The effectiveness of natural supplements on prevention and treatment of delayed onset muscle soreness and markers of muscle damage: a review of literature

Brandie C. Cheshier, Bert H. Jacobson*

School of Kinesiology, Applied Health and Recreation, Oklahoma State University Stillwater, Oklahoma, USA

* Corresponding author: bert.jacobson@okstate.edu

ABSTRACT

Objective. Unaccustomed or high-intensity eccentric exercise often leads to delayed onset muscle soreness (DOMS) that presents as pain, soreness, or swelling. Nonsteroidal anti-inflammatory medications (NSAIDs) are often used to treat DOMS. Due to the potential adverse effects of NSAIDs, commerically available supplements have been suggested as a potential alternative treatment of DOMS. The purpose of this review is to examine the effects of commerically available supplements on DOMS and markers of muscle damage and inflammation.

Method. Existing publications were examined and summarized regarding the effects of supplements such as curcumin, green tea extract, ginseng, ginger, branch chain amino acids, anatabine, pomegranate juice, and protease on DOMS and markers of both muscle damage and inflammation following eccentric exercise.

Results. Consuming branched chain amino acids (BCAA), pomegranate, and curcumin appear to have the greatest effect in preventing and treating DOMS. Anatabine and ginseng do not appear to decrease markers of muscle damage, inflammation, or DOMS.

Conclusion. Consuming supplements before or after exercise with anti-inflammatory and analgesia properties may be just as effective as NSAIDs in treating and preventing DOMS. Further studies should be conducted to determine the long-term effects of commerically available supplements and the safest dosage that can be consumed for maximal benefits.

Keywords

delayed onset muscle soreness; supplements; markers of muscle damage; eccentric exercise

DOI

10.14712/23366052.2021.4

INTRODUCTION

Delayed onset muscle soreness (DOMS) is an overuse injury that occurs after unaccustomed or high-intensity eccentric exercise (Cheung, Hume, & Maxwell, 2003), and can occur in novice and elite athletes alike. In individuals who are just beginning to exercise, DOMS can result in decreased motivation. The eccentric actions of plyometric exercise, squatting, jumping, downhill running, and the lowering phase of resistance training are all known to result in DOMS (Connolly, Sayers, & McHugh, 2003). DOMS presents itself as pain, muscle soreness, swelling, and stiffness 8 to 24 hours post-exercise and peaks 24–48 hr following an unaccustomed bout of eccentric exercise and resolves within 10 days following exercise (Manimmanakorn et al., 2016; Mchugh, Connolly, Eston, & Gleim, 1999; Meamarbashi, 2017).

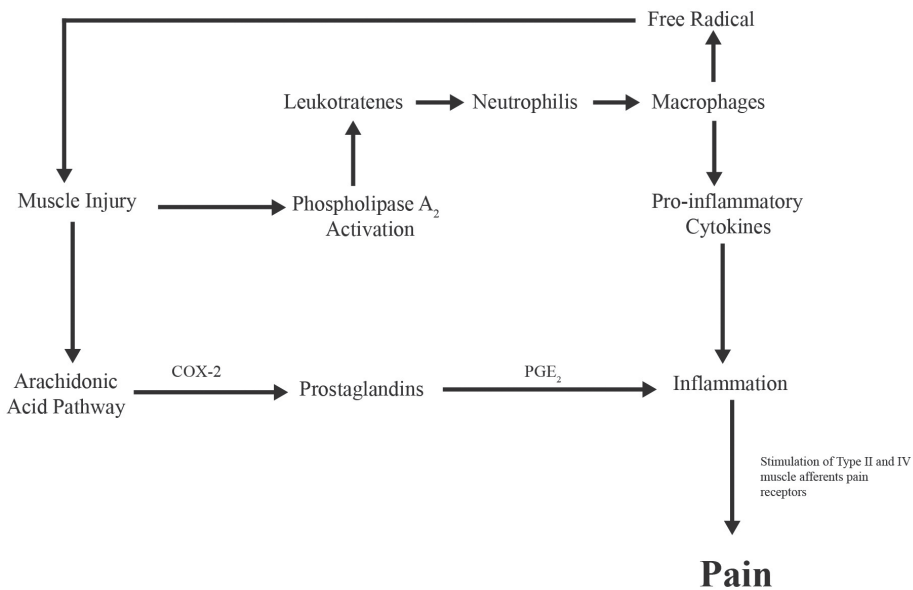

Figure 1 Schematic showing the possible sequence of injury leading to DOMS. COX-2, cycloxygenase; PGE_2; prostaglandin E_2

The underlying cause of DOMS is not fully understood. Most researchers agree that DOMS is caused by muscle damage (sarcomere disruption) and inflammation (Amalraj, Divya, & Gopi, 2020; Hoseinzadeh, Daryanoosh, Baghdasar, & Alizadeh, 2015) (Figure 1). During eccentric exercise, the sarcomeres become overstretched and fail to return to their resting length (Brooks, Fahey, & Baldwin, 2005). The overstretched sarcomeres allow calcium to accumulate in the injured portion of the muscle activating proteases and phospholipase (Cheung, Hume, & Maxwell, 2003; MacIntosh, Gardiner, & McComas, 2006). The activation of proteases and phospholipase lead to the production of both prostaglandins and leukotrienes (MacIntosh, Gardiner, & McComas, 2006). Neutrophils invade the injured area and increase vascular permeability, allowing fluids and intercellular components to enter the cells (MacIntosh,

Gardiner, & McComas, 2006). The fluid and intercellular components attract marcophages to invade the injuried area producing free radicals, proinflammatory cytokins and tumor nercosis factor-alpha (TNF-α) which further enhance muscle injury and stimulate type II and IV muscle afferent pain receptors, resulting in DOMS (Connolly, Sayers, & McHugh, 2003; MacIntosh, Gardiner, & McComas, 2006). Another pathway which is theorized to result in DOMS is the arachidonic acid pathway. Following muscle injury, arachidonic acid is released from the damaged cellular membranes (Maroon, Bost, Borden, Lorenz, & Ross, 2006). Archidonic acid is quickly transfomed into prostaglandins (PGE_2) and thromboxanes through the enxyme cyclooxygenase (COX-1 or COX-2) (Maroon, Bost, Borden, Lorenz, & Ross, 2006). COX-1 is a constitutive enzyme that protects the gastrointestinal lining and aids in platelet aggregation (Maroon, Bost, Borden, Lorenz, & Ross, 2006). In comparison, COX-2 is activated during muscle damage and aids in producing inflammation and stimulating type II and IV pain receptors (Maroon, Bost, Borden, Lorenz, & Ross, 2006).

Since the cause of DOMS is unknown, there is also a lack of knowledge for preventing DOMS. This lack of knowledge has led to multiple potential treatments, with mixed results (Cheung, Hume, & Maxwell, 2003). Over the years, treatments such as stretching, massage, nonsteroidal anti-inflammatory medications (NSAIDs), ultraound, hyperabaric oxygen, and exercise have all been examined as potential solutions to DOMS (Cheung, Hume, & Maxwell, 2003). Recently, athletes have increasingly sought natural remedies to treat pain and inflammation instead of NSAIDs, due to their potentially adverse effects within the gastrointestinal (stomach ulcers) and cardiovascular systems (blood clots leading to heart attacks and strokes). Many commerically available supplements are thought to have similar anti-inflammatory properties as NSAIDs, but without the adverse side effects. Some researchers believe that natural supplements may be an effective alternative to NSAIDs to control inflammation and oxidative stress induced by DOMS (Nakhostin-Roohi, Moradlou, Hamidabad, & Ghanivand, 2016). Therefore, the purpose of this review is to examine the effects of commerically available supplements on DOMS and markers of muscle damage and inflammation. The supplements examined include: anatabine, branched chain amino acids. curcumin, ginger, ginseng, green tea extract, pomegranate juice, and protease.

Anatabine

Anatabine is a minor tobacco alkaloid with a comparable chemical structure to nicotine (Jenkins et al., 2013). Anatabine is a member of the Solanaceae (nightshade) family and found in green tomatoes, peppers, and eggplants (Paris et al., 2013). Anatabine is thought to have anti-inflammatory properties; however, little research has been done in regard to anatabine's potential to decrease inflammation. The exact mechanism in which anatabine influences inflammation is unknown. Researchers speculate that anatabine's anti-inflammatory effect involves altering the signal transducer and activator of transcription 3 (STAT3) and nuclear factor Kappa-B (NF-kB) pathways, which play a major role in pro-inflammatory cytokine production and activating inflammatory cells (Paris et al., 2013).

The most compelling research to support the claim that anatabine has anti-inflammatory properties was conducted with 32-week old mice. Paris el al. (2013) discovered that anatabine reduced the production of pro-inflammatory cytokines IL-6,

IL-1, and TNF-α. The researchers also examined the anti-inflammatory activity of anatabine in vitro and found that anatabine prevented IL-1 production and STAT3 and NF-kB phosphorylation induced by lipopolysaccharide (LPS) or TNF-α (Paris et al., 2013). These results supported the claim that anatabine decreases inflammation by alternating both the STAT3 and NF-kB pathways. Jenkins et al. conducted two studies in 2013 and 2014 examining the effects of 6–12 mg of anatabine prior to and subsequent to unilateral eccentric elbow flexion. The results of both of these studies revealed that anatabine did not have any effect on DOMS or markers of muscle damage (CK, TNF-α, C-reactive protein (CRP), or myoglobin (MB)). The researchers concluded that the effectiveness of anatabine to block pro-inflammatory cytokines and decrease inflammation in humans after exercise was inconclusive (Jenkins et al., 2014) (Table 1).

