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Review Article

What is effective, may be effective, and is not effective for improvement of biochemical markers on muscle damage and inflammation, and muscle recovery? A Systematic Review of PubMed's Database

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Abstract

Introduction: The Homo sapiens has one of the most amazing characteristic, adaptability. And when adaptability comes to mind, exercising is just by side. Exercising brings many benefits for our body and it is the greater stimulus to trigger musculoskeletal adaptation, starting at mitochondrial level (i.e. biogenesis) to muscular level (i.e. hypertrophy). Mainly when the exercise is of high performance or strenuous, the athlete need a time to recover from fatigue, muscular damage, over-increase of muscular inflammation series of muscle and to prevent overtraining syndrome. Following the concept of "Evidence Based Practice" that is use the best available evidence in clinical decisions, what should be the methods that really have efficacy to prevent or reduce muscle damage, muscle biochemical markers of inflammation and recover? The aim of this article is to search in the PubMed database about what can help our patients/athletes to recover faster, to avoid or to reduce muscle damage and inflammation.

Methods: A search in the PubMed database with the keywords Muscle Skeletal, Inflammation, and Exercise; the keywords had none language translation but results in any language were accepted. Only clinical trials were searched.

Results: 272 articles, 174 excluded (by exclusion criteria). The 98 selected articles were divided into subtopics to discuss their efficacy.

Conclusion: This article evidences the most effective treatments or prevention techniques for improvement of muscle damage, inflammation biochemical markers and muscle recovery.

In our knowledge it is the first in PubMed database that assemble diverse health care subjects, and it may serve as an easy guideline for clinical decision making.

Introduction

The Homo sapiens has one of the most amazing characteristic, adaptability. And when adaptability comes to mind, exercising is just by side. When we exercise we have changes for adaptation, from cellular to systemic, in our entire body. It has benefits on mitochondrial biogenesis and activity [1], weight loss [2], sleeping quality [3], depression and anxiety

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[4], and a lot more beneficial effects in our system [5].

In 2017, about 174.05 million people were members of a health/fitness club worldwide [6].

The number of amateur, professional/elite athletes is uncountable but statistics shows that UNI World Athletes is a global collective of 85,000 elite/professional athletes [7].

Exercise is also the greater stimulus to trigger musculoskeletal adaptation, this adaptation also starts at mitochondrial level (i.e. biogenesis) to muscular level (i.e. hypertrophy). Mainly when the exercise is of high performance or strenuous, the athlete need a time to recover from fatigue, muscular damage, over-increase of muscular inflammation series of muscle and to prevent overtraining syndrome [8].

Knowing this, athletes from all over the world seek for health care professionals, aiming to reduce the recovery time, muscle soreness, and loss of muscle strength, after exercise-induced muscle damage and overtraining.

Following the concept of "Evidence Based Practice" that is use the best available evidence in clinical decisions [64] [9], what should be the methods that really have efficacy to prevent or reduce muscle damage, muscle biochemical markers of inflammation and recover?

The aim of this article is to search in the PubMed database about what can help our patients/athletes to recover faster, to avoid or to reduce muscle damage and inflammation.

Also, in a critical way, to highlight the most important findings.

Methods

A search in the PubMed database with the keywords Muscle Skeletal, Inflammation, and Exercise; the keywords had none language translation but results in any language were accepted. Only clinical trials were searched.

The exactly search was ((("muscles"[MeSH Terms] OR "muscles"[All Fields] OR "muscle"[All Fields]) AND skeletal[All Fields]) AND ("inflammation"[MeSH Terms] OR "inflammation"[All Fields]) AND ("exercise"[MeSH Terms] OR "exercise"[All Fields]) AND Clinical Trial[ptyp]).

The search returned 272 matches, dates from 1985 to 2020. First we read the abstract of all articles to remove those in the exclusion criteria.

The exclusion criteria were studies with animals, i.e. rats and horses; involving participants with any kind of previous or current injury, or any kind of disease or previous disease; involving sedentary or not healthy subjects; without DOI.

After reading the abstract of all articles and performing the exclusion criteria (174 excluded), 98 articles were selected.

Results

The following tables contains the article name, first author name, number of subjects (N), results and the DOI with a link to article's page.

Table 1 contents the articles selected with effective results in reducing muscle inflammation and muscle damage, 17 articles.

Table 2 contents the articles selected with non-clear effective results (may be effective) in reducing muscle inflammation and muscle damage, 33 articles.

