

Post-exercise fatigue, lactate, and natural nutritional strategy

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Abstract

Exercise-induced muscle fatigue is characterized by symptoms that persist simultaneously for up to two weeks after the first workout. As a primary consequence, in the athlete manifests the reduction of the function of the skeletal muscle and its power. Avoiding muscle fatigue pains is not easy since every exercise performed to train the muscles automatically creates muscle stress. The most important causes are muscle stress, inflammatory response to stress, excessive training load. Food is a great ally to obtain the desired results during training, and it also has an important function when it comes to muscle recovery. To make effort and fatigue even more effective, it is very important to combine sport with proper, healthy, natural, and balanced nutrition, and good supplementation that can assist exercise by making it more effective. Dietary strategies try to consider foods capable of acting on inflammation and the consequences of oxidative stress, physiological events that certainly appear in muscle fatigue, but which have their positive action on recovery and muscle adaptation to training. Natural supplements are products made from natural ingredients, often derived from plants or other biological sources, which are intended to supplement the diet and provide nutrients, vitamins, minerals, and other compounds beneficial to health. Thus, numerous phytochemicals and functional foods have been evaluated for their alleged ability to act and improve post-exercise recovery, which represents the goal of the various nutritional strategies proposed to athletes, especially if they practice agonistic sports. Conversely, the trade-off between adaptation and recovery are infrequently considered. Therefore, many researchers are trying to understand whether prolonged administration of functional foods or / and supplements, which act on muscle fatigue, is a good strategy. This is a topic at the center of numerous studies that deal with the search for a correct diet for the athlete, which certainly requires a careful and meticulous analysis of the potential *hormetic* effect of prolonged use of such nutritional aids on the performance of athletes and therefore the effective acceleration of recovery from muscle fatigue.

Key words: sport, nutrition, recovery, stress, antioxidants, polyphenols.

Introduction

Exercise-induced muscle fatigue.

Sporadic, strenuous high-intensity, or long-term exercise can cause possible damage to skeletal muscle, and this phenomenon is referred to as exercise-induced muscle fatigue. This phenomenon is manifested by a so-called primary response due to the mechanical stress that occurs during exercise and by a secondary inflammatory response, which presents the synthesis of numerous reactive oxygen species (ROS) and cytokines that can be synthesized at levels of neutrophils and phagocytic macrophages (D'Angelo et al., 2013; D'Angelo & Rosa, 2020^(a); Ingrosso et al., 1996). However, it must also be considered that ROS production and inflammatory responses are essential phenomena for muscle damage repair, tissue regeneration and adaptation of redox signaling pathways. But, if they are synthesized out of control, they can cause cell infiltrations into damaged tissues, incrementing secondary muscle damage. Muscle fatigue seems to cause pain, at the level of the muscles involved, called delayed onset (DOMS) and a drastic decrease in muscle proteins, such as creatine kinase and myoglobin. These negative feelings can affect the athlete's performance and therefore it is determined to find strategies that allow them to be minimized to optimize athletic performance and training itself (Tanabe et al., 2021). Prolonged or short-term intense exercise can therefore cause exercise-induced skeletal muscle damage and reduce the athlete's ability to train and/or adhere to a training program. Exercise-induced skeletal muscle damage causes pain to the tissues involved and a temporary loss of muscle function. In addition, it has been proposed that both inflammatory responses and free radicals produced during and after exercise may be involved in the phenomenon of DOMS.

Various post-exercise recovery strategies, like active recovery, massage, foam rolling, compression clothes, and cooling, are used to accelerate recovery after intense physical exercise. In recent years, nutritional strategy has also been considered. Dietary strategies capable of accelerating the recovery of skeletal muscle function and reducing pain sensation are often used in sports populations and may be useful for athletes participating in tournaments or when athletes are required to recover quickly, for example when involved in sequential competitive events. (D'Angelo, 2020^(a)).

The simultaneous intake of nutrients, therefore proteins, carbohydrates and lipids, and molecules with antioxidant power and / or anti-inflammatory nutrients, taken within physiological ranges, can accelerate the post-exercise recovery process. Numerous studies seem to show that a controlled diet can be an efficient recovery strategy. There are numerous nutritional strategies that have been proposed to athletes to improve

muscle recovery, alleviate the effects of DOMS and reduce muscle inflammation following physical exercise (D'Angelo & Rosa, 2020^(a)). According to the guidelines of the International Olympic Committee, some food supplements, such as creatine monohydrate, omega 3 fatty acids, vitamin D, vitamin C / collagen and some supplements that act as anti-inflammatories, for example curcumin and black cherry juice, can enhance and / or enhance the effects of training, muscle recovery, of pain. Reducing the effects of DOMS can be fundamental in athletes who practice sports, especially if they are of the agonistic type, as the pain can compromise performance both at the time and in subsequent sporting events. As a result, nutritional interventions that act on post-exercise inflammation and/or reactions to oxidative stress have received much consideration (Tanabe et al., 2021). Nowadays, it is frequent, among the sports population, the intake of dietary supplements as a nutritional strategy to improve and support performance, with the hope of obtaining a faster recovery after physical exercise. In addition, to achieve a better result, one must consider the individual characteristics of the athletes, in particular the level of physical fitness and the history of training (Tanabe et al., 2021).