Branched chain amino acids

Branched chain amino acids (BCAA) consist of leucine, isoleucine, and valine, which are three of the nine amino acids shown to be vital for protein synthesis and tissue repair (Leahy & Pintauro, 2013). Unlike other essential acids that are catabolized in the liver, BCAA are primarily catabolized in skeletal muscle (Harper, Miller, & Block, 1984). During exercise, the working skeletal muscles oxidize a greater proportion of BCAAs than any other amino acids (Shimomura, Yamamoto, & Bajotto, 2006). Therefore, researchers speculate that BCAA may prevent muscle damage by promoting skeletal muscle protein synthesis and suppressing protein degradation, in addition to aiding in reactive oxygen species (ROS) scavenging (Kadowaki & Kanazawa, 2003; Valerio, D'Antona, & Nisoli, 2011).

Numerous studies have examined the effects of BCAA on DOMS and markers of muscle damage. Most agree that BCAA have the potential to decrease muscle damage and DOMS following eccentric exercise. Greer and colleagues (2007) conducted a study examining the effects of 5.0 g of BCAA five min prior and one hr after cycling for 90 min on a cycle ergometer at 55% VO2max. The consumption of BCAA before and after an exhaustive bout of exercise decreased DOMS (24 hr post exercise) and lessened the increase in both creatine kinase (CK) and lactate dehydrogenase (LDH). Also, leg flexion torque was increased 48 hr post exercise with no effect on leg extension torque. Another group of investigators found that long distance runners who consumed a 2,500 ml drink containing 0.8% BCAA during a three day intensive training program experienced a decrease in DOMS, fatigue, CK, and lactate dehydrogenase (LDH) (Matsumoto et al., 2009). Others also found that BCAA consumption decreased DOMS after exercise (Asjodi, Khotbesara, Gargari, & Izadi, 2018; Howatson et al., 2012; Leahy & Pintauro, 2013; Nosaka, Sacco, & Mawatari, 2006; Shimomura et al., 2010). Shimomura et al. (2010) examined the effects of consuming 100 mg/kg BCAA 15 min after completing 140 squats. Although DOMS declined, consuming BCAA 15 min after performing exercise did not influence CK. In comparison, Howatson et al. (2012) found plasma CK levels were significantly lower when national rugby and football players consumed 20 mg of BCAA for 12 days (seven days prior and five days after 100 drop-jumps from a height of 0.6 m). Asjodi, Khotbesara, Gargari, and Izadi (2018) discovered that 10 mg/kg of BCAA increased CK levels 72 hr after a squat exercise (six sets at 75% 1RM) while significantly decreasing LDH up to 48 hr post

exercise. In summary, there is substantial evidence to suggest that BCAA may be effective in preventing muscle damage, thereby decreasing DOMS and fatigue following exercise. The exact amount of BCAA that is recommended for maximal benefit has not been established (Table 2).

Curcumin

Curcumin has been used for centuries in both traditional Chinese and Indian medicine to reduce pain and inflammation (Nicol, Rowlands, Fazakerly, & Kellett, 2015; Tanabe et al., 2019). Curcumin (diferuloylmethane) is extracted from the root of the curcumin plant (turmeric root) and is a natural polyphenolic substance with high anti-inflammatory and anti-oxidant properties (Delecroix, Abaidia, Leduc, Dawson, & Dupont, 2017; Nicol, Rowlands, Fazakerly, & Kellett, 2015; Singh & Aggarwal, 1995). Curcumin is believed to have similar anti-inflammatory properties as NSAIDs such as ibuprofen and Celebrex, but without the major cardiovascular and gastrointestinal side effects (Nakhostin-Roohi, Moradlou, Hamidabad, & Ghanivand, 2016). How curcumin influences inflammation is not agreed upon. However, it is believed that curcumin directly influences the activity of NF-kB, COX-2 or activator protein-1 (AP-1), which regulates the inflammation cascade (Davis et al., 2007). More specifically, curcumin may target NF-kB decreasing AP-1 binding to DNA decreasing the production COX-2, resulting in a blunted inflammation response to muscle injury following eccentric exercise (Singh & Aggarwal, 1995; Thaloor, Miller, Gephart, Mitchell, & Pavlath, 1999). The idea that curcumin inhibits NF-kB instead of COX-2 is why many researchers believe the supplement has a decreased risk of potential adverse side effects that NSAIDs possess (Davis et al., 2007).

Researchers have found conflicting results on the effects of curcumin and DOMS. For instance, Nicol, Rowlands, Fazakerly and Kellett (2015) examined the effects of curcumin on DOMS, sport performance, and markers of muscle damage and inflammation. They discovered that when moderately trained men consumed 2.5 g of curcumin twice a day for five days (two days prior and three days post exercise), curcumin decreased DOMS and increased jump height 24 hr and 48 hr after exercise. In addition, they found that curcumin blunted the increase of creatine kinase (CK), and interleukin-6 (IL-6). Likewise, Nakhostin-Roohi, Moradlou, Hamidabad and Ghanivand (2016) discovered that 150 mg of curcumin consumed immediately after eccentric exercise also decreased DOMS and markers of muscle damage (CK, alanine aminotransferase (ALT), and aspartate aminotransferase (AST)). In comparison, other researchers have shown that regardless of the dosage, curcumin did not have a significant effect on DOMS (Delecroix, Abaidia, Leduc, Dawson, & Dupont, 2017; Jager, Purpuna, & Kerksick, 2019; McFarlin et al., 2016; Tanabe et al., 2015).

While the effects of curcumin on DOMS are unclear, most researchers have shown that curcumin does decrease some markers of muscle damage (AST, ALT, CK) and inflammation (IL-6, interleukin-8 (IL-8) and TNF-α. McFarlin et al. (2016) examined the effects of 400 mg of curcumin daily (two days prior to and four days after exercise) and found that after eccentric leg press of 110% one repetition max (1-RM), curcumin significantly decreased CK, IL-6, IL-8 and TNF-α. However, there was no significant difference between the curcumin and placebo groups in regard to DOMS and activities of daily living soreness. Others authors (Nakhostin-Roohi, Moradlou,

Hamidabad, & Ghanivand, 2016; Nicol, Rowlands, Fazakerly, & Kellett, 2015; Tanabe et al., 2015; Tanabe et al., 2019) found similar results regarding the effects of curcumin on markers of muscle damage and inflammation. In comparison, Amalraj, Divya, and Gopi (2020) found that when 500 mg of curcumin was consumed for three days after a 45 min downhill (−10% grade) run, CK was not significantly different from the placebo. Delecroix et al. (2017) also found that 6 g of curcumin combined with 60 mg of peperline daily (two days prior and two days after exercise) did not result in a difference in CK from placebo.

Shortcomings of curcumin include its low bioavailability, poor solubility, and rapid elimination (Amalraj, Divya, & Gopi, 2020; Tanabe et al., 2019). Therefore, ingesting curcumin only before exercise has shown little or no effect on muscle damage (Tanabe et al., 2019). Tanabe et al. conducted two studies in 2015 and 2019 on the effects of curcumin (180 mg) before and after exercise. In both of the studies, DOMS was decreased when curcumin was consumed after exercise instead of before. The researchers also found that reduced CK lasted up to seven days after maximal elbow flexion only when curcumin was consumed following exercise (Tanabe et al., 2019). To gain maximal benefits from curcumin, researchers suggest it may be necessary to ingest curcumin continuously after exercise to keep curcumin concentrations in the blood elevated. (Tanabe et al., 2019). Overall, the general census in the literature is that curcumin can attenuate some, but not all, aspects of muscle damage and that more research should be done to determine the ideal dosage and consumption duration (Table 3).

Ginger

Ginger (zingiber officinale) is used in traditional Chinese medicine to treat arthritis, sprains, muscle aches, pain, and diabetes (Hoseinzadeh, Daryanoosh, Baghdasar, & Alizadeh, 2015; Mashhadi et al., 2013). Ginger and its constituents are shown to have both analgesic and anti-inflammatory properties (Hoseinzadeh, Daryanoosh, Baghdasar, & Alizadeh, 2015). The mechanism that is responsible for the analgesic and anti-inflammatory properties of ginger is through inhibiting COX-1 and COX-2, decreasing pro-inflammatory cytokines (TNF-α and IL-6) and blocking leukotriene synthesis (Ali, Blunden, Tanira, & Nemmar, 2008; Black & O'Connor, 2010; Hoseinzadeh, Daryanoosh, Baghdasar, & Alizadeh, 2015). Many studies have been conducted in an attempt to confirm the claimed benefits of ginger. Overall, the results of the reseaerch have been ambiguous. Mashhadi et al. (2013) had martial arts athletes consume 3 g of ginger daily six weeks before a sport-specific resistance training session during the competitive season. They found that DOMS was significantly lower when ginger was consumed before exercise, however ginger did not cause a significant decrease in IL-6. The authors suggested that 3 g may not have been large enough to have an influence on the pro-inflammatory cytokines. In comparison, Hoseinzadeh, Daryanoosh, Baghdasar, and Alizadeh (2015) compared the effects of 2 g of ginger extract in two conditions (one hr before a 20-min step test and immediately after exercise) in untrained adults. Muscle soreness was significantly lower only when ginger was consumed prior to exercise. Plasma IL-6 levels were significantly lower in both conditions. A possibility for inconsistent results between the two studies mentioned in regard to IL-6 could lie within the training status of the participants. Mashhadi and colleagues (2013) recruited martial art athletes for their study while (Hoseinzadeh,

Daryanoosh, Baghdasar, & Alizadeh (2015) recruited untrained women. Plasma IL-6 is released during muscle contractions and is shown to be lower after long-term training because of the chronic muscle contractions (Nicklas et al., 2008). Therefore, it seems likely that trained individuals would need a higher dose of ginger to see any significant pro-inflammatory cytokines reductions. Manimmanakorn et al. (2016) examined the effects of Plai (*zingiber cassumunar* Roxb) on markers of muscle damage and DOMS. Plai is within the ginger family and contains powerful phytochemicals (Manimmanakorn et al., 2016). The participants applied either 7% or 14% Plai cream on their quadriceps for seven days post eccentric knee extension exercise. They found no effect of Plai cream on CK levels but DOMS was significantly lower after the application of the 14% Plai cream, but not after the 7% cream. Additionally, applying 14% Plai cream to the quadriceps preserved quadricep strength while applying the 7% did not decrease strength loss. While the aforementioned studies confirmed that ginger can reduce DOMS, other studies have shown the opposite. Black and O'Connor (2010) determined that 2 g of ginger for two days following unilateral eccentric elbow flexion exercise did not have an effect on DOMS, range of motion (ROM), or arm volume. Others (Matsummura, Zavorsky, & Smoliga, 2015; Wilson, Fitzgerald, Rhodes, Lundstorm, & Ingraham, 2015) agreed that ginger (2.2 g and 4 g respectively) had no effect on DOMS. Due to the conflicting results, further research needs to be conducted to verify the potential benefits of ginger after exercise (Table 4).