Table 3 contents the articles selected with not effective results in reducing muscle inflammation and muscle damage, 48 articles.

Discussion

As the objective of this article is to show what are effective, may be effective, and not effective means to reduce muscle damage and muscle inflammation and recover means, we set the discussion into result themes subtopics.

Antioxidants

Extenuating exercises often causes oxidative damage to proteins, nucleic acids, and lipids, leading to impaired cellular functionality [10]. Antioxidants have been widely used in the amateur and professional athlete's daily supplementation, but are not well supported by literature.

Nine studies presented in this research, found non-significant/moderate results, in the use of antioxidants (beetroot juice, Vitamin C, N-acetyl-cysteine, Vitamin E, Grape consumption) for reducing biochemical markers of inflammation and muscle damage [11-20].

Clifford T, et al. 2016, show that in muscle damage by eccentric exercise, the beetroot juice is effective to reduce muscle soreness [21]. Toscano L. T, et al. 2015, article evidences that supplementation with purple grape juice promotes increased time-to-exhaustion and increased antioxidant activity [22].

Childs A, et al. 2001, findings suggest that supplementation with the antioxidants vitamin C and N-acetyl-cysteine immediately post-injury, may increase tissue damage and oxidative stress [13]. In contrast with the findings, Chou, et al. 2018, demonstrate the efficacy of a high dose of Vitamin C and E supplementation in short period (4 days) can attenuate tissue damage, and inflammatory response [23].

Studies with Panax ginseng, Avenanthramide, and Thiol-based antioxidant have also been carried. Panax ginseng may be effective in reduce exercise muscle damage and inflammatory responses [24]. Avenanthramide supplementation can attenuate inflammation markers, and increased antioxidant capacity during an eccentric exercise bout [25]. Thiol-based antioxidant may disrupts the skeletal muscle inflammatory response and repair capability [26].

Polyphenol-rich foods

The use of Montmorency Tart Cherry (polyphenol-rich foods) was found to be not effective or may be effective

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Table 1: Effective means in reducing muscle inflammation and muscle damage (17 articles).

