

# NUTRITIONAL SUPPLEMENTS ON MUSCLE DAMAGE AND PAIN INTENSITY AFTER PHYSICAL ACTIVITY: A SYSTEMATIC REVIEW

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## Abstract

This study aims to analyze and highlight the potential of nutritional supplements in reducing muscle damage and pain intensity after physical activity. This study uses a systematic review method by searching various journal databases such as Scopus, Pubmed, and DOAJ. The inclusion criteria in this study were articles published within the last 5 years and articles that discussed nutritional supplements, muscle damage, and pain intensity. The exclusion criteria for this study were articles published in unreliable journals. A total of 1881 articles from Scopus, Pubmed, and DOAJ databases were identified. A total of 7 articles that met the inclusion criteria were selected and analyzed for this systematic review. For operating standards, this study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) assessment. The results of this systematic research review reported that the anti-inflammatory effects of nutritional supplements consumed after the daily training session contained in protein resulted in reduced muscle damage. In addition, the anti-inflammatory properties of nutritional supplements can reduce the intensity of pain caused by inflammation and uncontrolled lactic acid due to intense physical activity and exercise. Nutritional Supplements work by breaking down lactic acid in the cytoplasm into energy, which shows significant pro-inflammatory effects such as TNF- $\alpha$ . We recommend that Nutritional Supplements be used in individuals to provide more effect against muscle damage caused by intense physical activity and exercise.

**Keywords:** Nutritional Supplements; Muscle Damage; Pain Intensity; Physical Activity.

## INTRODUCTION

Exercise that is infrequent, strenuous, high-intensity, or prolonged can result in damage to the muscles, known as EIMD (Exercise-Induced Muscle Damage) (Malheiro et al., 2024; Saberi et al., 2024; Sari, Kurniawan, et al., 2023). EIMD is characterized by the first reaction that occurs due to physical stress during exercise and the inflammatory reaction that follows (Oskuye et al., 2024). Physical force, mainly due to the muscle contraction that occurs when extending, produces the primary reaction (Espírito-Santo et al., 2024; Zhou et al., 2024). Specifically, excessive stretching and disruption of small muscle structures, followed by increased calcium influx into the muscle cells, leads to passive muscle tension and disruption of the muscle fibers (Gomez-Pinilla & Thapak, 2024; Murad & Alqurashi, 2024; Zhu & Song, 2024). This response then causes a second inflammatory reaction, involving the generation of reactive oxygen (ROS) and cytokines, which promote the activation of transcription factors (such as NF- $\kappa$ B, MAPK, and Nrf2) (Peinado et al., 2024; Sun et al., 2024; Talebi et al., 2024). In addition, phagocytic neutrophils and macrophages

can release ROS and cytokines (Guo et al., 2024; Hastings et al., 2024; Selviani et al., 2024). Responsive oxidative reactions (ROS) and inflammation triggered by physical activity are crucial for muscle repair, recovery, and redox pathway signaling (Guo et al., 2024; Metin & Kawano, 2024; Yue et al., 2024). However, if uncontrolled, they can cause damaged cells to enter the damaged tissue, which accelerates secondary muscle damage. The impact of EIMD appears to cause a number of symptoms, such as decreased muscle function (e.g. loss of strength and limited range of motion), late-onset muscle soreness (DOMS), and increased muscle protein breakdown (Bafirman et al., 2024; J.-W. Choi et al., 2024; Khan et al., 2024; Lee et al., 2024). In many situations, inflammation peaks 1-2 times within 24 hours of performing physical exercise (H. S. Choi et al., 2024; Metin & Kawano, 2024; Umar et al., 2023). Currently, about 30 million individuals worldwide are experiencing pain that is commonly treated with non-steroidal anti-inflammatory drugs (NSAIDs) (Muriana, 2024). Administration of non-steroidal anti-inflammatory drugs (NSAIDs) after exercise is not recommended for pain relief as these drugs may interfere with muscle growth and affect muscle hypertrophy and strength (Nazanin et al., 2024).