Ginseng

Ginseng (genus panax) is another supplement that has been used for thousands of years in traditional Chinese medicine to manage stress, relieve fatigue, and reduce pain and swelling (Caldwell et al., 2018; Pumpa, Fallon, Bensoussan, & Papalia, 2013). The active ingredient in ginseng, saponins (ginsenosides), has shown the potential to block calcium influx into smooth muscle by activating Na^+–K^+ ATPase, decrease intercellular calcium ion levels and heart rate (Chen, Chung, Li, Lin, & Tzan, 2009). The influx of calcium ions into the working skeletal muscles is reported as a potential explanation for DOMS following an exhaustive bout of exercise (Pumpa, Fallon, Bensoussan, & Papalia, 2013). If ginseng can potentially block excessive calcium influx into the working skeletal muscle, it may prevent or blunt DOMS following exercise (Pumpa, Fallon, Bensoussan, & Papalia, 2013). Again, the mechanism in which ginseng acts upon is unclear.

The literature to support the claimed benefits of ginseng (reduction of pain, inflammation and fatigue) is sparse. Only a few studies have been conducted to examine the effects of ginseng on sports performance, soreness, or inflammation after exercise. Pumpa, Fallon, Bensoussan, and Papalia (2013) examined the effects of 400 mg of ginseng after a downhill run (−10% grade) at 80% HR_{max}. The authors found that DOMS was significantly lower 96 hr post exercise in participants after consuming ginseng. However, ginseng did not influence markers of muscle damage such as CK, CRP, or MB. It is interesting to note that in this particular study, both IL-6 and TNF-α were significantly higher after the consumption of ginseng compared to the control group. To explain these results, the authors suggested that ginseng may intensify the release or delay the clearance of TNF-α and impact the timing or expression of IL-6 following exercise (Pumpa, Fallon, Bensoussan, & Papalia, 2013). Hsu, Ho, Lin, Su, and Hsu

(2005) studied the effects of 400 mg of American ginseng on CK four weeks prior to running at 80% VO2max until volitional fatigue. The authors found that American ginseng significantly reduced CK immediately and up to 120 min following exercise. Lastly, Caldwell et al. (2018) compared the effects of consuming a high dose (960 mg) and low dose (160 mg) Korean ginseng, GINST15 (modified to have an increased bioavailability, 14 days prior to resistance training on DOMS and sport performance (reaction time and jump power). Consuming GINST15 decreased DOMS significantly in both groups. However, GINST15 did not improve reaction time nor jump power. As the results from these studies are mixed, the authors recommend that further research be conducted to identify the specific mechanism ginseng acts upon to decrease inflammation, soreness and fatigue, as well as the appropriate dosage required to achieve the aforementioned benefits (Table 5).

Green tea extract

Green tea extract is obtained from *camellia sinensis* and is rich in polyphenols such as epigallocatechin gallate, epicatechin, epigallocatechin, and epicatechin (da Silva, Machado, Souza, Mello-Carpes, & Carpes, 2018). The properties of green tea extract make it a powerful anti-oxidant that gather free radicals such as superoxide hydroxyl (SOD) and hydrogen peroxide (H_2O_2), and inhibits pro-oxidant enzymes (da Silva, Machado, Souza, Mello-Carpes, & Carpes, 2018). The exact redox mechanism leading to exercise induced oxidative stress remains vague (He et al., 2016). Some researchers speculate that under stressful conditions such as eccentric exercise, the stimulation of xanthine oxidase (XO) contributes to the enhancement of reactive oxygen species (ROS) greater than the capacity of the anti-oxidant system to reduce ROS activity, resulting in oxidative stress and muscle cell damage (He et al., 2016). The damage to the muscle cells caused by oxidative stress decreases athletic performance and increases muscle soreness (Jowko et al., 2012). Increasing the anti-oxidant concentration by consuming green tea extract may offset fatigue and the accumulation of free radical production for a faster exercise recovery (Kerksick, Kreider, & Willoughby, 2010). The anti-oxidant properties of green tea extract are believed to prevent ROS formation, thereby decreasing fatigue and preserving sport performance by inhibiting XO (Gomez-Cabrera, Domenech, & Vina, 2008; Panza et al., 2008). There have been several studies examining the effects of green tea extract on measurements of oxidative stress. The results from these studies are conflicting. Furthermore, the exact dosage and duration that green tea needs to be consumed to combat oxidative stress and improve DOMS is unknown at this time. For instance, da Silva, Machado, Souza, Mello-Carpes, & Carpes (2018) examined the effects of 500 mg green tea extract over the course of 15 days post eccentric exercise. They found green tea extract did not improve markers of muscle damage (CK, lactate dehydrogenase (LDH)) or decrease oxidative stress (ROS, or ferric reducing antioxidant power (FRAP)). These results were in agreement with a study done by Jowko et al. (2012) in which the authors evaluated the effects of 640 mg of green tea extract 1.5 hr before a muscular endurance test. The researchers found that 640 mg of green tea extract prior to exercise did not have an effect on markers of muscle damage (CK), oxidative stress (SOD, uric acid (UA) or total anti-oxidant capacity (TAC)). Other authors (Jowko, Dlugolecka, Makaruk, & Cieslinski, 2015; Kerksick, Kreider, & Willoughby, 2010) also found that green tea

extract had no significant effect on markers of muscle damage and oxidative stress. In contrast, Panza et al. (2008) had 14 healthy adults consume 600 ml of green tea daily, seven days before a bout of exhaustive bench press exercise. They found that FRAP was significantly higher after 14 days of consuming 600 ml of green tea and XO was significantly decreased. The authors also discovered that CK and AST were significantly lower after exercise. The authors concluded that consuming at least 600 ml of green tea may offer protection against oxidative stress after exercise. Due to the reduction in markers of muscle damage, the authors also suggested that the oxidative mechanism may play a role in the development of muscle damage following exercise. Herrlinger, Chirouzes, and Ceddia (2015) confirmed these results when they conducted a study examining the effects of 1,000 mg or 2,000 mg of green tea extract daily for four days following a 40 min downhill run (−10% grade) at 65% VO2max. Both doses of green tea extract significantly reduced CK and LDH and enhanced FRAP.

To date, there have been three studies regarding the effects of green tea extract on DOMS. Kerksick, Kreider, and Willoughby (2010) found after 14 days of 1800 mg of green tea extract following eccentric unilateral knee extension, DOMS was significantly decreased at 24 hr post exercise, but markers of inflammation were not influenced by green tea extract. Similarly, Herrlinger, Chirouzes, and Ceddia (2015) also found that green tea (2,000 mg) improved muscle soreness at both 48 hr and 96 hr after exercise. However, da Silva and colleagues (2018) found that muscle damage was minimized without any detectable significant changes in DOMS following 15 days of 500 mg of green tea after performing calf raises to voluntary fatigue. Green tea extract may offer some protection against oxidative stress and reduce muscle damage and DOMS. Future research needs to determine the exact consumption dosage and duration required for green tea to have maximal benefits against oxidative stress and muscle soreness (Table 6).

Pomegranate juice

Pomegranate juice contains high levels of polyphenols and offers many health benefits and can aid in preventing and treating conditions such hypertension and dyslipidemia (Ammar et al., 2016). In addition, some believe that pomegranate juice has properties that can decrease both inflammation and oxidative stress (Ammar et al., 2016). Pomegranate extract (liquid or dry form) has recently become a popular alternative source for obtaining the polyphenols found in pomegranate juice (Ammar et al., 2018). One of the benefits of pomegranate juice or extract over other polyphenols such as green tea is the high bioavailability with an anti-oxidant activity three times higher than green tea, making it more effective in destroying free radicals, inhibiting cellular oxidative stress, and decreasing lipid peroxidation (Seeram et al., 2008). Pomegranate juice is thought to act similarly to green tea in that it inhibits cellular transcription factors NF-kB, TNF-α, and COX-2, thereby preventing inflammation and pain (Adams et al., 2006; Afaq et al., 2005).

Although researchers have noted a beneficial effect of pomegranate juice, few have examined the potential effects of pomegranate juice after exercise. Lamb et al. (2019) examined the effects of a daily consumption of 500 ml pomegranate juice four days prior and five days after unilateral eccentric elbow flexion. The authors found that nine days of pomegranate juice did not have an effect on elbow flexion strength, DOMS,

ROM, or plasma CK levels. In comparison, Trombold, Barnes, Critchley, and Coyle (2010) investigated the effects of 100 ml of ellagitanni (pomegranate extract) four days prior and five days post unilateral eccentric elbow flexion. Nine days of ellagitanni consumption significantly decreased DOMS 2 hr after exercise and increased elbow flexor strength at 24 and 48 hr following exercise. However, ellagitanni was not successful at influencing markers of muscle damage (CK, CRP) or pro-inflammatory cytokines (IL-6). Trombold conducted a second study (2011) and found that 500 ml of pomegranate juice for 15 days (seven days prior and eight days after exercise) decreased DOMS in elbow flexors and improved elbow flexion strength up to seven days post unilateral maximal eccentric elbow flexion exercise.