Lactate: friend or foe of the performance?

The story of lactate and its role in physiology and medicine has changed dramatically in the last three decades (Brooks, 2018; Brooks, 2020; Hall et al., 2016). No longer conceived of as a dead-end metabolite, a fatigue agent, or metabolic poison, in contemporary physiology, lactate is seen as a major metabolic intermediate that has wide ranging impacts in energy substrate use, cell signaling, and adaptation; simply, lactate is at the fulcrum of metabolic integration. Now, rather than regarded as an oddity of exercise metabolism, the presence of lactate shuttling is recognized in fields as diverse as wound healing, cancer biology, insulin secretion, management of sepsis, learning and memory, and treatment of traumatic brain injury (Brooks & Martin, 2015). Hence, in contemporary biology, the role of lactate in metabolism needs to be understood and viewed as a 'phoenix risen' (Brooks, 2002; Brooks, 2018)

Hence, we now realize that lactate produced in working muscle is a major fuel energy source, but also that lactate release from working muscle fuels other organs such as the heart and brain normally, but also in illness and following injury. Moreover, lactate released from working muscles and other driver cells such as the integument is the major gluconeogenic precursor. It has been shown that the L-enantiomer of the lactate anion is formed and is used continuously in various cells under aerobic conditions and therefore lactate synthesis does not occur only in oxygen-restricted muscle. Most cultured mammalian cells produce a large amount of lactate even when abundant oxygen is present in the cellular environment (Rabinowitz & Enerbäck, 2020). The L-enantiomer of the lactate anion has been shown to form under fully aerobic conditions and is used continuously in different cells, tissues, organs and throughout the body (Brooks, 2020; Brooks et al, 2022^(a), Brooks et al., 2022^(b)). Lactate can be considered as the link between glycolytic and aerobic pathways being the product of a metabolic pathway, namely "glycolysis", and substrate for a downstream pathway, that is "mitochondrial respiration". According to the lactate shuttle hypothesis, this link occurs under completely aerobic conditions and can transcend compartmental barriers and occur within and between tissues, cells, and organs (Brooks, 2018; Brooks, 2020). In opposition to its reflection as a metabolic waste molecule and fatigue mediator, this molecule has been suggested as the focal messenger in a complex feedback loop. Short-term challenges to adenosine triphosphate (ATP) supply encourage lactate synthesis, leading to instantaneous, short- and long-term cellular changes to support the homeostasis of ATP (Gladden, 2004). Energy can be obtained from glucose by activating two metabolic processes: fermentation and respiration. Both begin with glucose catabolism by glycolysis, resulting in two pyruvate molecules and production of two ATP molecules and two NADH molecules. During fermentation, NADH is used to reduce pyruvate to lactate, which is then eliminated. This process results in a net yield of two molecules of ATP and two molecules of lactate for one molecule of glucose, without using oxygen. In respiration, the NADH electrons and pyruvate generated during the glycolytic process are transferred to the mitochondria, where they are consumed to generate abundant usable energy from cells (about 25 ATP molecules per glucose) (Rabinowitz & Enerbäck, 2020).

Under aerobic conditions, NADH electrons can be rapidly used by the electron transport chain in the mitochondria, producing energy. Therefore, in aerobic state, fermentation is the only metabolic possibility. In the presence of oxygen, ATP synthesis by oxidative phosphorylation may however be partial by the rate of oxygen uptake. Therefore, in conditions of high oxygen demand, such as during intense exercise, fermentation represents a metabolic pathway capable of accelerating energy production. Therefore, in the condition where the muscle is pushed beyond the aerobic threshold, such as during a short sprint or towards the end of a long hard run, lactate is synthesized as metabolic waste (Rabinowitz & Enerbäck, 2020). The two carbon metabolites circulating at high concentrations are glucose (5 mM) and lactate (1 mM). Glucose and lactate can be interconverted by the processes of glycolysis and gluconeogenesis. A convenient way to coordinate these two processes is: 1. most cells extract energy from carbohydrates by absorbing glucose and then completely oxidizing it into CO₂; 2. cells subjected to particularly urgent energy needs absorb extra glucose and release a small amount of lactate as waste, moreover, as observed by Gerty and Cori, fasting muscle releases glycogen reserves as lactate; 3. The liver "cleanses" this lactate, converting it back into glucose, through gluconeogenesis.

In this scenario, lactate is valuable only as a substrate for generating glucose. Rapid production of circulating lactate must be offset by comparably rapid consumption. Lactate can be converted into glucose, and glucose can be converted into lactate. Such analysis has shown that the brain directly oxidizes glucose as its primary fuel.

