-inflammatory regulators related to sports anemia (Kokkinos, 2008). In this context, Diaz-Castro et al. (2020) found that plasma ubiquinol (reduced form of CoQ_{10}) levels increased in the experimental group at the end of circular strength training interventions consisting of 10 repetitions and 10 different stations with a perceived difficulty of 6-7 points (according to OMNI-RES, a perceived exertion scale) compared to placebo. Based on the assumption that ubiquinol-10 supplementation would increase plasma CoQ_{10} levels, Suzuki et al. (2021) administered 300 mg/kg ubiquinol-10 daily to 16 male university students who were long-distance runners and observed that CoQ_{10} concentrations increased up to 5.62 µg/mL in plasma samples obtained from participants who ran 25 km on day 7 and 45 km on day 9. Additionally, 300 mg/day ubiquinone supplementation given to 31 well-trained university athletes for 12 weeks significantly increased the plasma CoQ_{10} levels of the experimental group compared to placebo (Ho et al., 2020). When Drobnic et al. (2020) compared CoQ_{10} given 100 mg/kg for 30 days to elderly volunteer runners with a control group, the plasma CoQ_{10} levels of the experimental group moved significantly upwards. The supplement group, comprising sedentary young men, displayed a noteworthy rise in plasma CoQ_{10} levels following 4 weeks of receiving 200 mg/kg CoQ_{10} supplementation. This increase was observed after engaging in eccentric exercises (Okudan et al., 2018). As a result, under exercise conditions, compared to placebo groups, participants receiving CoQ_{10} supplementation exhibited an upward increase in plasma CoQ_{10} levels.

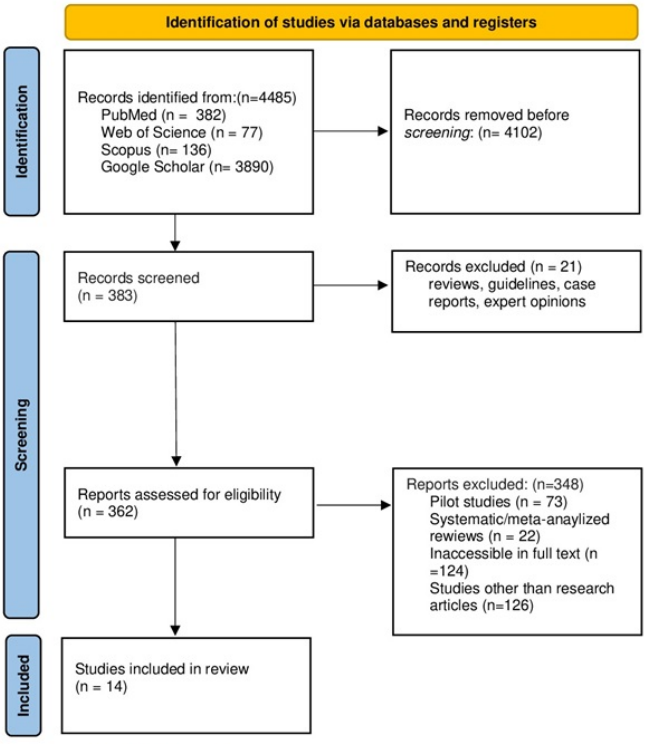

Figure 1. PRISMA flow diagram.

Table 1
The characteristics of the included studies.