In a study conducted by Amar and associates (2016), Olympic weight lighters consumed 500 ml of pomegranate juice prior to training and another 450 ml for two days following training. Pomegranate juice decreased knee extensor DOMS, rate of perceived exertion (RPE) and markers of muscle damage (CRP, CK, LDH and AST). In regard to elbow flexor DOMS, pomegranate juice had no effect. Based on the few studies conducted, it appears that pomegranate juice may be an effective treatment for muscle soreness and fatigue following exercise. However, more research needs to be completed to verify the effectiveness of pomegranate juice for recovery after exercise (Table 7).

Protease

Protease consists of a group of four biologically active enzymes (seline, cysteine, aspartic acid, and metalloproteases) that initiate protein catabolism through the hydrolysis of peptide bonds that link amino acids together in a polypeptide chain (Buford et al., 2009). Protease is believed to decrease inflammation and attenuate pain (Miller, Bailey, Barnes, Derr, & Hall, 2004). How protease decreases inflammation remains unknown. It is hypothesized that protease reduces inflammation by blocking COX-2 stimulation to decrease edema and pain (Buford et al., 2009; Miller, Bailey, Barnes, Derr, & Hall, 2004). A few studies have been conducted on the effects of protease on muscle damage and inflammation after exercise. Miller, Bailey, Barnes, Derr, and Hall (2004) studied the effects of protease on performance and DOMS after a 30 min downhill run (−10% grade). They discovered after four days of protease supplementation, DOMS was decreased 24 to 72 hr post exercise. In addition, knee flexion power and torque were maintained after exercise with no change in agility run time, or knee extension torque. Shing and colleagues (2016) studied bromelain, a mixture of proteases obtained from pineapples, and its effect on highly trained road cyclists. The cyclists completed a cycle of 10 stages over the span of six days while consuming 1000 mg of bromelain daily. Fatigue was decreased on day four only and the supplement did not influence CK, MB, or LDH. Beck et al. (2007) found similar results when 29 recreationally active men consumed a protease supplement that contained both 325 mg of protease 6.0 and 340 mg protease 4.5 four days after completing damaging eccentric forearm flexion exercise. While the protease supplement increased forearm flexion strength, it had no effect on DOMS, joint angle, or arm circumference. In addition, plasma CK and MB levels were not blunted after supplementation. Budfold et al. (2009) also found that 24 days of 5.828 mg of protease had no effect on DOMS or some markers of muscle damage and inflammation (CK, SOD, IL-8, IL-10, IL-1, and TNF-α).

Intriguingly, protease did decrease three markers of inflammation (IL-6, IL-12 and COX-2) and improved quadriceps flexion strength. The authors concluded that while not all pro-inflammatory cytokines were decreased by protease, the decrease in IL-6 and IL-12, as well as COX-2, supported the concept that protease has the ability to decrease muscle inflammation and improve muscle function following exercise. Based on available evidence, it appears that protease may decrease inflammation and improve performance after a damaging bout of exercise. To gain a better insight in the potential post exercise benefits of protease, again, more research should be conducted (Table 8).

DISCUSSION

Finding ways to prevent and treat the negative effects of DOMS can maximize training performance in athletes, prevent injury, and help exercise novices maintain motivation (Nicol, Rowlands, Fazakerly, & Kellett, 2015). The series of events that cause DOMS is unclear. However, researchers have come to the conclusion that both mechanical injury to the sarcomere and the inflammation cascade are key players in the development in DOMS (Cheung, Hume, & Maxwell, 2003). Without knowing the exact cause of DOMS, finding the ideal treatment ramains difficult. Therefore, many proposed treatments for DOMS exsist (NSAIDs, massage, ultraound, hyperabaric oxygen, and exercise) and their effects on DOMS has produced mixed results (Cheung, Hume, & Maxwell, 2003). NSAIDs are often used as the first line of defense in the treatment of inflammation and soreness following exercise. However, other than their potential adverse effects, NSAIDs may supress muscle protein synthesis (Mackey, 2013), thereby slowing the healing processes (Paulsen et al., 2010) following an injury, making them less than ideal. Many commerically available supplements have similar anti-inflammatory properties as NSAIDs without the possible adverse effects and remain safer alternativse for treating pain and inflammation. While they may be safer alternatives, as shown throuhgout this review, the exact mechanism in which these supplements target and the safest maximal dosages remain unknown.

It appears that many of the supplements reviewed may decrease DOMS following eccentric exercise, as well as decrease markers of muscle damage and inflammation. BCAA, pomegranate juice/extract and curcumin appear to have the greatest effect on DOMS. In comparision, anatabine and ginseng do not appear to have a significant effect on inflammation or DOMS following exercise. However, due to a lack of consistent study design and dosing for each supplement, it is diffuclt to draw a final conclusion on the effectiveness of these supplements on DOMS. Future research should examine the effects of consuming natural supplements on relieving the symptoms of DOMS on clinical populations such as those with diabetes and peripheral artery disease. In addition, for all populations, the safety of consuming natural supplements needs to be examined regarding adverse side effects, long-tem effects, as well as the optimal dosage.

REFERENCES

Adams, L. S., Seeram, N. P., Aggarwal, B. B., Takada, Y., Sand, D., & Heber, D. (2006). Pomegranate Juice, Total Pomegranate Ellagitannins, and Punicalogin Suppress Inflammatory Cell Signaling in Colon Cancer Cells. *Journal of Agricultural and Food Chemistry*, *54*(3), 980–985.

Afaq, F., Malik, A., Syed, D., Maes, D., Matsui, M. S., & Mukhtar, H. (2005). Pomegranate Fruit Extract Modulates UV-B-Mediated Phosphorylation of Mitogen-Activated Protein Kinases and Activation of Nuclear Factor Kappa B in Normal Human Epidermal Keratinocytes. *Photochemistry and Photobiology*, *81*(1), 38–45.

Ali, B. H., Blunden, G., Tanira, M. O., & Nemmar, A. (2008). Some Phytochemical, Pharacological and Toxicological Properties of Ginger (Zingiber officinale Roscoe): A Review of Recent Research. *Food and Chemical Toxicology*, *46*(2), 409–420.

Amalraj, A., Divya, C., & Gopi, S. (2020). The Effects of Bioavailable Curcumin (Cureit) on Delayed Onset Muscle Soreness Induced by Eccentric Continuous Exercise: A Randomized, Placebo-Controlled, Double-Blind Clinical Study. *Journal of Medicinal Food*, *23*(5), 1–9.

Ammar, A., Bailey, S. J., Chtourou, H., Trabelsi, K., Turki, M., Hokelmann, A., Souissi, N. (2018). Effects of Pomegranate Supplementation on Exercise Performance and Post-Exercise Recovery in Healthy Adults: A Systematic Review. *British Journal of Nutrition*, *120*(11), 1201–1216.

Ammar, A., Turki, M., Chtourou, H., Hammouda, O., Trabelsi, K., Kallel, C., ... Souissi, N. (2016). Pomegranate Supplementation Accelerates Recovery of Muscle Damage and Soreness and Inflammatory Markers After a Weightlifting Training Session. *PloSONE*, *11*(10), e0160305.

Asjodi, F., Khotbesara, R. D., Gargari, B. P., & Izadi, A. (2018). Impact of Combined or Single Supplementation of Branched-Chain Amino Acids on Delayed Onset Muscle Soreness and Muscle Damage Following Resistance Exercise. *Progress in Nutrition*, *20*(2), 263–272.

Beck, T. W., Housh, T. J., Johnson, G. O., Schmidt, R. J., Housh, D. J., Coburn, J. W., ... Mielke, M. (2007). Effects of a Protease Supplement on Eccentric Exercise-Induced Markers of Delayed-Onset Muscle Soreness and Muscle Damage. *Journal of Strength and Conditioning Research*, *2*(13), 661–667.

Black, C. D., & O'Connor, P. J. (2010). Acute Effects of Dietary Ginger on Muscle Pain Induced by Eccentric Exercise. *Phytotherapy Research*, *24*(11), 1620–1626.

Brooks, G. A., Fahey, T. D., & Baldwin, K. M. (2005). Muscle Strength, Power and Flexibility. In: G. A. Brooks, T. D. Fahey, & K. M. Baldwin (Eds.), *Exercise Physiology: Human Bioenergetics and Its Application* (pp. 456–491). New York, NY: McGraw-Hill.

Buford, T. W., Cooke, M. B., Redd, L. L., Hudson, G. M., Shelmadine, B. D., & Willoughby, D. S. (2009). Protease Supplementation Improves Muscle Function After Eccentric Exercise. *Medicine and Science in Sports and Exercise*, 1908–1914.

Caldwell, L. K., DuPont, W. H., Beeler, M. K., Post, E. M., Barnhart, E. C., Hardesty, V. H., ... Kraemer, W. J. (2018). The Effect of a Korean Ginseng, GINST15, on Perceptual Effort, Psychomotor Performance, and Physical Performance in Men and Women. *Journal of Sport Science and Medicine*, *17*(1), 92–100.

Chen, R. J., Chung, T.-Y., Li, F.-Y., Lin, N.-H., & Tzan, J. T. (2009). Effect of Sugar Positions in Ginsenosides and their Inhibitory Potency on Na+/K+ -ATPase Activity. *Acta Pharmaceutica Sinica*, *1*, 61–69.