To maintain tight concentration homeostasis, overall production and consumption of lactate must be synchronized. (Rabinowitz & Enerbäck, 2020).

Lactate metabolism certainly performs three capabilities: 1. lactate is one of the primary sources of energy; 2. lactate is the principal gluconeogenic precursor; 3. lactate is a signaling metabolite with paracrine, autocrine, and endocrine capabilities and for this reason it is considered as a "*lactormon*". The role of lactate as the preferred fuel energy source for muscle exercise and as a major gluconeogenic precursor has been recently revised (Brooks, 2020).

Lactate can cause numerous adaptive responses, which manage metabolism such as, for example, functional adaptation to exercise in skeletal muscle cells (e.g., mitochondrial reticulum proliferation and the complex leading to lactate oxidation). Consequently, the signaling cascade of this molecule involves the production of ROS, cytosolic Ca^{++} and other products that converge on transcription factors that affect mitochondrial biogenesis. The physiological starting signal is lactate that drives cellular adaptation by conditioning the expression of many specific genes. (Brooks, 2020).

Rather than a dead-end metabolite produced in muscle because of oxygen insufficiency, it has currently been shown that lactate is synthesized continuously under fully aerobic conditions, particularly during exercise when glycogenolysis and glycolysis rates are high. Lactate and pyruvate are interconverted across bilayer lipid membranes by proton-bound, guided transport requiring the activity of a monocarboxylate (MCT) transport protein family.

As part of the Lactate Shuttle mechanism, MCT1 facilitates the absorption of lactate into functioning human skeletal muscle from the interstitium and plasma. Exercise and muscle contraction have been shown to increase the expression of the lactate transporter MCT1 in mammalian skeletal muscle (Hashimoto et al., 2007).

Within tissues, lactate can be exchanged between white and red fibers within a muscle bed and between astrocytes and neurons in the brain (Brooks, 2020). Endurance exercise has long been recognized to stimulate mitochondrial biogenesis. Hence, the following question arose: 'Could the lactatemia of exercise stimulate mitochondrial biogenesis?' Hashimoto and colleagues observed that lactate increased ROS production and upregulated 673 genes, many known to be responsive to exercise and exercise training via ROS and Ca^{++} stimulation. Among the many effects, lactate increased the mRNA and protein expression of MCT1 and COx. Increases in COx expression coincided with increases in peroxisome proliferator activated-receptor gamma coactivator-1 alpha expression and the DNA binding activity of nuclear respiratory factor-2. Based upon these results, Hashimoto et al. concluded that the presence of a lactate signaling cascade implicates ROS synthesis and converges on transcription molecules implicating in the mitochondrial biogenesis (Brooks, 2020).

Material & methods

The source articles were found using the online databases MEDLINE (Pubmed), Scopus and Web of Science, using keywords, including "exercise induced fatigue", "physical activity", "lactate", "polyphenols", and "phytochemicals". Pertinent papers were reviewed and restricted to peer-reviewed manuscripts published from 2013 to 2023.

Results

Functional foods

So-called "functional foods" have the potential to exert a positive physiological effect related to the improvement or preservation of human health and disease prevention (Bell et al., 2014). Numerous researchers, especially physical activity researchers, have demonstrated the ability of these foods to act synergistically to manage the negative effects associated with intense physical activity. This is of specific interest for sports where muscle damage can affect repeated workouts and competition. This manuscript will discuss recent data on selected, contemporary, and emerging functional foods applied in exercise recovery protocols, with reference to foods rich in natural polyphenols (Owens et al., 2019).

Dietary strategy: fruits, vegetables, and plant-derived polyphenols effects.

Polyphenols are described as secondary metabolites and are concerned in a wide range of critical processes in plants, involving pigmentation, growth, pollination, and resistance to pathogens and environmental stressors (Tsao, 2010; Williamson, 2017). In recent years, numerous researchers have faced research related to the antioxidant power associated with phenolic molecules present in foods in the human diet; In particular, evidence has been observed in favor of the contribution of polyphenol intake in the prevention of some syndromes, such as cardiovascular diseases, tumors, neurodegenerative syndromes and metabolic diseases such as diabetes mellitus (D'Angelo & Madonna, 2020; Boccellino et al., 2021; Martino et al., 2019; D'Angelo S. et al., 2001; Boccellino & D'Angelo, 2020; Ferrara et al., 2022_(b); D'Angelo 2020_(b); D'Angelo & Tafuri, 2020; D'Angelo & Cusano 2020_(a); D'Angelo, 2020_(a); D'Angelo & Cusano, 2020_(b); D'Angelo & Cusano, 2020_(c); Orlandella et al., 2019) (**Figure 1**). Total daily dietary intake of polyphenols can be as high as 1 g/day, which is ~10 to ~100 times higher than the intakes of other 'phytochemicals' and known dietary antioxidant nutrients, i.e., E and C vitamins, and carotenoids. From a chemical point of view, polyphenols have two (or more) hydroxyl groups bound to one (or more) benzene rings. Differences in this principal chemical configuration have led to the grouping of these molecules into four main classes, containing phenolic acids, flavonoids, stilbenes, lignans. Due to the low