Therefore, the administration of NSAIDs will reduce the benefits of the exercise performed (AlSalhi et al., 2024; Park et al., 2024; Puri et al., 2024; Yehya et al., 2023). There is a need to find other solutions to resolve this issue. Nutritional Supplements are one type of dietary supplement that is highly favored by athletes, recreationally active adults, and military personnel (Lan et al., 2024; Pisoschi et al., 2024; Sundarammal et al., 2012). During the survey, people commonly cited the hope of enlarging muscles, speeding up recovery from training, and improving performance as reasons for using nutritional supplements. They also said that they rely on advice from coaches, teammates, and family or friends to seek information about these products (Guo et al., 2024; Malík et al., 2021; Pranoto et al., 2024). Specifically, customers also believe that nutritional supplements can promote the growth of lean muscle mass by increasing protein production reducing protein breakdown, and speeding up the process of muscle recovery and physical performance after training by reducing muscle damage and soreness (Mao et al., 2024; Tice & Steiner, 2024; Wilson et al., 2024). Several studies have shown that Nutritional Supplements can reduce inflammation (Ferguson et al., 2024; Pires et al., 2021; Visconti et al., 2021). In this condition, anti-inflammatory cytokines such as interleukin 10 (IL-10) play an important role in controlling inflammatory reactions (Nam et al., 2022; Pisani, 2023). Nutritional Supplements are also well known for having high levels of antioxidants (Häussler et al., 2023; López-Cisneros et al., 2023). Conversely, Nutritional Supplements play a role in inhibiting pro-oxidant activity by increasing the gene expression of heme oxygenase 1 (HO-1) and glutathione peroxidase (GPx) (Borja-Magno et al., 2023; Morella et al., 2023). This shows the importance of nutritional supplements in protecting the body from the effects of pro-oxidants (Ma et al., 2022; Verceles et al., 2023; Yurista et al., 2023). Nutritional supplements are also used in the medical and health field to reduce digestive disorders (Sari, Bafirman, et al., 2023; Stefani et al., 2021). Other studies mentioned that Nutritional Supplements have been shown to have various beneficial properties such as the ability to kill germs and bacteria, relieve inflammation, dilate blood vessels, lower blood pressure, fight cancer, and protect the body from free radicals (Boccardi & Marano, 2024; Halade et al., 2024). Nutritional Supplements have the ability to fight antioxidants due to the content of polyphenol and flavonoid compounds in them (Lacerda et al., 2023; Nieves-Anaya et al., 2023). In this situation, we have the opportunity to closely examine the benefits of Nutritional

Supplements that can reduce oxidative stress and inflammation after exercise. This provides an opportunity to thoroughly explore their impact through structured research.

This study aims to analyze and highlight the potential of nutritional supplements in reducing muscle damage and pain intensity.

## METHODS

This study adopted the systematic review method by searching various journal databases such as Scopus, Pubmed, and DOAJ. The inclusion criteria in this study included articles that had been published within the last 5 years and articles that addressed the topics of nutritional supplements, inflammation, oxidative stress, and physical activity. Exclusion criteria for this study were articles published in less reliable journals. Titles, summaries and full texts of the articles were screened first, then checked and stored using Mendeley software. In the first stage, a total of 1881 articles were found from Scopus, Pubmed, and DOAJ databases. Furthermore, in the second stage, 355 articles were screened based on the suitability of the title and abstract. In the third stage, 134 articles were verified for further processing. In the fourth stage, 37 articles were screened based on the suitability of the full article (theory, dosage, and data). Furthermore, in the final stage, 7 articles that met the inclusion criteria were selected and analyzed for this systematic review. For operating standards, this study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) assessment.