Cheung, K., Hume, P. A., & Maxwell, L. (2003). Delayed Onset Muscle Soreness: Treatment Strategies and Performance Factors. *Journal of Sports Medicine*, *33*(2), 145–164.

Connolly, D. A., Sayers, S. P., & McHugh, M. P. (2003). Treatment and Prevention of Delayed Onset Muscle Soreness. *Journal of Strength and Conditioning Research*, *17*(1), 197–208.

Da Silva, W., Machado, A. S., Souza, M. A., Mello-Carpes, P. B., & Carpes, F. P. (2018). Effect of Green Tea Extract Supplementation on Exercise-Induced Delayed Onset Muscle Sorenes and Muscular Damage. *Physiology and Behavior*, *194*, 77–82.

Davis, J. M., Murphy, E. A., Carmichael, M. D., Zielinski, M. R., Groschwitz, C. M., Brown, A. S., ... Mayer, E. P. (2007). Curcumin Effects on Inflammation and Performance Recovery Following Eccentric Exercise-Induced Muscle Damage. American Journal of Physiology: Regulatory. *Integrative and Comparative Physiology*, *292*(6), R2168–R2173.

Delecroix, B., Abaidia, A. E., Leduc, C., Dawson, B., & Dupont, G. (2017). Curcumin and Piperine Supplementation and Recovery Following Exercise Induced Muscle Damage: A Randomized Controlled Trial. *Journal of Sports Science and Medicine*, *16*(1), 147–153.

Drobnic, F., Riera, J., Appendino, G., Togni, S., Franceschi, F., Valle, X., ... Tur, J. (2014). Reduction of Delayed Onset Muscle Soreness by a Novel Curcumin Delivery System: A Randomized, Placebo-Controlled Trial. *Journal of the International Society of Sports Nutrition*, *11*(31), 3–10.

Gomez-Cabrera, M. C., Domenech, E., & Vina, J. (2008). Moderate Exercise is an Antioxidant: Upregulation of Antioxidant Genes by Training. *Free Radical Biology and Medicine*, *44*(2), 126–131.

Greer, B. K., Woodard, J. L., White, J. P., Arguello, E. M., & Haymes, E. M. (2007). Branched-Chain Amino Acid Supplementation and Indicators of Muscle Damage After Endurance Exercise. *International Journal of Sport Nutrition and Exercise Metabolism*, *17*(6), 595–607.

Harper, A. E., Miller, R. H., & Block, K. P. (1984). Branched-Chain Amino Acids Metabolism. *Annual Review of Nutrition*, *4*, 409–454.

He, F., Li, J., Liu, Z., Chuang, C. C., Yang, W., & Zuo, L. (2016). Redox Mechanism of Reactive Oxygen Species in Exercise. *Frontiers in Physiology*, *7*, 486.

Herrlinger, K. A., Chirouzes, D. M., & Ceddia, M. A. (2015). Supplementation with Polyphemolic Blend Improves Post-Exercise Strength Recovery and Muscle Soreness. *Food and Nutrition Research*, *59*, 30034.

Hoseinzadeh, K., Daryanoosh, F., Baghdasar, P. J., & Alizadeh, H. (2015). Acute Effects of Ginger Extract on Biochemical and Functional Symptoms of Delayed Onset Muscle Soreness. *Medical Journal of the Islamic Republic of Iran*, *29*, 261.

Howatson, G., Hoad, M., Goodall, S., Tallent, J., Bell, P. G., & French, D. N. (2012). Exercise-Induced Muscle Damage is Reduced in Resistance-Trained Males by Branched Chain Amino Acids: A Randomized, Double-Blind, Placebo Controlled Study. *Journal of the International Society of Sport Nutrition*, *9*(20).

Hsu, C.-C., Ho, M.-C., Lin, L.-C., Su, B., & Hsu, M.-C. (2005). American Ginseng Supplementation Attenuates Creatine Kinase Level Induced by Submaximal Exercise in Human Beings. *World Journal of Gastroenterology*, *34*, 5327–5331.

Jager, R., Purpuna, M., & Kerksick, C. M. (2019). Eight Weeks of a High Dose of Curcumin Supplementation May Attenuate Performance Decrements Following Muscle-Damaging Exercise. *Nutrients*, *11*(1692), 1–14.

Jenkins, N. D., Housh, T. J., Cochrane, K. C., Bergstom, H. C., Traylor, D. A., Lewis, R. W., ... Cramer, J. T. (2014). Effects of Anatabine and Unilateral Maximal Eccentric Isokinetic Muscle Actions on Serum Markers of Muscle Damage and Inflammation. *European Journal of Pharmacology*, *728*, 161–166.

Jenkins, N. D., Housh, T. J., Johnson, G. O., Traylor, D. A., Bergstrom, H. C., Cochrane, K. C., ... Cramer, J. T. (2013). The Effects of Anatabine on Non-Invasive Indicators of Muscle Damage: A Randomized, Double-Blind, Placebo-Controlled, Crossover Study. *Journal of the International Society of Sport Nutrition*, *10*, 33.

Jowko, E., Dlugolecka, B., Makaruk, B., & Cieslinski, I. (2015). The effect of Green Tea Extract Supplementation on Exercise-Induced Oxidative Stress Parameters in Male Sprinters. *European Journal of Nutrition*, *54*(5), 783–791.

Jowko, E., Sacharuk, J., Balasinska, B., Wilczak, J., Charmas, M., Ostaszewski, P., & Charmas, R. (2012). Effect of a Single Dose of Green Tea Polyphenols on the Blood Markers of Exercise-Induced Oxidative Stress in Soccer Players. *International Journal of Sport Nutrition and Exercise Metabolism*, *22*, 486–496.

Kadowaki, M., & Kanazawa, T. (2003). Amino Acids as Regulators of Proteolysis. *The Journal of Nutrition*, *133*(6), 2052S–2056S.

Kerksick, C. M., Kreider, R. B., & Willoughby, D. S. (2010). Intramuscular Adaptations to Eccentric Exercise and Antioxidant Supplementation. *Amino Acids*, *39*(1), 219–232.

Lamb, K. L., Ranchordas, M. K., Johnson, E., Denning, J., Downing, F., & Lynn, A. (2019). No Effect of Tart Cherry Juice or Pomegranate Juice on Recovery from Exercise-Induced Muscle Damage in Non-Resistance Trained Men. *Nutrients*, *11*(7), 1593.

Leahy, D. T., & Pintauro, S. J. (2013). Branched-Chain Amino Acid Plus Glucose Supplement Reduced Exercise-Induced Delayed Onset Muscle Soreness in College-Age Females. *ISRN Nutrition*, 2013, 921972.

Mackey, A. L. (2013). Does an NSAID a Day Keep Satellite Cells at Bay? *Journal of Applied Physiology*, *115*(6), 900–908.

MacIntosh, B. R., Gardiner, P. F., & McComas, A. J. (2006). Injury and Repair. In: B. R. MacIntosh, P. F. Gardiner, & A. J. McComas (Eds.), *Skeletal Muscle: Form and Function* (pp. 313–321). Champaign, IL: Human Kinetics.

Manimmanakorn, N., Manimmanakorn, A., Boobphachart, D., Thuwakum, W., Laupattarakasem, W., & Hamlin, M. J. (2016). Effects of Zingiber Cassumunar (Plai Cream) in the Treatment of Delayed Onset Muscle Soreness. *Journal of Integrative Medicine*, *14*(2), 114–120.

Maroon, J. C., Bost, J. W., Borden, M. K., Lorenz, K. M., & Ross, N. A. (2006). Natural Antiinflammatory Agents for Pain Relief in Athletes. *Neurosurgeon Focus*, *21*(4), E11.

Mashhadi, N. S., Ghiasvand, R., Askari, G., Feizi, A., Hariri, M., Darvishi, L., ... Hajishafiee, M. (2013). Influence of Ginger and Cinnamon Intake on Inflammation and Muscle Soreness Enduced by Exercise in Iranian Female Athletes. *International Journal of Preventive Medicine*, *4*, S11-S15.

Matsummura, M. D., Zavorsky, G. S., & Smoliga, J. M. (2015). The Effects of Pre-Exercise Ginger Supplementation on Muscle Damage and Delayed Onset Muscle Soreness. *Phytotherapy Research*, *29*(6), 887–893.

Matsumoto, K., Koba, T., Hamada, K., Sakurai, M., Higuchi, T., & Miyata, H. (2009). Branched-Chain Amino Acid Supplementation Attenuates Muscle Soreness, Muscle Damage and Inflammation During an Intensive Training Program. *Journal of Sport Medicine and Physical Fitness*, *49*(4), 424–431.

McFarlin, B. K., Venable, A. S., Henning, A. L., Best Sampson, J. N., Pennel, K., Vingren, J. L., & Hill, D. W. (2016). Reduced Inflammatory and Muscle Damage Biomarkers Following Oral Supplementation with Bioavailable Curcumin. *BBA Clinical*, *5*, 72–78.

McHugh, M. P., Connolly, D. A., Eston, R. G., & Gleim, G. W. (1999). Exercise-Induced Muscle Damage and Potential Mechanisms for The Repeated Bout Effort. *Sport Medicine*, *27*(3), 157–170.

Meamarbashi, A. (2017). Herbs and Natural Supplements in the Prevention and Treatment of Delayed-Onset Muscle Soreness. *Avicenna Journal of Phytomedicine*, *7*(1), 16–26.

Miller, P. C., Bailey, S. P., Barnes, M. E., Derr, S. J., & Hall, E. E. (2004). The Effects of Protease Supplementation on Skeletal Muscle Function and DOMS Following Downhill Running. *Journal of Sport Science*, *22*(4), 365–372.