amounts that are limited food sources, the contribution of stilbenes and lignans to the total intake of polyphenols is much lower. Instead, phenolic acids and flavonoids are the most present in the human diet, with prevalent sources in fruits, vegetables, fruit juices, tea, coffee, red wine, cereals, and chocolate (Kashi et al., 2019). The effects of health advantages of a diet rich in vegetables and fruits in decreasing the risk of several diseases are abundantly demonstrated (Vuoso et al., 2020a; Vuoso et al., 2020_(b); Meccariello & D'Angelo, 2021). These positive effects have been attributed to the polyphenol content of such diets, as observed by in vitro experimental models and epidemiological studies linking dietary intake of fruit-derived polyphenols with a decreased risk of non-communicable diseases (D'Angelo et al., 2017; D'Angelo & Sammartino D'Angelo, 2005; et al., 2019_(b); D'Angelo et al., 2019_(a); Naxos et al., 2021; Augimeri et al., 2023). However, the bio effectiveness of such phytochemicals is strictly dependent on their bioavailability. Indirect evidence of the absorption of phenolic compounds across the intestinal barrier is provided by the increase in the antioxidant power of plasma after consumption of foods rich in these molecules, such as tea, red wine, blackcurrant, and apple juice. More direct evidence on the bioavailability of some polyphenols has been observed by evaluating their concentrations in plasma and urine after ingestion of pure compounds or foods with a known content of the compound of interest (Kashi et al., 2019).

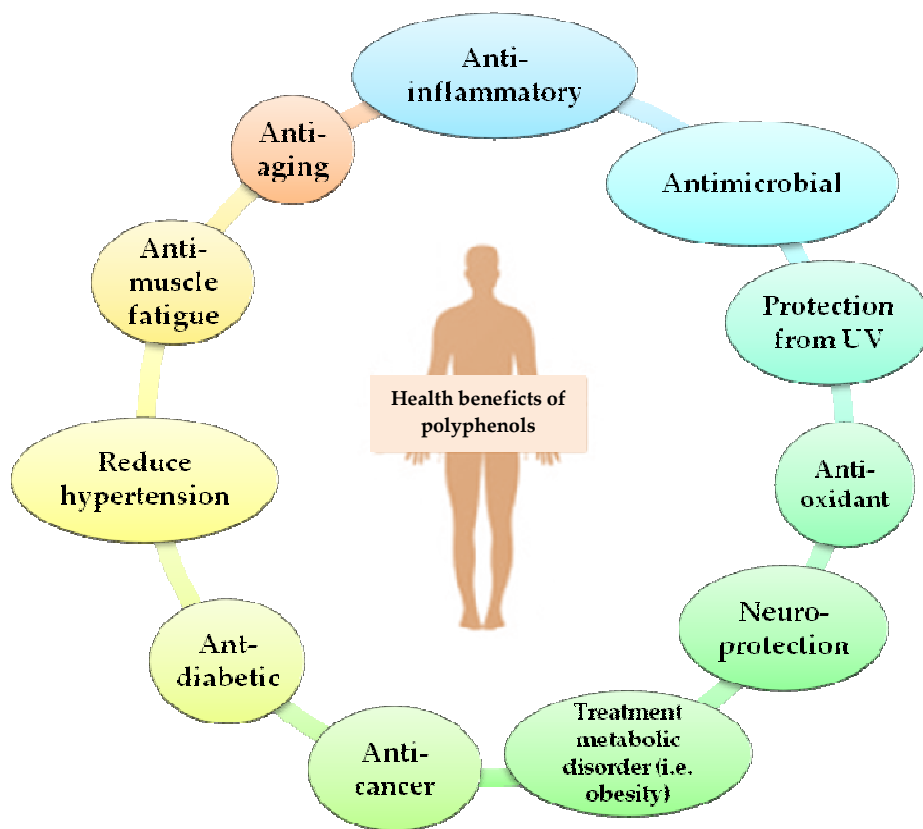


Figure 1. Potential healthy attribute of polyphenols toward human health and disease.

Initially, polyphenols are conjugated with sugar molecules within plants (glycosides) and must be hydrolyzed to separate the sugar group (glycon) from the polyphenol (aglycone) before absorption. This process is mediated by lactase phloridzin hydrolase in the brush edge of the epithelial cells of the small intestine. Aglycones can be poured into the bloodstream; However, they undergo conjugation processes, resulting in the formation of sulfate, glucuronide and/or methylated metabolites both within epithelial cells and the liver. A high percentage of these molecules is not absorbed inside the small intestine and reached the colon is attacked by enzymes present within the microbiota to release aglycones; These will then produce bioavailable metabolites such as phenolic acids. It is essential to underline that there is a high degree of interindividual variation in bioavailability, determined by differences in the gut microbiome and food processing of phenolic compounds. The knowledge of the absorption phases and metabolism of polyphenols is complicated due to the numerous different polyphenolic compounds present within plants, their interactions within the food matrix and their conjugation to form different metabolites after absorption. Fruits and vegetables and fruit-derived polyphenol supplements have a mixture of polyphenols and therefore the pharmacokinetics and metabolism after ingestion of whole foods or fruit-derived supplements are even more complicated to study and understand (Kashi et al., 2019).