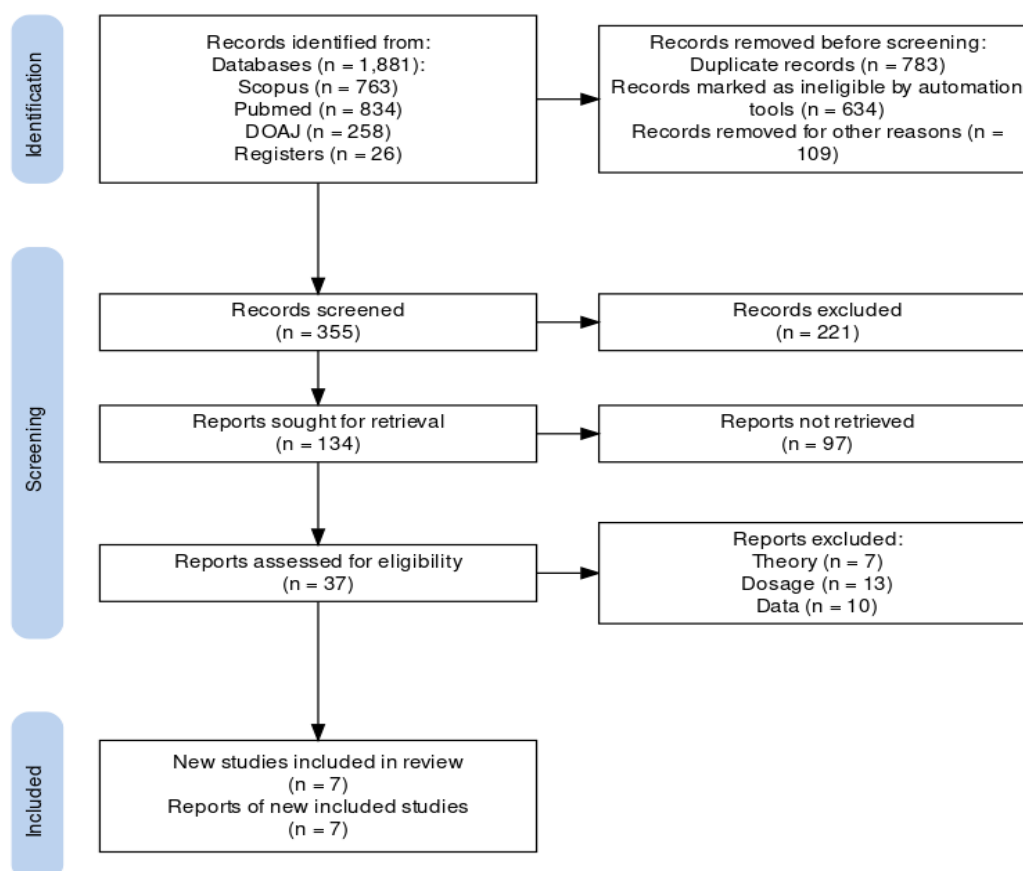


Figure 1: PRISMA flow chart for article selection process

## RESULT

**Table 1: Review of the effects of nutritional supplements on muscle damage and pain intensity**

Author	Sample Characteristics	research design	Intervention	Result
(Forbes et al., 2023)	Healthy normal-weight males	Experimental	500 mg of curcumin or placebo, three times/day after half marathon for 29 day	effective against IL-10 as a prevention of inflammation in order to reduce muscle damage and seen in VAS measurements there is a decrease so that it is effective against pain intensity.
(Martin-Rincon et al., 2020)	Physically active students, males and females	Experimental	140 mg of quercetin with 140 mg of Zynamite or Placebo for 2 day. Run a 10-km race followed by 100 drop jumps	muscle damage as assessed by blood markers (CK, LDH, and Mb). The effect of quercetin on pain intensity has been shown to be effective in a parallel study only.
(Wael Daab Mohamed Amine Bouzid & Rebai, 2021)	Male soccer players	Experimental	150 mL Bee Troot Juice or placebo, twice/day. 7 d (3 d pre-Ex, Ex-d and 3 d post-Ex)	beetroot juice may reduce muscle damage caused by endurance exercise. Meanwhile, most crossover studies have found that beetroot juice supplementation promotes faster recovery of sprint, CMJ, MVIC
(Tanabe et al., 2019)	Healthy males	Experimental	90 mg of curcumin or placebo, twice/day, 7 d post-Ex Eccentric Ex (elbow flexors)	there is effectiveness on creatin kinase as a marker of muscle damage and there is a decrease in VAS value as a measurement of pain intensity.
(Kyriakidou et al., 2021)	Healthy males (n = 14, 25.07 ± 4.05 years)	Experimental	3 g/day n-3 supplementation (N-3, n = 7) or placebo (PLA, n = 7). Following 4 weeks supplementation, a downhill running protocol (60 min, 65% $\dot{V}O_{2max}$ , - 10% gradient) was performed	omega-3 supplementation for 4 weeks may successfully attenuate minor aspects of EIMD. Whilst not improving performance, these findings may have relevance to soreness-associated exercise avoidance.
(Czuczejko et al., 2019)	47 male football players from second and third league teams (Zawisza Bydgoszcz Sports Club, Bydgoszcz, Poland) and 19 male	Experimental	The athletes were supplemented with 5 mg melatonin daily, taken orally in a single dose, 1 hour before bedtime and cycle ergo meter exercise 70-90% HR	Our research results Our research shows that melatonin supplementation reduces lipid peroxidation, modulates