Nakhostin-Roohi, B., Moradlou, A. N., Hamidabad, S. M., & Ghanivand, B. (2016). The Effects of Curcumin Supplementation on Selected Markers of Delayed Onset Muscle Soreness (DOMS). *Annals of Applied Sport Science*, *4*(2), 25–31.

Nicklas, B. J., Hsu, F.-C., Brinkley, T. J., Church, T., Goodpaster, B. H., Kritchevsky, S. B., & Pahor, M. (2008). Exercise Training and Plasma C-reactive Protein and Interleukin-6 in Elderly. *Journal of the American Geriatrics Society*, *56*(11), 2045–2052.

Nicol, L. M., Rowlands, D. S., Fazakerly, R., & Kellett, J. (2015). Curcumin Supplement Likely Attenuates Delayed Onset Muscle Soreness (DOMS). *European Journal of Applied Physiology*, *115*(8), 1769–1777.

Nosaka, K., Sacco, P., & Mawatari, K. (2006). Effects of Amino Acid Supplementation on Muscle Soreness and Damage. *International Journal of Sport Nutrition and Exercise Metabolism*, *16*(6), 620–635.

Panza, V. S., Wazlawik, E., Schutz, G. R., Comin, L., Hecht, K. C., & da Silva, E. L. (2008). Consumption of Green Tea Extract Favorable Affects Oxidative Stress Markers in Weight-Trained Men. *Nutrition*, *24*(5), 433–442.

Paris, D., Beaulieu-Abdelahad, D., Abdullah, L., Bachmeier, C., Ait-Ghezala, G., Reed, J., ... Mullan, M. (2013). Anti-Inflammatory Activity of Anatabine via Inhibition of STAT3 Phosphorylation. *European Journal of Pharmacology*, *698*(1–3), 145–153.

Paulsen, G., Egner, M., Drange, M., Langberg, H., Benestad, B., Fjeld, J. G., ... Raastad, T. (2010). A COX-2 Inhibitor Reduced Muscle Soreness, But Does Not Influence Recobery and Adaptation After Eccentric Exercise. *Scandinavian Journal of Medicine and Science in Sports*, *20*(1), e195-e207.

Pumpa, K. L., Fallon, K. E., Bensoussan, A., & Papalia, S. (2013). The Effects of Panax Notoginseng on Delayed Onset Muscle Soreness and Muscle Damage in Well-Trained Males: A Double Blind Randomized Controlled Trial. *Complementary Therapies in Medicine*, *21*(3), 131–140.

Seeram, N. P., Aviram, M., Zhang, Y., Henning, S. M., Feng, L., Dreher, M., & Heber, D. (2008). Comparison of Antioxidant Potency of Commonly Consumed Polyphenol-Rich Beverages in United States. *Journal of Agricultural and Food Chemistry*, *56*(4), 1415–1422.

Shimomura, Y., Inaguma, A., Watanabe, S., Yamamoto, Y., Muramatsu, Y., Bajotto, G., ... Mawatari, K. (2010). Branched-Chain Amino Acid Supplementation Before Squat Exercise and Delayed-Onset Muscle Soreness. *International Journal of Sport Nutrition and Exercise Metabolism*, *20*(3), 236–244.

Shimomura, Y., Yamamoto, G., & Bajotto, G. (2006). Nutraceutical Effects of Branched-Chain Amino Acids on Skeletal Muscle. *Journal of Nutrition*, *136*(2), 529S–532S.

Shing, C. M., Chong, S., Driller, M. W., & Fell, J. W. (2016). Acute Protease Supplementation Effects on Muscle Damage and Recovery Across Consecutive Days of Cycle Racing. *European Journal of Sport Science*, *16*(2), 206–212.

Singh, S., & Aggarwal, B. (1995). Activation of Transcription Factor NF-kB is Supressed by Curcumin (Diferulolymethane). *The Journal of Biomedical Chemistry*, *270*(50), 24995–25000.

Stauber, W. T., Fritz, V. K., Dahlmann, B., & Reinauer, H. (1988). Immunoflourescent Localization of an Alkaline Proteinase in Skeletal Muscle from Diabetic Rats. *Basic and Applied Histochemistry*, *20*, 345–352.

Tanabe, Y., Chino, K., Ohnishi, T., Ozawa, H., Sagayama, H., Maeda, S., & Takahashi, H. (2019). Effects of Oral Curcumin Ingested Before or After Eccentric Exercise on Markers of Muscle Damage and Inflammation. *Scandinavian Journal of Medicine & Science in Sports*, *29*(4), 524–534.

Tanabe, Y., Chino, K., Sagayama, H., Lee, H., Ozawa, H., Maeda, S., & Takahashi, H. (2019). Effective Timing of Curcumin Ingestion to Attenuate Eccentric Exercise-Induced Muscle Soreness in Men. *Journal of Nutritional Science and Vitaminology*, *65*(1), 82–89.

Tanabe, Y., Maeda, S., Akazawa, N., Zempo-Miyaki, A., Choi, Y., Ra, S.-G., ... Nosaka, K. (2015). Attenuation of Indirect Markers of Eccentric Exercise-Induced Muscle Damage by Curcumin. *European Journal of Physiology*, *115*(9), 1949–1957.

Thaloor, D., Miller, K. J., Gephart, J., Mitchell, P. O., & Pavlath, G. K. (1999). Systemic Administration of the NF-kB Inhibitor Curcumin Stimulates Muscle Regeneration After Tramatic Injury. *American Journal of Physiology-Cell Physiology*, *2*, C320–C329.

Trombold, J. R., Barnes, J. N., Critchley, L., & Coyle, E. F. (2010). Ellagitannin Consumption Improves Strength Recovery 2–3d after Eccentric Exercise. *Medicine and Science in Sports and Exercise*, *42*(3), 493–498.

Trombold, J. R., Reinfeld, A. S., Casler, J. R., & Coyle, E. F. (2011). The Effect of Pomegranate Juice Supplementation on Strength and Soreness After Eccentric Exercise. *Journal of Strength and Conditioning Research*, *25*(7), 1782–1788.

Valerio, A., D'Antona, G., & Nisoli, E. (2011). Branched-Chain Amino Acids, Mitochondrial Biogenesis and Healthspan: An Evolutionary Perspective. *Aging*, *3*(5), 464–478.

Wilson, P. B., Fitzgerald, J. S., Rhodes, G. S., Lundstorm, C. J., & Ingraham, S. J. (2015). Effectiveness of Ginger Root (Zingiber officinale) on Running-Induced Muscle Soreness and Function: A Pilot Study. *International Journal of Athletic Therapy & Training*, *20*(6), 44–50.

Table 1 Effects of Anatabine on Performance, Soreness, and Markers of Inflammation and Muscle Damage

Authors	Subjects	Dosage	Duration	Design	Exercise Protocol	Performance	Fatigue/Soreness/ ROM	Markers of Inflammation / Muscle Damage
Jenkins et al. (2013)	18 healthy men	1d–2d: 6 mg 3d–4d: 9 mg 5d–10d: 12 mg	10d	Double-blinded, PLAC controlled, crossover design (2wk–4wk washout)	Unilateral elbow flexion (6 × 10)	↔ flexion strength	↔ HJA ↔ DOMS ↔ AC	↔ CK
Jenkins et al. (2014)	17 healthy men	1d–2d: 6 mg 3d–4d: 9 mg 5d–10d: 12 mg	10d	Double-blinded, PLAC controlled, crossover design (2wk–4wk washout)	Unilateral eccentric elbow flexion (6 × 10)	N/A	N/A	CK ↔ LDH ↔TNF-α ↔ MB ↔ CRP

↑ significantly higher than placebo; ↓ significantly lower than placebo; ↔ no significant difference from placebo; ex, exercise; MB, myoglobin; PLAC, placebo; DOMS, delayed onset muscle soreness; CK, creatine kinase; LDH, lactate dehydrogenase; TNF-α, Tumor necrosis factor-alpha; CRP, C-reactive protein; AC, arm circumference; HJA, hanging joint angle.

Table 2 Effects of Branched Chain Amino Acids on Performance, Soreness, and Markers of Inflammation and Muscle Damage

Authors	Subjects	Dosage	Duration	Design	Exercise Protocol	Performance	Fatigue/Soreness/ROM	Markers of Inflammation / Muscle Damage
Shimomura et al.	12 untrained females	100 mg/kg body weight	15 min prior to ex	Randomized, double-blind, PLAC controlled crossover design (11wk washout)	Squat exercise (7×20)	↑ knee extension torque	↓ DOMS	↔ MB ↔ CK
Asjodi et al.	50 untrained men	10 mg/kg body weight 2×	30 min prior to ex and 0h	Randomized, PLAC controlled design	Squat exercise 6 sets at 75% 1-RM until fatigue	N/A	↓ DOMS 48hr post ex ↑ ROM 24hr–72hr post ex	↑ CK 72hr post ex ↓ LDH 24hr-48hr post ex
Greer et al.	9 untrained men	2.5 g 2×	5 min prior and 60 min post ex	PLAC controlled crossover design (8wk washout for each trial)	Three 90 min cycling bouts at 55% VO_{2max}	↑ leg flexion torque 48hr post ex ↔ leg extension torque	↓ DOMS 24hr post ex	↓ CK 4hr–48hrr post ex ↓ LDH 4hr post ex
Leahy et al.	20 healthy adults	1.22 mg	4d post ex	Randomized, PLAC controlled, double-blind crossover design (3wk washout)	Squat exercise (3×12)	N/A	↓ DOMS females 24hr post ex	N/A
Matsumoto et al.	12 long distance runners	0.8% BCAA drink; 2,500 ml/day	3d of training	Randomized, PLAC controlled, double-blind, crossover design (3wk washout)	Intensive training period 2 sets of 3d	N/A	↓ DOMS ↓ Fatigue	↓ CK ↔ MB ↓ LDH
Nosaka et al.	38 untrained men	Exp.1: 3.6 g 2× Exp. 2: 3.6 g 3× daily	Exp. 1: 30 min prior and 0h Exp. 2: 30 min prior, 0h, and 4d after ex	Randomized, PLAC controlled, double-blind crossover design (3-4wk washout)	Isometric arm curl at 90% 1-RM for 30min	↔ Exp. 1 and Exp. 2 max forearm strength	↔ Exp. 1; ↓ Exp 2 (1d–3d post ex): DOMS ↔ ROM ↔ Exp. 1; ↓ Exp. 2 (72hrs–96hrs) AC	↔ Exp. 1; ↓ Exp. 2 (3–4d post ex): CK ↔ Exp. 1; ↓ Exp. 2 (3–4d post ex): MB ↔ Exp. 1; ↓ Exp. 2 (3–4d post ex) ALD
Howatson et al.	12 national rugby and football players	10 g 2× daily	12d (7d prior to ex, 5d after ex)	Randomized, PLAC controlled, double-blind design	Drop jumps from 0.6m with immediate vertical jump with max force (5×20)	↔ JH ↑ dominant knee extensors force 24h post ex	↔ TC ↔ CC ↓ DOMS 24–48h post ex	↓ CK 24hr post ex