Could a different diet prevent lactate in the muscles? Maybe not directly, but it can play a big part in improving the threshold at which this accumulates. A better availability of oxygen in the muscles is a result to be

pursued with correct nutrition or supplementation. Taking many leafy vegetables (e.g., some types of salad, spinach, etc.) and beetroot in a significant volume (even 500g per day) can increase the presence of nitrites in the blood and so muscle oxygenation. Acute supplement with nitrate (NO_3^-)-rich beetroot juice would increase quadriceps muscle oxygenation, pulmonary oxygen uptake kinetics and exercise tolerance in normoxia and that these progresses would be augmented in hypoxia and attenuated in hyperoxia (Cocksedge et al., 2020)

Furthermore, vegetables can be rich in alkalizing substances, e.g., magnesium, the contribution of which is potentially useful in counteracting lactate acidosis. Above all, we must not forget that correct hydration, which allows lymphatic circulation and the necessary supply of carbohydrates and carbohydrates, will place the body in the right condition to manage physical effort and the by-product, the lactate, is an adaptation of the body to effort.

Dietary polyphenols.

Phenolic compounds are contained in abundant vegetables and fruits that are ingested regularly in a well-adjusted diet. They have been revealed to act as antioxidants and anti-inflammatories (Meccariello & D'Angelo, 2021). Several polyphenols own the capacity to decrease arachidonic acid pathways by impeding the production of cyclooxygenase 1 and 2 in concentrations like over-the-counter nonsteroidal anti-inflammatory drugs. Foods rich in polyphenols incorporate tea, grapes, coffee, nuts, cocoa, cherries blueberries, and pomegranates.

Considering the phenomena that cause muscle fatigue, it is quite unlikely that a dietary intervention can interact with the primary phase of mechanical stress that occurs during exercise (Bongiovanni et al., 2020; Mazzeo, 2019). What is more likely, however, is an interaction with the secondary cascade, which causes inflammation and ROS production and consequent further exacerbation of the damage, which can be modulated and thus help the recovery process (Owens et al., 2019).

Quercetin. Quercetin is a polyphenol belonging to the group of flavonoids. This molecule is abundant in green tea, white and red onions, apples, peppers, blueberries, dark green vegetables (Williamson, 2017). Quercetin possesses anti-inflammatory and antioxidant properties. This phytochemical has cardioprotective, antitumor and hepatoprotective effects, has antipathogenic abilities that can affect the immune system and resistance to pathogens. Therefore, this polyphenol is considered a dietary supplement capable of acting and controlling the health of the immune system in athletes (IOC Consensus Statement). Studies on athletes who practice prolonged resistance exercises (such as running on treadmills or cycling) have reported that chronic supplementation (3 weeks) of pure quercetin does not protect against oxidative stress induced by exercise and inflammation. However, the action of this polyphenol seems to be affected by the time of intake and/or if another nutritional supplement is co-ingested. More newly, research has shown that in triathletes' supplementation with quercetin-based supplement, specifically designed to increase the bioavailability of polyphenol, can reduce oxidative stress and muscle pain simultaneously after training, with an improvement in total time in three individual sporting events (cycling, swimming, and running) simulating a triathlon. It has been observed that any strategy that increases the bioavailability of this flavonoid is important to increase its effectiveness. (Tanabe et al., 2021). It should be noted that quercetin ingestion does not cause anti-inflammatory effects after resistance exercises or local exercises (e.g., elbow flexors and fall jumps) in a parallel study design. Several studies in which muscle damage has not been analyzed have reported that supplementation of this polyphenol improves resistance exercise performance or anaerobic capacity. due to improvement in mitochondrial and antagonizing biogenesis of adenosine receptors. However, it may be appropriate to consider the quercetin intake times due to the short half-life of this molecule (3.5 hours). Therefore, to optimize the intake of this phytochemical, both the co-ingestion of added nutritional supplements and the timing of the intake of this polyphenol can be fundamental (Tanabe et al., 2021; Ferrara et al., 2021).