Authors, Year	Research Design	Participant, Gender	Exercise History	Dose of CoQ_{10}, Duration	Exercise Type and Duration	Antioxidant Capacity	Performance	Oxidative Stress	Muscle Damage
Gül et al. (2011)	Randomized, double-blind, crossover design	Healthy Male (n=50)	Sedentary	100 mg/kg during 8 weeks	Wingate test	GPx ↔ SOD ↔	NO ↔	MDA ↓	
Bloomer et al. (2012)	Randomized, double-blind, cross-over design	Healthy Male/Female (n=15)	Well trained runners	300 mg/kg during 4 weeks	Aerobic running and HIIT		HR; bpm ↔ PP (watts) ↔ TW (kJ) ↔		
Díaz-Castro et al. (2012)	Randomized, placebo-controlled design	Healthy Male (n=20)	Well trained amateur athletes	5 capsules of 30 mg (1 capsule 2 days before the test, 3 capsules on the previous day (breakfast, lunch, and dinner), 1 capsule the same day of the run.	The total distance of the test was 50 km across the highest road in Europe with an initial altitude of 640 m and final altitude (arrival) of 3,393 (increase of 2,800 m).	TNF-α ↓ CAT ↑ GPx ↔	IsoPs ↓	8-OHdG ↓ OSI ↓ TOS ↑ H_2O_2 ↓	
Armanfar et al. (2015)	Randomized and quasi-experimental design	Middle-distance Male (n=18)	Well trained runners	5 mg/kg during 14 days	Competitive 3000 meters running	TNF-α ↓ IL-6↓	LA ↓	CRP ↓	CK ↓
Pala et al. (2016)	Randomized, experimental design	Wistar rats (n=28), Male	Well trained rats	300 mg/kg during 42 days	6-week chronic exercise	NFκB ↓ IκB ↑ Nrf2 ↑ HO-1 ↑			
Emami et al. (2018)	cross-sectional and experimental design with a controlled design	Elite athletes Male (n=36)	Well trained swimmers	300 mg/kg during 14 days	Freestyle swimming (800+200+50m)	TAS ↑ Plasma CoQ_{10} ↑	cTnL ↓	LPO ↓	CK ↓ LDH↓

Table 1
Continued.

Authors, Year	Research Design	Participant, Gender	Exercise History	Dose of CoQ_{10}, Duration	Exercise Type and Duration	Antioxidant Capacity	Performance	Oxidative Stress	Muscle Damage
Okudan et al. (2018)	Randomized, double-blind and placebo-controlled design	Young participant Male (n=21)	Sedentary	200 mg/kg during 4 weeks	Eccentric exercise protocols (90° flexion and 180° extension, velocity 60°/s) through isokinetic exercise dynamometry	Plasma CoQ_{10} ↑			
Diaz-Castro et al. (2020)	Randomized, double-blind, and placebo-controlled design	Healthy participant Male (n=100)	Well trained fireman	200 mg/kg during two weeks	Two identical strenuous exercise tests (CWT) with a rest period between tests of 24 h	IL-1, IL-8 ↓ Plasma CoQ_{10} ↑	VEGF ↑ NO ↑ EGF ↑	MCP-1 ↓	
Ho et al. (2020)	Randomized, double-blind, placebo-controlled	University students Male/Female (n=31)	Soccer and Taekwondo teams	300 mg/kg during 12 weeks	Regular Soccer and Taekwondo training practices for 12 weeks	Plasma ubiquinone (CoQ_{10}) ↑			
Drobnic et al. (2020)	Randomized, intervention-controlled, single-center clinical design	Healthy aging participant Male (n=20)	Performing regular exercise for more than 4 hours per week runners	100 mg/kg during 30 days	Incremental maximal test until exhaustion on a motorized treadmill	TAS ↑ TNF-α ↓ IL-6-8-10 ↓ Plasma ubiquinone (CoQ_{10}) ↑		MDA ↓	
Suzuki et al. (2021)	Placebo-controlled, double-blind design	University students Male (n=16)	Long-distance runners	300 mg/kg during 12 days	Comprised 25- and 40-km runs on days 7 th and 9 th	Plasma ubiquinone (CoQ_{10}) ↑			
Broome et al. (2021)	Randomized, double-blind, placebo-controlled crossover design	Healthy participant Male (n=19)	Distance cycled per week for 6 months before study, Cyclists	20 mg/kg during 12 days	The performance trial consisted of 45 min cycling at a fixed workload eliciting 70% VO2peak followed by an 8 km time trial.		LA ↓ CO ↓ NEFA ↓ FO ↑ PO ↑ RPE ↑	F_2IsoP↓ LPO ↓	

Table 1
Continued.