↑ significantly higher than placebo; ↓ significantly lower than placebo; ↔ no significant difference from placebo; 0hr, immediately after exercise, DOMS, delayed onset muscle soreness; PLAC; placebo; CK, creatine kinase, AC, arm circumference; TC, thigh circumference; CC, calf circumference; MB, myoglobin; BCAA, branched chain amino acids; ROM range of motion; LDH, lactate dehydrogenase; JH, jump height.

Table 3 Effects of Curcumin on Performance, Soreness, and Markers of Inflammation and Muscle Damage

Authors	Subjects	Dosage	Duration	Design	Exercise Protocol	Performance	Fatigue, Soreness and Range of Motion	Markers of Inflammation / Muscle Damage
Nicol et al.	19 moderately trained men	2.5 g 2× daily	5 d (2 d prior, 3 d after ex.)	Double-blind, randomized, PLAC controlled crossover design (14d washout)	Unilateral eccentric leg press (7 × 10)	↑ JH 24hr and 48hr post ex	↓ DOMS 24hr and 48hr post ex	↓ CK 24 hr and ↓ 1L-6 24hr post ex.
Nakhostin-Roohi et al.	10 healthy males	150 mg	Immediately after ex	Double-blind, randomized PLAC controlled crossover design (14d washout)	Eccentric squat machine 50% 1-RM (7 × 20)	N/A	↓ DOMS 48 hr post ex	↓ AST 24hr post ex ↓ CK 48hr and 72rh post ex
McFarlin et al.	20 healthy adults	400 mg	6d (2d prior, 4d after ex)	Randomized-controlled design	Eccentric leg press 110% 1-RM (6 × 10)	N/A	↔ DOMS ↔ ALDS	↓ TNF-α 1d, and 4d post ex ↓ CK 1d-4d post ex ↓ IL-8 1d-2d post ex. ↔ 1L-6 ↔ 1L-10
Jager et al.	63 active adults	Low dose: 250 mg High dose: 1,000 mg	8wks prior to ex	Double-blind, randomized, PLAC controlled, parallel design	Downhill running (−15% grade) for 45 mins	↔ High; ↓ Low: isokinetic peak flexion torque ↔ High; ↓ low: isokinetic peak extension torque	↔ DOM	N/A
Tanabe et al. (2015)	14 untrained men	150 mg	1hr prior to ex 12hr after ex	Single-blinded, randomized, crossover design (4wk washout)	50 max eccentric elbow flexion	↑ MVC torque of elbow flexor 0h and 48hr–96hr post ex	↔ ROM ↔ DOMS ↔ RC	↓ CK ↔ IL-6 ↔ TNF-α
Tanabe et al. (2018)	20 healthy men	180 mg	Exp. 1: 7d prior to ex Exp. 2: 7d after ex	Double-blind crossover, parallel design (4wk wash out)	30 max eccentric elbow flexion	↑ Exp. 2; ↔ Exp. 1: MVC torque of elbow flexor	↓ Exp. 2 (3d–6d post ex); ↔ Exp. 1: DOMS ↑ Exp.2 (3d–7d post ex); ↔ Exp. 1: ROM	↓ Exp. 2 (5d–7d post ex); ↔ Exp. 1: CK ↓ Exp. 1 (12hrs post ex); ↔ Exp. 2: IL-8 ↔ TNF-α
Tanabe et al. (2019)	24 healthy men	180 mg	PRE: 7d prior POST: 4d after ex	Randomized, single-blinded, parallel design	30 max eccentric elbow flexions	↔ torque of elbow flexor	↔ PRE; ↓ (3d post ex) POST: DOMS ↔ PRE; POST ↑ (3d–4d post ex): ROM	↔ CK

Authors	Subjects	Dosage	Duration	Design	Exercise Protocol	Performance	Fatigue, Soreness and Range of Motion	Markers of Inflammation / Muscle Damage
Delecroix et al.	10 elite rugby players	2g 2× daily curcumin 20 mg 3× daily piperine	4d (2d prior, 2d after ex)	Randomized, balanced crossover design (15d washout)	25 unilateral jumps on −8% downhill slope	↔ CMJH ↔ concentric peak torque isometric peak torque	↔ DOMS	↔ CK
Amalraj et al.	33 healthy adults	500 mg	3d post ex	Randomized, PLAC controlled, double-blind design	Downhill running (−10% grade), 6 km/h increasing by 1 km/h each min until max maintainable effort – for 45mins	↑ VO_{2max}	↓ DOMS	↔ CK
Drobnic et al.	20 moderately trained men	200 mg	4d (2d prior and 2d after ex)	Randomized, PLAC controlled, single blinded design	Downhill running (−10% grade) for 45 minutes	N/A	↓ DOMS	↓ IL-8 ↔ CK

↑ significantly higher than placebo; ↓ significantly lower than placebo; ↔ no significant difference from placebo; ex, exercise; CK, creatine kinase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALDS, activities of daily living soreness; PLAC, placebo; ROM, range of motion; IL-6, Interleukin-6; IL-8, Interleukin-8; IL-10, Interleukin-10; TNF-α, Tumor necrosis factor-alpha; MVC, maximal voluntary contraction; VO_{2max}, maximal oxygen consumption; AC, arm circumference; CMJH, counter movement jump height; 0hr, immediately after exercise.

Table 4 Effect of Ginger Supplement on Performance, Soreness, and Markers of Inflammation and Muscle Damage

Authors	Subjects	Dosage	Duration	Design	Exercise Protocol	Performance	Fatigue/Soreness/ROM	Markers of Inflammation / Muscle Damage
Black et al.	27 healthy adults	2 g	2d post ex	Double-blind, crossover design	Unilateral elbow flexion (6 × 8) 120% 1-RM	N/A	↔ AV ↔ VASP ↔ ROM	N/A
Manimmanakorn et al.	75 untrained adults	7% Plai cream 14% Plai cream	7d post ex	Randomized, PLAC controlled design	Dominant max knee extension (4 × 25)	↑ 14%; ↔ 7% quadricep strength ↔ JH (7% and 14%)	↓ 14%; ↔ 7%: DOMS ↔ TC	↔ CK
Wilson et al.	20 marathon trained men	2.2 g	3d prior, day of ex, and 24hr after ex	Randomized, double-blind, PLAC controlled design	20–22 mi training run	↔ JH ↔ Peak Force ↔ RFD	↔ DOMS ↓ RPE 24hr post ex	N/A
Matsumura et al.	20 untrained adults	4 g	5d prior to ex	Randomized, double-blind, PLAC controlled design	Non-dominant elbow flexion (4 × 10 or to failure) at 80% and 100% of 1-RM	↑ elbow flexion strength 24h post ex	↔ DOMS ↑ ROM 24hr post ex ↔ AC	↔ CK ↔ LDH
Mashhadi et al.	49 martial artists	3 g	6wk	Randomized, double-blind, PLAC controlled design	Specific resistance exercise for the competitive season	N/A	DOMS	IL-6
Hoseinzadeh et al.	36 untrained women	60 mg	GIBE:1hr prior ex GIAE: 0hr post ex	Randomized, double blind, PLAC controlled design	20 min step test with 46 cm step with a rate of 15 steps per min	↔ isometric thigh strength	↔ ROM ↓ GIBE; ↔ GIAE: DOMS ↔ TC	↓ IL-6 (1hr both groups an 1hr post ex and 48hr in GIBE group ↔ CK

↑ significantly higher than placebo; ↓ significantly lower than placebo; ↔ no significant difference from placebo; 1-RM, one repetition max; ex, exercise; DOMS, delayed onset muscle soreness; ROM, range of motion; AV, arm volume; PLAC, placebo; RFD, rate of force development; RPE, rating of perceived exertion; LDH, lactate dehydrogenase; 1L-6, Interleukin-6; 0hr, immediately following exercise; GIAE, ginger immediately after exercise; GIBE, ginger immediately before exercise; CK, creatine kinase; AC, arm circumference; TC, thigh circumference; VASP; visual analog scale pain; JH, jump height.