Curcuma. Curcumin (*Curcuma longa L.*) is a phenolic compound extracted from turmeric. This polyphenol has numerous physiological effects and its mechanisms of action have been the subject of study for many years in the field of clinical medicine. This phytochemical has mainly anti-inflammatory and antioxidant effects and the consequences of its action are generally observed through a decrease in the expression of numerous pro-inflammatory genes. Taking curcumin has been shown to be effective in treating numerous syndromes, including cancer, heart failure and Alzheimer's dementia. (D'Angelo, 2020_(c)). This molecule can regulate inflammatory cascades and therefore has the ability in athletes to limit post-exercise inflammation, resulting in reduced sensitivity to pain and DOMS (Meccariello & D'Angelo, 2021). Since curcumin can act as an antioxidant, it could reduce the effects of secondary muscle damage, and for this property this polyphenol is classified as a nutritional supplement capable of improving performance, training capacity, post-exercise recovery, muscle pain and the management of any injuries (IOC Declaration of Consent). As for the antioxidant action of curcumin after exercise, curcumin ingestion has been reported to reduce the concentrations of derivatives of the reactive oxygen metabolites, thioredoxin-1 and glutathione, while increasing the biological antioxidant potential after walking on the treadmill or running to 65% $\text{VO}_{2\text{max}}$. The piperine, the active constituent of black pepper, may improve the bioavailability of this polyphenol when the curcumin and the piperine are co-ingested (Tanabe et al., 2021). To have an optimal effect, to reduce inflammatory responses, it seems necessary to start taking curcumin at least 2 days before training, regardless of the category of sport. Regarding DOMS, the action of this polyphenol on DOMS diminution, due to its affected analgesic's, may be reduced in elite or highly trained players. In addition, DOMS was only relieved when this phytochemical was administered soon after sport event.

Therefore, continuous ingestion of this phytochemical during the post-exercise time may be essential to decrease DOMS (Tanabe et al., 2021). This polyphenol has been shown to control inflammation and cytokine flow by conditioning of COX-2 marker. An experimental report indicated how discreetly active males, who take this polyphenol (200 mg curcumin/day for 4 days) before running downhill, after 2 days of integration, reported reduced quadriceps pain 48 hours after exercise.

Supplementation of this phytochemical (5 g curcumin/day) for 5 days moderately reduced post-exercise pain during 48 hours of recovery and reduced creatine kinase flow caused by eccentric single-leg exercises in recreationally active men, while the post-exercise interleukin 6 concentration was elevated compared to placebo. Similarly, preservation of muscle function and reduced creatine kinase (peak) activity were demonstrated in untrained subjects who took 150 mg of this polyphenol 1 hour before and 12 hours after elbow extensions. Clearly, this polyphenol shows promise as an integrative strategy to improve the negative effects of exercise. Of course, more information is needed, developing studies involving a larger number of subjects (Harty et al., 2019).

Montmorency cherries and juice. Montmorency tart cherries (*Prunus cerasus L.*) have been proposed as a recovery supplement because of their high concentrations of phytochemicals and flavonoids, anthocyanins, and other phenolic compounds. Numerous scientific works have shown how anthocyanins with high antioxidant power are able to reduce and limit the production of ROS (Meccariello & D'Angelo, 2021). The flavonoids and anthocyanins abundant in tart cherry juice presented the ability to inhibit the activities of certain enzymes, such as cyclooxygenase-2 and phospholipase A2, and could act as anti-inflammatories (Williamson, 2017). Cherry tart juice can result in a better resistance to the inflammatory response and redox balance, thus decreasing recovery time after strenuous exercise. The IOC consensus statement mentions that the anti-inflammatory effects of tart cherry juice can be useful for speeding up recovery times, although the benefits very often depend on the type of sport practiced and the training performed. The dose of black cherry juice needed to accelerate recovery after physical exercise is on average equal to 250-350 ml (30 ml if concentrated), to be taken twice a day, for 4-6 days before the sporting event or for 2-3 days after the race or training. The amount of intake of tart cherry juice, especially the total phenolic content, is a key factor in ensuring positive effects. In fact, in a recent review article the authors concluded that to improve recovery times from muscle damage through antioxidant and anti-inflammatory mechanisms may require >1000 mg of polyphenols per day for 3 or more days before and after the sporting event. Review articles concluded that tart cherry juice may attenuate inflammatory and oxidative responses to muscle fatigue, accelerating faster recovery after periods of harmful muscle exercise (Tanabe et al., 2021; Meccariello & D'Angelo, 2021). These results led to many lines of investigation that applied Montmorency cherries in exercise recovery (Buongiovanni et al., 2020). Chronic consumption of tart cherry juice (about 60-65 ml of concentrated juice/day or 500 ml of juice/day for 7-9 days) also appears to improve decreases in muscle function, reduce biomarkers of muscle fatigue, and reduce pain sensation both simultaneously after and during 48 hours of recovery after intermittent or prolonged resistance exercise in a variety of populations.

Considering all these reflections, tart cherry juice shows promise as an emerging strategy to reduce muscle fatigue (Harty et al., 2019). However, the effect of tart cherry juice might be hardly detectable under conditions where sport-specific exercises, such as soccer and rugby match, are employed. In the future, studies will be needed to delineate the optimal amount and duration of tart cherry juice intake in terms of the effect on DOMS in athletes (Tanabe et al., 2021).