Authors, Year	Research Design	Participant, Gender	Exercise History	Dose of $CoQ_{10,}$ Duration	Exercise Type and Duration	Antioxidant Capacity	Performance	Oxidative Stress	Muscle Damage
Suzuki et al. (2021)	Placebo-controlled, double-blind trial	Healthy participant Male (n=16)	Well trained Runners	300 mg/kg during 12 days	Comprised 25 and 40 km runs on days 7 th and 9 th	Plasma ubiquinone (CoQ_{10}) ↑			CK ↓ ALT ↓ LDH ↓
Ovchinnikov et al. (2022)	Randomized, placebo-controlled	Healthy participant Male (n=30)	Well trained Runners	60 mg/kg during 10 days	HIIT (three repetitions of 100 m)		HR; bpm ↓ LA ↓	SI ↓	

CWT; Circuit weight training, TNF-α; tumor necrosis factor alpha, CRP; C-reactive protein, IL-6; interleukin 6, 8-OH-dG; 8-hydroxyguanosine, OSI; oxidative stress index, IsoPs; isoprostanes generation, H_2O_2; hydroperoxides, TOS; total oxidant status, VEGF; Vascular endothelial growth factor, NO; nitric oxide, IL-1; interleukin 1, IL-8; interleukin 8, EGF; epidermal growth factor, MCP-1; monocyte chemoattractant protein-1, IL-10; interleukin 10, LPO; lipid peroxidation, LA; lactate, NEFA; non- esterified fatty acid, FO; Fat oxidation, CO; Carbohydrate oxidation, PO; power output (both each km of the time trial and during the time trial following 6 weeks), RPE; respiratory, gasses and measures of rating of perceived exertion, F_2IsoP; F_2-isoprostane concentration TAS; total antioxidant status, MDA; malondialdehyde, CK; Creatine kinase, cTnL; troponin, LD; Lactate dehydrogenase, SOD; superoxide dismutase, GPx; glutathione peroxidase, CAT; catalase, SI; stress index, NFκB; nuclear factor kappa-light chain-activated B cells, IκB; kappa B inhibitors, Nrf2; nuclear factor erythroid 2, HO-1; heme oxygenase; PP; peak power, TW; total work.

Exercise, CoQ_{10} Supplementation and Inflammatory Responses

Regular and planned exercise (Matheson et al., 2011) has many beneficial effects such as reducing age-related changes in nuclear pore complex proteins, protecting the neuromuscular junction and increasing the lifespan of sensitive motoneurons, and maintaining neuromuscular integrity and innervation status (Gillon et al., 2018) LaRoche et al., 2018). Exercise also plays an important role in accelerating blood flow, improving vascular integrity, increasing angiogenesis (Yasul, 2021; Yasul et al., 2023), reversing rarefaction and hypertension, and improving cerebral blood flow and cognition (Norling et al., 2020). On the other hand, exercise induces oxidative stress, hematologic changes and a series of inflammatory effects involved in activating catabolic pathways leading to muscle damage (Abbasi et al., 2014). Moreover, exercise causes muscle soreness, long-term loss of muscle function, increased free radical output, suppression of pro-inflammatory signaling, impairment of immune functions including immunoglobulin production or T-cell function, and structural damage to muscle cells with leakage of muscle proteins into the circulation (Simon, 2015). In this context, physical activity of short duration and high or prolonged moderate intensity was associated with an increase in oxidative stress, inflammation and pro-inflammatory modulators (Zhou et al., 2005; Powers & Jackson, 2008) and it was reported that exercise caused membrane cell damage or inflammatory responses in muscle cells (Gomez-Cabrera et al., 2005). According to the literature, CoQ_{10} supplementation may be an important opportunity to eliminate the negative processes resulting from exercise effects, improve hematological parameters, reduce performance-related inflammatory signals and support muscle regeneration processes (Sarmiento et al., 2016). Armanfar et al. (2015) determined that tumor necrosis factor alpha (TNF-α), C-reactive protein (CRP) and interleukin 6 (IL-6) levels decreased in middle-distance runners after 14 days of CoQ_{10} supplementation. Díaz-Castro et al. (2012) similarly observed that CoQ_{10} supplementation to highly trained male amateur athletes decreased 8-hydroxyguanosine (8-OH-dG) levels in addition to TNF-α levels and suppressed oxidative stress that causes RNA damage. Recently, Díaz-Castro et al. (2020) investigated the effect of circular strength training on inflammation markers and the role of CoQ_{10} supplementation on these markers and found that athletes receiving CoQ_{10} had an increase in growth factors such as VEGF (vascular endothelial growth factor), NO (nitric oxide), EGF (epidermal growth factor) and a decrease in IL-1, IL-8 and monocyte chemoattractant protein-1 (MCP-1). Drobnic et al. (2020) reported that not only being physically active but also regular CoQ_{10} supplementation significantly decreased inflammatory markers such as IL-6, IL-8, IL-10 and TNF-α. In conclusion, it can be observed that the metabolic load due to exercise activates inflammatory markers. Furthermore, the effort of CoQ_{10} to keep this mobilization within acceptable limits is noteworthy.