	rowers from the Bydgoszcz Rowing Club (Bydgoszcz, Poland)		max for 30 days. Serum levels of melatonin, isoprostanes, antioxidant-LDL antibodies, interleukin-6, and C-reactive protein were measured. In erythrocytes, concentrations of reduced glutathione (GSH) and malondialdehyde (MDA), as well as activities of glutathione peroxidase (GSH-Px), cytoplasmic superoxide dismutase (SOD-1), and glutathione reductase (GR) were determined.	inflammatory processes and strengthens defense mechanisms against oxidative stress induced by intense physical effort
(Mohamed Cheikh Khoulood Makhlof & Hammouda, 2020)	Fourteen male teenage volleyball players (14.5 ± 0.52 years; 181.57 ± 7.38 cm; 65.68 ± 7.72 kg; mean ± SD) from a Tunisian league 1 squad were enrolled in the study	Experimental	Intervention tablet 10 mg MEL after late night sports volleyball practice for 7 days	a single dose of MEL-10 mg ingestion after vigorous late-evening exercise could serve as a pharmacological solution that provide protection against exercise-induced inflammation, lipid peroxidation, and muscle damage the following morning in teenage male athletes

## DISCUSSIONS

This systematic review study aims to evaluate and highlight the possibility of nutritional supplements in reducing inflammation due to muscle damage and pain intensity after physical activity. Nutritional supplements containing compounds (Omega-3, quercetin, creatin, curcumin, and melatonin) that have the ability to reduce (MVIC torque, ROM, DOMS, CK, and swelling), and inflammatory markers (IL-8 and TNF- $\alpha$ ) in the body (Visser et al., 2024). It is known that doing physical exercise can increase the formation of Reactive Oxygen Species (ROS) in the body (Missong et al., 2024; Sari & Muchlis, 2022). Excessive increase in ROS production can damage muscle fibers and cause fatigue (Massironi et al., 2023). Conversely, a small stimulus of low ROS formation can stimulate the production of natural antioxidants (Del Bianco et al., 2024; Lavorato et al., 2021). However, if physical activity is performed at a high intensity, it can result in an imbalance between the excessive production of ROS and the oxidant defense system and will cause inflammation, known as oxidative stress. Pain intensity can be determined by examining biological clues such as measuring the level of interleukin-6 in the bloodstream (Jadon et al., 2024).

Inflammation plays an important role in worsening the condition or even causing death (Caris et al., 2020). One of the important inflammatory markers in this case is interleukin-6 (IL-6) and interleukin-10 (IL-10). These cytokines are released in conditions of acute infection, chronic inflammation, obesity and physiological stress. These cytokines are associated with various biological effects on the vascular wall,

including increased oxidative stress (Khalafi et al., 2024; Lacerda et al., 2023; Oliveira et al., 2020). The main function of cytokines is to regulate inflammation and therefore play an important role in regulating immune responses in health and disease (da Silva et al., 2023). There are pro-inflammatory and anti-inflammatory cytokines. Therefore, IL-6 and IL-10 are well suited as inflammatory markers (Pereira et al., 2023; Shirvani et al., 2020).

The results showed that nutritional supplements contain antioxidants that are quite strong. Research conducted on healthy men with normal body weight found that giving nutritional supplements, namely curcumin at a dose of 500 mg / kg three times a day after marathon resistance training for 29 days as long as it can be effective against IL-10 as a prevention of inflammation so as to reduce muscle damage and seen in VAS measurements decreased so that it is effective against pain intensity (Forbes et al., 2023). The results of this study are supported by research on physically active students which shows that giving quercetin with an amount of 140 mg after the usual physical exercise of 10 km followed by 100 drop jumps for 2 days can reduce the level of pain intensity seen from CK as a biomarker of (Martin-Rincon et al., 2020). Furthermore, this study is supported by research showing that the provision of nutritional supplements to male soccer players who were given 150 ml of Bee Troot Juice and exercise for 7 days showed that beetroot juice nutritional supplements may reduce muscle damage caused by endurance exercise (Wael Daab Mohamed Amine Bouzid & Rebai, 2021). From a physiological point of view, what is interesting is how flavonoids in nutritional supplements can increase the concentration of mitochondrial calcium ions (Ca<sup>2+</sup>) in cells, thereby triggering hyperpolarization of cell membranes. Thus, an increase in Ca<sup>2+</sup> concentration in the mitochondria could potentially reduce inflammatory oxidative stress (Cai et al., 2023; Xing et al., 2024).