Beetroot juice. Beet juice. Red beetroot (*Beta vulgaris rubra*) is classified as a functional food as it has high levels of nitrates and bioactive phytochemicals, such as betalain, ascorbic acid, carotenoids, phenolic acids, and flavonoids. The nitrate in beet juice increases the bioavailability of nitric oxide, a molecule capable of improving vascular function, mitochondrial efficiency, glucose homeostasis and muscle contractility of type II fibers, thus improving physical performance, especially endurance exercise performance (in the range of 5-30 minutes). For these properties, nitrate is classified as a dietary supplement capable of directly improving sports performance (IOC declaration of consent). Taking beet juice can improve sprinting and cognitive performance. This juice, to be effective, must be ingested by the athlete at least 90 minutes before the sporting event. On the other hand, betalain, the most potent antioxidant molecule found in beetroot, is thought to be able to attenuate ROS scavenging and upregulate endogenous antioxidant enzymes. Nitrites have also demonstrated inhibitory power of ROS formation. Therefore, beet juice should be able to accelerate the recovery of muscle damage by directly or indirectly reducing the production of exercise-induced ROS and DOMS. The data suggest that the effect of such juice on markers of muscle damage present in blood flow strongly depends on the design of the study. Most crossover studies have found that beet juice supplementation promotes faster recovery of sprint, time trial duration, and VO₂max after muscle damage exercise. Therefore, the intake of this juice may be active in ameliorating the athletic performance even under muscle fatigue situations (Tanabe et al., 2021).

Black Currant. Preliminary scientific data suggest that consumption of blackcurrant extract may reduce indirect markers of muscle injury. Blackcurrant (*Ribes nigrum L.*) is abundant in anthocyanins, specific polyphenols with powerful anti-inflammatory and anti-oxidant powers. In a paper published in 2016, researchers showed that discreetly active, non-endurance-trained subjects who taking blackcurrant juice (470 ml twice daily for 8 days) before eccentric squat exercise, performed after 4 days of supplementation, showed reduced levels of

circulating creatine kinase at both 48 hours and 96 hours after exercise. compared to placebo (Harty et al., 2019).

Pineapple. The pineapple (*Ananas comosus*) is a good source of antioxidant, showing a high presence of phenolics in the fruit. Based on the physicochemical composition and nutritional values, pineapple can be considered as one of the most useful fruits for manufacturing value-added compounds such as antioxidants, organic acids, bromelain, and phenolic compounds (Mohd et al., 2020). The typical bioactive compounds of pineapple are mainly phenolic compounds and flavonoids that are present in the morphological parts of the fruit. Pineapple fruit also has a proteolytic enzyme namely bromelain which helps in the digestion process as well as being essential for the therapeutic effects associated with bromelain. Bromelain has various potential uses as an anti-inflammatory, antioxidant, anti-cancer activity, and cardioprotective agent. Bromelain supplementation resulted in improved muscle function, reduced pain, and increased pain threshold after exercise, compared to placebos. It has been observed that in untrained subjects who took a supplement containing this molecule for 30 days before squat smith machine exercise reported less pain. Therefore, bromelain supplements show positive effects in subjects, but of course further investigation is also needed in this case (Harty et al., 2019).

Pomegranate juice. Numerous recent studies show that periodic intake of pomegranate juice can improve the value of bio-functional markers and reduce biomarkers related to muscle damage. Pomegranate juice (*Punica granatum L.*) is rich in ellagitannins, a particular phytochemical with antioxidant and anti-inflammatory power. Active subjects who took apple juice (800 ml/day for 9 days) were shown to maintain significantly better muscle function after eccentric exercise on day 5 of intake compared to subjects who took a placebo (D'Angelo & Rosa, 2020_(b); Ferrara et al., 2022_(a)). It was shown that the intake of about 30 ml of pomegranate juice concentrate had an efficacy like a double consumption (60 ml / day) in active men for recreational purposes. After 3 days of supplementation, the subjects performed a specific physical activity protocol. During the 4-day recovery phase, the researchers noted that both treatment groups showed greater knee extension and maximum voluntary contraction of elbow flexion compared to subjects who took placebo. A recent report also indicated that elite weightlifters who took this juice (750 ml/day, 500 mL) 1h before sport event, in the 48h prior to high-intensity weightlifting training described lower individual pain (Harty et al., 2019).

Green Tea. Green tea (*Camellia sinensis*) is a plant whose leaves are rich in polyphenols, especially catechins, which exert powerful antioxidant properties (Meccariello & D'Angelo, 2021). Preventive intake of polyphenols from green tea has been indicated to relieve signs and symptoms of muscle exhaustion. Some it was found that non-resistance-trained males, who intake epigallocatechin gallate, a phytochemical contained in green tea (1800 mg/day), for 14 days, reported considerably lower values of muscle soreness 24h after exercise matched with placebo. Ingestion of green tea before downhill running conserved muscle power, decreased circulating creatine kinase enzyme concentration, and reduced pain 48h after training likened to placebo, in recreationally dynamic subjects. Hence, green tea-derived polyphenols show merit in reducing muscle fatigue, although more work is needed to find optimal dosing strategies (Harty et al., 2019).