Exercise, CoQ_{10} Supplementation and Antioxidant Responses

While the scientific community acknowledges the positive impact of regular exercise on diverse health indicators, it's also established that exercise induces a considerable systemic increase in levels of reactive oxygen species (ROS) (Powers & Jackson, 2008). High levels of ROS production suppress the endogenous antioxidant defense network, resulting in damage to cellular proteins, lipids and DNA and impaired cellular function. Therefore, chronic oxidative stress triggers the pathogenesis of various diseases, especially muscle contractile functions (Powers et al., 2011). However, it should not be ignored that transient and exercise-induced increases in skeletal muscle ROS production are necessary for optimal contractile function (Meo et al., 2017; Andrade et al., 2001). Although there are suggestions that antioxidant supplementation attenuates exercise-induced redox signaling and training adaptations (Merry & Ristow 2016) and impairs training-induced recovery (Laaksonen et al., 1995; Malm et al., 1997), the increased demand for O_2 and hydrogen peroxide (H_2O_2), especially in acute exercise, impairs calcium release in the sarcoplasmic reticulum and myofibrillar calcium sensitization, leading to muscle fatigue (Allen et al., 2008; McKenna et al., 2006). Therefore, exogenous antioxidant supplementation increases the capacity of skeletal muscle to neutralize ROS. It is also an important strategy to improve athletic performance by delaying the onset of muscle fatigue (Braakhuis & Hopkins, 2015; Mason et al., 2020).

CoQ_{10} consists of a ubiquinone moiety conjugated to a lipophilic triphenylphosphonium cation (Ross et al., 2005). The triphenylphosphonium cation facilitates the accumulation of mitoQ in mitochondria to a greater extent than in the cytoplasm, driven by plasma and mitochondrial membrane potentials (Ross et al., 2005). Within mitochondria, mitoQ is reduced to ubiquinol,