In addition, one of the most important origins of oxidative stress comes from the immune system, and inflammation is the immune system's primary response in restoring cells damaged by rigorous exercise back to normal (Stringham et al., 2024). That's right, when damage occurs to organ cells, the immune system will be activated. These cells will encourage macrophages to increase the production of cytokine proteins that cause inflammation and cytokine proteins that fight inflammation (Muhammad et al., 2021; Stringham et al., 2024; Zhang et al., 2024). It is reported that TNF- $\alpha$  is one of the pro-inflammatory cytokines that increase pain in muscles. In this situation, Nutritional Supplements that have inflammation-reducing properties can be used as an attempt to control the uncontrollable inflammatory process due to exercise activity. A research study showing that the administration of Curcumin Nutritional Supplements at a dose of 90 mg/kg to healthy men for 7 days after eccentric physical exercise, namely elbow exercise, can reduce VAS values as a measurement of pain intensity. (Tanabe et al., 2019). Supported by research conducted on healthy men with omega-3 supplementation of 3 g / day in downhill sports for 4 weeks found that it can weaken the minor aspects of EIMD and can avoid pain after exercise. (Kyriakidou et al., 2021).

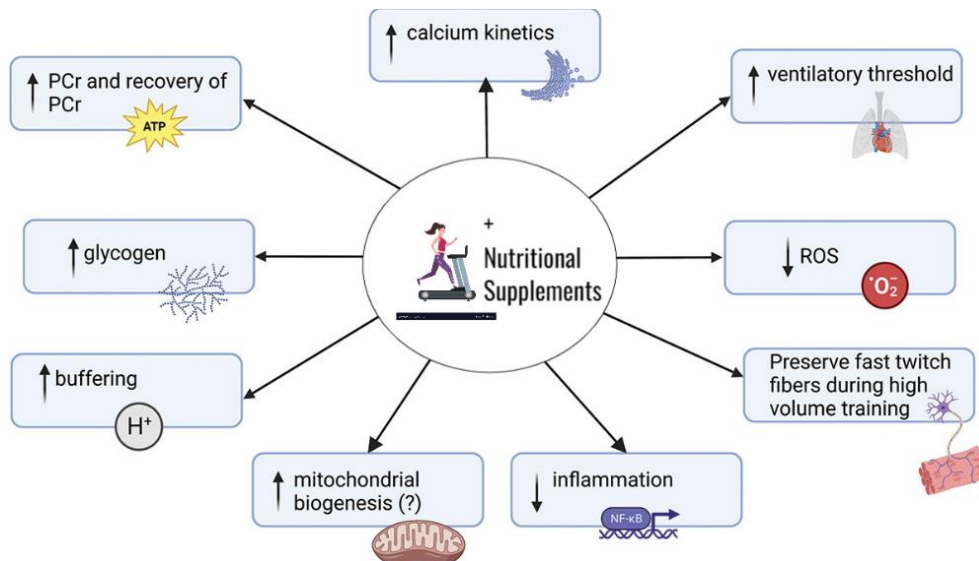
The results of a study on elite football athletes showed that the anti-inflammatory properties of nutritional supplements can significantly reduce TNF- $\alpha$  levels in the blood when they experience trigger-induced inflammation as evidenced by the 66 respondents who were given 5 mg/kg of melatonin which had an effect on lipid peroxidation, modulated the inflammatory process and strengthened defense mechanisms against oxidative stress caused by intense physical effort (Czuczejko et

al., 2019). In addition, a supporting study with 14 volleyball athletes from the tunism league 1 who were given melatonin nutritional supplements at a dose of 10 mg/kg after volleyball in the evening for 7 days pharmacological solutions provided protection against exercise-induced inflammation, lipid peroxidation, and muscle damage the next morning in adolescent male athletes (Mohamed Cheikh Khouloud Makhoulouf & Hammouda, 2020). Regarding NF-kB signaling, NF-kB is initially activated when tissue damage occurs and then plays a crucial role in regulating inflammation by promoting the release of pro-inflammatory cytokines such as TNF- $\alpha$ . By using Nutritional Supplements to inhibit NF-kB signaling, it will also have an impact on reducing pro-inflammatory cytokines and reducing pain in the muscles (Adams et al., 2022).