Discussion

Dietary reflections to control exercise-induced muscle fatigue: *hormetic* approach. The long-term use of recovery protocols on training adaptation and athletic expansion is an area of much interest and perhaps concern. Researchers are trying to understand the interventions to be implemented capable of diminishing the stress response induced by physical exercise, which can decrease adaptive potential, assuming that the two events are related. Many dietary strategies, as highlighted in this short manuscript, can modulate oxidative stress and inflammation, known to be significant and determined in the adaptive reaction to an exercise stimulus. For example, smoothing out the pro-inflammatory phase of the repair process can be problematic as a reduction in the number of immune cell infiltrates leads to a reduction in the diameter of new myofibers and the growth of fibrosis. Therefore, the problem arises of understanding whether the habit of taking natural supplements can, in the long term, cause a maladaptive response and influence the development of the athlete's skills.

Frequent use of nutritional strategies that accelerate recovery can affect muscle adaptation. Therefore, the goal of the nutritional strategy should be carefully evaluated in the context of the compromise between muscle recovery and post-exercise adaptation. Contemplating the possible *hormetic* outcome of the long-term use of the benefits obtained from the nutritional strategies followed, it is likely that a periodized approach to the sports diet will produce the greatest benefits for the athlete (Ji et al., 2016). The concept of hormesis describes the ability of an organism to respond to a specific stimulus in a different way based on its intensity. In other words, hormesis is a dose-response phenomenon according to which low doses of a certain stimulus induce opposite effects compared to high doses of the same stimulus. If the main goal is to increase the stimulus to training, then a certain degree of attention is required, so athletes and professionals must co-consider a periodized approach to nutrition to adequately support training and competition and to maximize the potential for adaptation. This notion can be conceptualized with the idea of hormesis, which was first applied to exercise paradigms (Radak et al., 2005). The concept of *hormetic* physical activity therefore casts many doubts on the need for athletes to take supplements based on anti-oxidants. (Radak et al., 2005). The *hormesis theory* purports that biological organizations respond with a bell-shaped curve to exposure to chemicals, toxins, and radiation. Then it is possible to extend the hormesis theory to include ROS. It is possible that the beneficial effects of regular exercise

are partly based on the ROS generating capability of exercise, which is in the stimulation range of ROS production. Therefore, the exercise-induced ROS production can play a role in the induction of antioxidants, in DNA repair and in the protein degrading enzymes. This idea suggests that biological systems respond in a way that forms a kind of bell curve, where a positive adaptive response is experienced when exposed to a stimulus. However, when exposure becomes high (i.e., when muscle fatigue impairs function for a prolonged period) there is a need to intervene to cancel out potential adverse effects. Since exercise-induced muscle damage can shape the fundamental understanding of skeletal muscle adaptation, it is important to discover how nutritional strategies might differently influence adaptation to harmful resistance and resistance training (Owens et al., 2019). Therefore, it is significant to understand whether foods with anti-inflammatory properties negatively affect with the pro-inflammatory phase of muscle repair and thus help the renovation process. The same can be said for foods with "antioxidant" power, as recent research highlights the fundamental importance of oxidative stress in adaptations to exercise (Margaritelis et al., 2017). Mitohormesis, i.e., mitochondrial hormesis, occurs in response to any stress that can impinge upon mitochondrial function and stimulates adaptive responses that improve not only mitochondrial function but also global resistance to stress (Musci et al., 2019). Interestingly, it has been observed that a local stress can have also systemic effects. In other words, the beneficial effects of the response can be extended also to distal organs and tissues that are not directly affected by the stressor. This paradoxical phenomenon whereby a local, mild stress can decide an increased resistance to the same (but also other) stresses in distal cells has been observed in several animal experimental models (Powers et al., 2020).

Conclusions

Muscle fatigue can have a profound effect on the ability to perform next bouts of exercise and therefore adhere to an exercise training program. A variety of interventions have been used prophylactically and/or therapeutically to reduce the negative effects associated with muscle fatigue. Further research is called for to elucidate the rightest dose and frequency of interventions to attenuate muscle fatigue and if these interventions attenuate the adaptation process. The decision to implement dietary strategies to reduce the effects of muscle fatigue must be made considering the potential negative effects of these strategies, as chronic use of many of these nutrients can compromise training adaptations. Decisions on which nutritional strategy to use should also be made considering the other physiological effects of the substance. Future research in this area should optimally encompass the combined actions of multiple nutritional or supplementation strategies on skeletal muscle fatigue outcomes. It is possible that prophylactic supplementation with sufficient and different nutrients acting simultaneously on different physiological mechanisms may cause a synergistic effect on symptoms of muscle fatigue in addition to that of nutrients alone. In addition, more information is needed about the interaction between nutritional/supplementation strategies and other treatment options for muscle fatigue, such as massage or cryotherapy.

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