which acts as a chain-breaking antioxidant, directly or indirectly preventing lipid peroxidation (James et al., 2004). Williamson et al. (2020) reported that mitoQ protected against exercise-induced increases in mitochondrial DNA damage. Broome et al. (2021) found that 20mg/g CoQ_{10} supplementation administered to 19 middle-aged recreational cyclists for 28 days resulted in a protective effect against lipid peroxidation (LPO) in the supplement group compared to placebo after an 8 km trial. The researchers also reported that mitochondrial lipids were essential molecules in maintaining the integrity of mitochondrial membranes and maintaining the proper function of mitochondria. Therefore, CoQ_{10} supplementation appears to be an important antioxidant response modulator in exercise applications (Broome et al. ,2021) Sarmiento et al. (2016) reported that CoQ_{10} supplementation increased total antioxidant levels (TAS) and prevented peroxidative damage to membrane phospholipids and free radical-induced oxidation in exercise groups. Similarly, Drobnic et al. (2020) found that there was a significant increase in TAS in the group receiving CoQ_{10}, but a significant decrease in malondialdehyde (MDA) level. Emami et al. (2018) observed that swimmers given CoQ_{10} supplementation had a significant decrease in LPO and a significant increase in TAS. In a group of sedentary participants given 100 mg/g CoQ_{10} for 8 weeks, it was found that MDA decreased, while NO, superoxide dismutase (SOD) and glutathione peroxidase (GPx) levels did not change in serum samples taken immediately after an acute Wingate test applied at different times (Gül et al., 2011). In a study involving 50 km (between 640-2100 m altitude) ultra-endurance and mountain running with well-trained amateur male participants, it was found that 5 CoQ_{10} capsules of 30 mg given as supplements at different times significantly increased the catalase (CAT) level in the supplementation group compared to placebo, while GPx did not change and H_2O_2 level decreased significantly. Therefore, oxidative stress and cell peroxidation were decreased and TAS was significantly increased (Díaz-Castro et al., 2012). In conclusion, CoQ_{10} given as a supplement in different exercise models or conditions, at different doses and in different participant groups (different in terms of age, physical activity level, region, duration, and intensity) appears to improve antioxidant behaviors in metabolism.

Exercise, Physiological Skeletal Muscle Injury and CoQ_{10} Supplementation

CoQ_{10}, an essential component of the mitochondrial electron transport chain, plays a crucial role in ATP production, particularly in muscle cells characterized by elevated metabolic demands, such as those experiencing high-intensity and vigorous exercise (Zhou et al., 2005). The increased demand for CoQ_{10} in skeletal muscle (Paredes-Fuentes et al., 2020) compared to sarcomere and other cells with less metabolic demand under exercise conditions is related to the lack of saturation kinetics of mitochondrial concentration (Lenaz et al., 1999). Intense exercise induces structural damage to muscle cells, evident through symptoms like muscle pain and swelling, sustained reduction in muscle function, heightened production of free radicals, activation of pro-inflammatory signaling pathways, compromised immune functions including effects on immunoglobulin production and T-cell function, as well as the release of muscle proteins into the bloodstream (Simon, 2015). This is because metabolic stress, which increases with exercise, decreases CoQ_{10} levels and increases free radical release. Karlsson et al. (1996) stated that individuals with high muscle tissue or high peripheral oxygen availability, i.e. physically good aerobic conditioning, have higher ubiquinone levels than sedentary individuals. Again, in a study with long-distance runners, it was reported that 12 days of ubiquinol-10 supplementation significantly decreased plasma CK, ALT and lactate dehydrogenase (LDH) levels compared to the placebo group (Suzuki et al., 2021). CoQ_{10} supplementation of 5 mg/kg/day given to middle-distance runners 3 times at 3 different meals for 14 days significantly reduced LA and CK levels compared to an acute 3000m test (Armanfar et al., 2015). In conclusion, the demand for CoQ_{10} in skeletal muscle following exercise routines is necessary both to maintain energy efficiency and to cope with inflammation due to chemical reactions. Furthermore, CoQ_{10} is an important supplement in terms of improving compliance and damage in muscle contraction.

Exercise, Physiological Heart Muscle Injury and CoQ_{10} Supplementation

Strenuous exercise causes the whole organism or a part of it to overheat above physiological norms. This situation negatively affects myocardial functions by further stimulating oxidative stress markers (Emami et al., 2018). In particular, excessive ROS production may adversely affect intracellular Ca^{2+} homeostasis and cause