Table 5 Effects of Green Tea on Performance, Soreness, Markers of Inflammation, Muscle Damage and Oxidative Stress

Authors	Subjects	Dosage	Duration	Design	Exercise Protocol	Performance	Fatigue/ Soreness/ROM	Markers of Inflammation / Muscle Damage	Oxidative Stress
da Silva et al.	20 non-trained men	500 mg	15d post ex	Randomized triple blind PLAC controlled design	calf raises until voluntary fatigue	N/A	↔ DOMS	↓ CK 0h, 48h post ex ↔ LDH	↔ ROS ↔ FRAP
Jowko et al. (2012)	16 soccer players	640 mg	1.5 hrs. prior to ex	Randomized, double-blind design	Bench press and back squat (3 sets to exhaustion) at 60% 1-RM	N/A	N/A	↔ CK	↔ SOD ↔ UA ↔ TAS
Jowko et al. (2015)	16 sprinters	250 mg 2× daily	4wk prior ex	Double-blind, randomized, PLAC controlled crossover design (4wk washout)	RST 4 × 15 with 1-min rest intervals	↔ RST	N/A	↔ CK	↓ SOD ↑ TAC (rest) ↓ MDA ↔ AL ↔ UA ↔ GPx
Herrlinger et al.	37 active men	Low: 250 mg 4× daily High: 500 mg 4× daily	13wk after ex	Randomized, double-blind, PLAC controlled design	Downhill run (−10% grade) for 40mins at 65% VO_{2max}	↑ High; ↔ Low: peak torque	↑ High; ↔ Low: DOMS	↓ CK ↔ IL-6 ↔ IL-10 ↔ TNF-α	↑ FRAP
Kerksick et al.	30 active men	1800 mg NAC 1800 mg EGCG	14d after ex	Double-blind parallel design	Unilateral knee extensions (10X10)	↔ peak isometric torque	↓ DOMS	↔ CK ↔ LDH ↔ TNF-α	↔ SOD
Panza et al.	14 healthy adults	200 mL 3× daily	7d prior to ex	PLAC controlled crossover design	Bench press 4 sets of 10, 8, 6, 4 reps at 75%, 80%, 85%, and 90% 1-RM	N/A	N/A	↓ CK ↓ AST	↑ FRAP ↓ UA ↓ XO

↑ significantly higher than placebo; ↓ significantly lower than placebo; ↔ no significant difference from placebo; PLAC, placebo; ex, exercise; DOMS, delayed onset muscle soreness; CK, creatine kinase; LDH, lactate dehydrogenase; 0hr, immediately following exercise; RST, repeated sprint test; ROS, reactive oxygen species; SOD, superoxide dismutase; TAC, total antioxidant capacity; MDA, malondialdehyde; UA, uric acid; AL, albumin; GPx, glutathione peroxidase; FRAP, ferric-reducing ability of plasma; AST, aspartate aminotransferase; XO, xanthine oxidase; NAC, N-acetyl-cysteine; EGCG, epigallocatechin gallate.

Table 6 Effects of Ginseng on Performance, Soreness, and Markers of Inflammation and Muscle Damage

Authors	Subjects	Dosage	Duration	Design	Exercise Protocol	Performance	Fatigue/Soreness/ROM	Markers of Inflammation / Muscle Damage
Hsu et al.	13 active men	400 mg 4× daily	4wk prior to ex	Randomized, double-blind, PLAC controlled, crossover design (4wk washout)	Running test at 80% VO_{2max} until volitional fatigue	N/A	N/A	↓ CK 0h, 30 min, 60 min, and 120 min post ex
Pumpa et al.	20 trained men	100 mg 4× daily	1hr prior, 0hr, 24–48hr post ex: every 4hrs. (waking) 48–27hr post ex: every 2hrs (waking)	Randomized, double-blind, PLAC controlled design	Downhill run (-10% grade) at 80% HR_{max}, (5 bouts of 8mins)	↑ JH: 0hr	↓ DOMS 96hr post ex	↔ IL-1 ↑ IL-6 24hr post ex ↑ TNF-α 24hr post ex ↔ CK ↔ CRP ↔ MB
Caldwell et al.	19 active adults	High: 160 mg 6× daily Low: 160 mg daily	14d prior to ex	Randomized, double-blind, PLAC controlled cross over design (7d washout)	Leg press at 70% 1-RM (5 × 12)	↔ High and Low RT ↔ High and Low BJH	↓ High and Low DOMS ↓ High; ↔ Low RPE	N/A

↑ significantly higher than placebo; ↓ significantly lower than placebo; ↔ no significant difference from placebo; ex, exercise PLAC, placebo; IL-1 Interleukin-1; TNF-α, Tumor necrosis factor-alpha; IL-6, Interleukin-6; 0hr, immediately after exercise; DOMS, delayed onset muscle soreness; MB, myoglobin; CK, creatine kinase; CRP, C-reactive protein; 1-RM, one repetition max; RT, reaction time; BJH, ballistic jump height; RPE, rating of perceived exertion; JH, jump height.

Table 7 Effect of Pomegranate Juice on Performance, Soreness, and Markers of Inflammation and Muscle Damage

Authors	Subjects	Dosage	Duration	Design	Exercise Protocol	Performance	Fatigue/Soreness/ ROM	Markers of Inflammation / Muscle Damage
Lamb et al.	36 non-resistance trained men	250ml 2× daily	9d (4d prior and 5d post ex)	Randomized, double-blind, PLAC controlled parallel design	Unilateral elbow flexion (5 × 10)	↔ elbow flexion strength	↔ ROM ↔ DOMS	↔ CK
Ammar et al.	9 elite male weightlifters	150ml 3× daily + 500ml 1hr prior ex	1hr prior ex 2d post ex	Non-randomized, PLAC controlled, crossover design (48hr washout)	3 Olympic weight lifting ex (snatch, clean, and jerk squat) 5 set each 2 at 85% 1-RM 4 at 90% 1-RM	↑ total and maximal load lift	↓ RPE ↓ knee extensors; ↔ elbow flexors DOMS	↓ CRP 3min post ex ↓ CK 3min and 48hr post ex ↓ LDH 3min and 48hr post ex ↓ AST 3min and 48hr post ex
Trombold et al. (2010)	16 recreationally trained men	500 ml 2× daily at 12hr interval	9d (4d prior and 5d post ex	Randomized, double-blind, PLAC controlled crossover design (14d washout)	Unilateral max elbow flexion (2 × 20)	↑ elbow flexion strength at 48hr and 72hr post ex	↓ DOMS 2hr post ex	↔ CK ↔ IL-6 ↔ CRP
Trombold et al. (2011)	17 physically resistance trained men	250 ml 2× daily at 12hr intervals	15d (7d prior to ex. 8d after ex)	Randomized double-blind, counterbalanced, PLAC controlled crossover design (14d washout)	Unilateral max elbow flexion (3 × 20) Unilateral max knee extensions (6 × 10) at 110% 1-RM	↑ elbow flexion strength 2h-168hr post ex knee extension strength	↓ elbow flexors; ↔ knee extensors: DOMS	N/A

↑ significantly higher than placebo; ↓ significantly lower than placebo; ↔ no significant difference from placebo; ex, exercise; PLAC, placebo; 1-RM, one repetition max; CRP, c-reactive protein; DOMS, delayed onset muscle soreness; RPE, rating of perceived exertion; LDH, lactate dehydrogenase; CK, creatine kinase; AST, aspartate aminotransferase, 1L-6, Interleukin-6.

Table 8 Effects of Protease Supplement on Performance, Soreness, and Markers of Inflammation and Muscle Damage

Authors	Subjects	Dosage	Duration	Design	Exercise Protocol	Performance	Fatigue/ Soreness/ROM	Markers of Inflammation / Muscle Damage
Shing et al.	15 highly trained road cyclist men	500 mg 2× daily	6d	Randomized, double-blind, PLAC controlled design	Cycle race of 10 stages for 6d with average of 96.7 km·day	N/A	↓ Fatigue 4d stage 7	↔ CK ↔ MB ↔ LDH
Buford et al.	29 recreationally active men	5.828 g	24d (21d prior and 3d after ex)	Randomized, double-blind, PLAC controlled design	Downhill run (−17%) grade for 45 min at 60% VO_{2max}	↑ quadriceps flexion strength ↔ quadriceps extension strength	DOMS	↔ CK ↔ SOD ↓ IL-6 ↔ IL-8 ↔ 1L-10 ↔ IL-12 12hr post ex ↔ IL- ↔ TNF-α ↓ COX-2
Beck et al.	20 untrained men	324 mg Protease 6.0 340 mg Protease 4.5	4d after ex	Randomized, double-blind, PLAC controlled, crossover design (2wk washout)	Unilateral max forearm flexion (6X10)	↑ FFS	↔ AC ↔ JA ↔ DOMS	↔ CK ↔ MB
Miller et al.	20 healthy men	325 mg pancreatic enzymes 75 mg trypsin 50 mg papain 50 mg bromelain 10 mg amylase 10 mg lysozyme 2 mg chymotrypisn	4d (1d prior and 3d after ex)	Randomized, double-blind, PLAC controlled design	Downhill run (−10% grade) for 30min at 80% HR_{max}	↔ agility run time ↑ knee flexion power 24hr-48hr post ex ↔ knee extension power ↑ knee flexion torque 24hr-48hr post ex ↑ knee extension torque 48hr post ex	↓ DOMS anterior thigh 24h–48h post ex ↓ DOMS posterior thigh 24h–72h post ex	N/A

↑ significantly higher than placebo; ↓ significantly lower than placebo; ↔ no significant difference from placebo; ex, exercise; MB, myoglobin; CK, creatine kinase; LDH, lactate dehydrogenase; PLAC, placebo; VO_2max, maximal oxygen consumption; DOMS, delayed onset muscle soreness; SOD, superoxide dismutase; 1L-6, Interleukin-6; IL-8, Interleukin-8; TNF-α, tumor necrosis factor-alpha; IL-12, Interleukin-12; IL-10, Interleukin-10; IL-, Interleukin 1- COX-2, cyclooxygenase 2; HR_{max}, maximal heart rate; AC, arm circumference; JA, joint angle.