According to recent research the antioxidants found in Suplemen Nutrisi are Flavonoids, a type of antioxidants that are further classified into flavonoids, flavones, flavonols, and isoflavonoids (Kung et al., 2020). The Suplemen Nutrisi contains  $23.3 \pm 0.92$  GAE  $\mu\text{g}/\text{mg}$  total of phenolics and  $1.28 \pm 0.09$  RE  $\mu\text{g}/\text{mg}$  of total flavonoid. Pinobanksin and organic acids and their esters, for example, octanoic acid, 2-hexanoic acid, their esters, dodecanoic acid, and their esters, 1,2-benzene dicarboxylic acid, and benzoic acid are the main phenolic compounds contained in Nutritional Supplements and also the main cytokines as anti-inflammatory (Manzoor et al., 2023). IL-10 is an important type of cytokine that has anti-inflammatory effects and can reduce both heritable and customized immune system reactions. Immune protection against pathogens or antigens can relieve inflammation and reduce damage to tissues. Some components of Nutritional Supplements can stimulate the formation of anti-inflammatory cytokines and initiate the release of anti-inflammatory compounds from targeted cells to maintain the body's balance (Caris et al., 2020; Stringham et al., 2024).

Regarding plasma IL-6 concentrations peaked immediately after EIMD for the PLA group (Catherine Prater et al., 2024). Plasma IL-6 peaks after training. However, there was no significant difference in plasma IL-6 concentrations between the N-3 and PLA groups. This is in line with there being no significant difference between groups in plasma IL-6 concentrations immediately after exercise (Kyriakidou et al., 2021; Visconti et al., 2021). In a similar manner to plasma IL-6, there was no difference in post-EIMD plasma TNF- $\alpha$  concentrations between the N-3 and PLA groups (Rodway et al., 2021). There is conflicting evidence on the behavior of the TNF- $\alpha$  response after muscle-damaging exercise. Other studies have shown that plasma TNF- $\alpha$  increases after prolonged exercise, others observed no change and others noted a decrease in TNF- $\alpha$  (kianmehr et al., 2022). In other studies TNF- $\alpha$  was not significantly increased, which is a similar result to this study, where no significant increase was shown in plasma TNF- $\alpha$  concentration (Karimi et al., 2024; Nederveen et al., 2024). This could be due to the feedback mechanism, that IL-6 inhibits TNF- $\alpha$ . Thus, it is possible that plasma TNF- $\alpha$  is not an optimal marker to measure EIMD-induced inflammation (Caldas et al., 2022; Kyriakidou et al., 2021; Visconti et al., 2021).

Thus, Nutritional Supplements that have antioxidant properties can reduce the impact of oxidative stress as well as anti-inflammatory properties. Nutritional Supplements have the ability to reduce uncontrolled inflammation due to physical activity, manage muscle damage and reduce pain intensity. Furthermore, to clarify the benefits of Nutritional Supplements in relieving oxidation stress and inflammation, please refer to Figure 2.



**Figure 2: Nutritional supplement response to inflammation**

## CONCLUSIONS

Nutritional supplements contain flavonoids that have anti-oxidant properties that can reduce oxidative stress. In addition, there are many studies that show potential mechanisms to support the use of nutritional supplementation to improve athlete performance specifically reducing muscle damage and pain intensity. Mechanistically, nutritional supplementation increases PCr and glycogen content which alters calcium handling and power production, reduces oxidative stress and inflammation, increases transport of ATP from mitochondria to sites of use, increases hydrogen ion buffering, and may be able to influence mitochondrial biogenesis, whole-body oxygen kinetics and respiratory thresholds. Overall, studies on the effects of NS on muscle damage and pain intensity show mixed results. However, NS (Omega-3, bee troot juice, quercetin, creatin, curcumin, and melatonin) are promising to improve the ability to reduce muscle damage and pain intensity caused by NF-Kb. Future research is needed to investigate more diverse supplementation in various athlete performances.

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## Conflict of Interests

The creators uncover that there's no struggle of intrigued.

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