many contractile dysfunctions such as cardiomyopathy, arrhythmia, ischemia-reperfusion and mitochondrial DNA damage (Burgoyne et al., 2012). Ultra-endurance exercises such as cycling, running, swimming and semi-ironman triathlon cause exercise-induced cardiac fatigue and oxidative damage in both blood and heart muscle (Shave et al., 2004). In this context, exercise impacted several markers associated with myocardial damage, including LDH-1 isoenzyme, α-hydroxybutyrate (HBD), aspartate transaminase (AST), creatine kinase (CK), cardiac troponin I (cTnI), cardiac troponin T (cTnT), and myoglobin (Mb) levels (Kemp et al., 2004). Additionally, oxidative stress markers like malondialdehyde (MDA), CK, and LD exhibited significant increases immediately after a swimming session in men, while antioxidant defense responses, such as ascorbate (vitamin C), also increased (Tauler et al., 2008). In other words, while exercise triggers inflammation markers, it also stimulates antioxidant responses. However, increased antioxidant responses due to exercise alone may not be sufficient during intense exercise periods. For this reason, researchers or coaches often resort to CoQ_{10} supplementation to cope with the negative effects of oxidative stress caused by continuous and heavy training and to increase the strength of antioxidant responses (Díaz-Castro et al., 2012). CoQ_{10}, primarily concentrated in the myocardium, plays a crucial role in mitochondrial redox components and acts as an endogenous lipid-soluble antioxidant, scavenging oxygen radicals (Borekova et al., 2008). Its responsibilities extend to maintaining cell membrane stability and replenishing other antioxidants like tocopherol and ascorbate (Borekova et al., 2008). A decade-long study involving 36 male national swimmers indicated a notable decrease in CK, cTnL, Mb, and LD levels in the CoQ_{10} supplemented group (Emami et al., 2018). CoQ_{10} has been demonstrated in the literature to elevate ATP levels by preventing adenine nucleotide pool loss in cardiac cells (Bonakdar & Guarneri, 2005). It also indirectly stabilizes calcium pathways, reducing intracellular calcium imbalance or overload (Petrofsky et al., 2011). Elevating 2,3-diphosphoglycerate levels in erythrocytes, CoQ_{10} shifts the dissociation curve of oxyhemoglobin (HBO2) to the right, enhancing oxygen transfer at a given pressure (PO2). This mechanism, observed in cardiac muscle, leads to increased oxygen, ATP synthesis, and reduced lactate production, thereby enhancing maximal oxygen consumption (VO2 max) (Zheng et al., 2008). Studies have reported CoQ10's capacity. Therefore, this mechanism helps to explain the significant decreases in CK, cTnl, Mb and LPO levels in CoQ_{10} supplemented groups (Emami et al., 2018). In a study with 30 intermediate runners, 10 days of CoQ_{10} 60 mg/kg and royal jelly supplementation modulated the sympathetic effect on the heart and significantly reduced heart rate (HR; bpm) compared to placebo (Ovchinnikov et al., 2022). In addition to CoQ_{10} supplementation in patients with advanced chronic heart failure, moderate-intensity exercise (5 days/4 weeks) with a VO_2max of 60% was found to improve peak VO_2max by +9%, endothelium-dependent dilatation of the brachial artery by +38% and systolic wall thickening score index by -12% compared to placebo (Belardinelli et al., 2006). Pala et al. (2016) found that 6-week chronic exercise and daily 300 mg/kg CoQ_{10} supplementation improved nuclear factor kappa-light chain-activated B cells (NFκB), kappa B inhibitors (IκB) in cardiac muscle in rats, nuclear factor erythroid 2 (Nrf2) and heme oxygenase 1 (HO-1), and thus IκB, Nrf2 and HO-1 were reported to be significantly increased and NFκB decreased in response to exercise and CoQ_{10} supplementation. Conclusively, the supplementation of CoQ_{10} alongside exercise demonstrates dual benefits: it not only mitigates heightened inflammation markers within the heart muscle but also significantly contributes to the energy production processes within cardiomyocytes. This combined effect of exercise and CoQ_{10} synergistically enhances the contractile functions of cardiomyocytes, particularly under strenuous exercise conditions, leading to more robust responses to new or increased exercise load.

Exercise, CoQ_{10} Supplementation and Performance

One of the curious issues about CoQ_{10} is whether it affects physical performance. Because the increase in ATP demand during exercise reduces O_2 production by mitochondria (Mason et al., 2020; Goncalves et al., 2015). Since CoQ_{10} plays an important role in mitochondrial bioenergetics and acts as an antioxidant in plasma membranes, the hypothesis that CoQ_{10} supplementation could be a dietary strategy with the potential to improve athletic performance has also attracted great interest (Frei et al., 1990). In this context, a graded exercise running test (under aerobic conditions) and a repeated interval sprint test (10 min sprint, 2 min rest) were applied to fifteen trained participants who were supplemented with 300 mg/day CoQ_{10} to follow their performance improvements. At the end of the study, aerobic assessment at 8 and 14 min and peak HR (bmp) and perceived difficulty according

to the Borg scale showed no significant difference compared to placebo. The same authors also found no statistically significant differences in HR and perceived difficulty, as well as peak power (watts), mean power (watts) and total work (kJ) capacity of the myocardium compared to placebo when they performed anaerobic assessment (Bloomer et al., 2012). Based on the currently available literature, the correlation between CoQ_{10} supplementation and athletic performance lacks sufficient comprehensive studies. However, the existing evidence suggests that CoQ_{10} supplementation does not appear to significantly impact athletic performance.

Conclusion

We concluded that there are dramatic responses of CoQ_{10} supplementation to novel metabolic expressions that emerge due to exercise stress. There was an increased response in plasma CoQ_{10} level at different doses and different exercise loads in sedentary or athletes. In athletes, CoQ_{10} intake at different doses significantly reduced LA levels. Oxidative stress parameters such as MDA, 8-OhdG, OSI, LPO, H_2O_2 and SI, which occur in athletes due to exercise, decreased significantly with CoQ_{10} supplementation. On the other hand, CoQ_{10} intake in healthy individuals with high levels of physical activity reduced CRP, an expression of inflammation, and MCP-1, a chemokine that is effective in the progression of many diseases. Moreover, in athletes, CoQ_{10} intake decreased pro-inflammatory markers such as IL-1, IL-6, IL-8, TNF-α and anti-inflammatory markers such as IL-10. These responses are associated with an increase in TAS and a decrease in markers of oxidative damage. CoQ_{10} has also been observed to have a significant ability to improve indicators of exercise-induced muscle damage such as CK, LDH and ALT. Although there has been a limited amount of research on growth factors and gene expression, in athletes, CoQ_{10} is observed to trigger growth factors such as VEGF, EGF and NO, as well as affect DNA gene expression factors such as NFκB, and improve IκB level and HO-1 level depending on pro/anti-inflammation inducers. When CoQ_{10} intake was evaluated in terms of energy efficiency and performance in prolonged exercise, it decreased CO, NEFA, F_2IsoP and IsoPs levels, but increased FO and caused significant improvements in PO and RPF. When looking at the effect of CoQ_{10} on the heart health of elite athletes, it was found to significantly reduce cTnL levels and regulate and lower heart rate (HR; bmp) in athletes.

To summarize, future research should focus on examining the specific factors within the VEGF and MMP's family that are most affected by CoQ_{10}, particularly in athletes. It is crucial to investigate CoQ_{10} impact on aerobic and anaerobic performance tests in order to determine its effectiveness. Furthermore, the effect of CoQ_{10} on lactate change at various time points immediately after an acute high-intensity interval training (HIIT) load should be explored. Additionally, it is important to evaluate CoQ_{10} influence on recovery speed and lipid metabolism in non-healthy obese subjects. Furthermore, future investigations should examine the role of CoQ_{10} in the metabolic aging process in individuals, especially the elderly who engage in physical exercise.

Recommendations

Some recommendations for future research: Especially in athletes, which factor from the VEGF and MMP's family CoQ_{10} affects the most, its success in aerobic and anaerobic performance tests, its effect on lipid metabolism in non-healthy obese subjects, its role in the metabolic aging process in exercising elderly subjects are still not clarified. In addition, further randomized controlled trials could be conducted to more comprehensively evaluate the effect of CoQ_{10} on sports performance.

Author's Contribution

Study Design: YY, VC, ÖS; Data Collection: YY, BY, MEY; Manuscript Preparation: YY, BY, MEY.

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No ethical approval is required.

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Conflict of interest

There is no conflict between the authors.

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