Article	Author(S)	N	Results	DOI
Pre-Exercise Infrared Low-Level Laser Therapy (810 nm) in Skeletal Muscle Performance and Postexercise Recovery in Humans, What Is the Optimal Dose? A Randomized, Double-Blind, Placebo-Controlled Clinical Trial.	[102]	28	Pre-exercise LLLT, mainly with 50 J dose, significantly increases performance and improves biochemical markers related to skeletal muscle damage and inflammation	10.1089/pho.2015.3992
Oral consumption of electrokinetically modified water attenuates muscle damage and improves postexercise recovery.	[87]	40	Oral consumption of EMW significantly reduced exercise-induced muscle damage and inflammation and improved functional recovery.	10.1152/japplphysiol.00083.2013
Vibration therapy reduces plasma IL6 and muscle soreness after downhill running.	[57]	29	Vibration Therapy reduces muscle soreness and IL6. It may stimulate lymphocyte and neutrophil responses and may be a useful modality in treating muscle inflammation.	10.1136/bjsm.2008.052100
Effects of lemon verbena extract (Recoverben®) supplementation on muscle strength and recovery after exhaustive exercise: a randomized, placebo-controlled trial.	[88]	44	Lemon verbena extract (Recoverben®) has been shown to be a safe and well-tolerated natural sports ingredient, by reducing muscle damage after exhaustive exercise	10.1186/s12970-018-0208-0
Short-Term High-Dose Vitamin C and E Supplementation Attenuates Muscle Damage and Inflammatory Responses to Repeated Taekwondo Competitions: A Randomized Placebo-Controlled Trial.	[23]	18	We demonstrated that short-term (4-days) vitamin C and E supplementation effectively attenuated exercise-induced tissue damage and inflammatory response during and after successive TKD matches.	10.7150/ijms.26340
The effects of beetroot juice supplementation on indices of muscle damage following eccentric exercise.	[21]	30	Acute beetroot juice supplementation attenuated muscle soreness and decrements in CMJ performance induced by eccentric exercise; further research on the anti-inflammatory effects of beetroot juice are required to elucidate the precise mechanisms.	10.1007/s00421-015-3290-x
Pre-Exercise Infrared Photobiomodulation Therapy (810 nm) in Skeletal Muscle Performance and Postexercise Recovery in Humans: What Is the Optimal Power Output?	[103]	28	PBMT with 100 mW power output per diode (500 mW total) before exercise achieves best outcomes in enhancing muscular performance and postexercise recovery. Another time it has been demonstrated that more power output is not necessarily better.	10.1089/pho.2017.4343
Iron Supplementation Effects on Redox Status following Aseptic Skeletal Muscle Trauma in Adults and Children.	[89]	25	Iron supplementation can alter redox responses after muscle-damaging exercise in both adults and children. This could be of great importance not only for healthy exercising individuals, but also in clinical conditions which are characterized by skeletal muscle injury and inflammation, yet iron supplementation is crucial for maintaining iron homeostasis.	10.1155/2017/4120421
Protein ingestion preserves proteasome activity during intense aseptic inflammation and facilitates skeletal muscle recovery in humans.	[92]	11	Milk PRO supplementation following exercise-induced muscle trauma preserves proteasome activity and attenuates strength decline during the pro-inflammatory phase.	10.1017/S0007114517001829
Vibration Therapy Is No More Effective Than the Standard Practice of Massage and Stretching for Promoting Recovery From Muscle Damage After Eccentric Exercise.	[59]	50	Cycloidal vibration therapy is no more effective than the standard practice of stretching and massage to promote muscle recovery after the performance of muscle-damaging exercise. Prescription of vibration therapy after maximal exercise involving eccentric muscle damage did not alleviate signs and symptoms of muscle damage faster than the standard prescription of stretching and massage.	10.1097/JSM.0000000000000149
Combined effect of Bacillus coagulans GBI-30, 6086 and HMB supplementation on muscle integrity and cytokine response during intense military training.	[93]	26	Results indicated that CaHMB attenuated the inflammatory response and that BC30 combined with CaHMB may be more beneficial than CaHMB alone in maintaining muscle integrity during intense military training.	10.1152/japplphysiol.01116.2016
Black Currant Nectar Reduces Muscle Damage and Inflammation Following a Bout of High-Intensity Eccentric Contractions.	[90]	16	Consumption of BCN prior to and after a bout of eccentric exercise attenuates muscle damage and inflammation.	10.3109/19390211.2014.952864
Comparison of Pro-Regenerative Effects of Carbohydrates and Protein Administrated by Shake and Non-Macro-Nutrient Matched Food Items on the Skeletal Muscle after Acute Endurance Exercise.	[94]	35	The uptake of protein and carbohydrate by shake or food reduces exercise induced skeletal muscle damage and has pro-regenerative effects.	10.3390/nu11040744
Avenanthramide supplementation attenuates eccentric exercise-inflicted blood inflammatory markers in women.	[25]	16	Long-term AVA supplementation can attenuate blood inflammation markers, decrease ROS generation and NFkB activation, and increased antioxidant capacity during an eccentric exercise bout.	10.1007/s00421-015-3244-3
Effects of powdered Montmorency tart cherry supplementation on acute endurance exercise performance in aerobically trained individuals.	[35]	27	Results revealed that short-term supplementation of Montmorency powdered tart cherries surrounding an endurance challenge attenuated markers of muscle catabolism, reduced immune and inflammatory stress, better maintained redox balance, and increased performance in aerobically trained individuals.	10.1186/s12970-016-0133-z

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Diclofenac sodium (Voltaren) reduced exercise-induced injury in human skeletal muscle.	[43]	54	Pre administration of diclofenac (in accordance with tissue half-life pharmacokinetics) significantly reduces quantitative indices of exercise-induced skeletal muscle damage in human muscle.	10.1097/00005768-200007000-00001
Short term effects of various water immersions on recovery from exhaustive intermittent exercise.	[52]	41	The practice of cold water immersion and contrast water therapy are more effective immersion modalities to promote a faster acute recovery of maximal anaerobic performances (MVC and 30" all-out respectively) after an intermittent exhaustive exercise. These results may be explained by the suppression of plasma concentrations of markers of inflammation and damage, suggesting reduced passive leakage from disrupted skeletal muscle, which may result in the increase in force production during ensuing bouts of exercise.	10.1007/s00421-010-1754-6

Table 2: May be effective means in reducing muscle inflammation and muscle damage (33 articles).

Article	Author(S)	N	Results	DOI
cstress and inflammatory responses to repeated days high-intensity stochastic cycling.	[30]	16	The attenuated oxidative and inflammatory responses suggest MC may be efficacious in combating post-exercise oxidative and inflammatory cascades that can contribute to cellular disruption. Additionally, we demonstrate direct application for MC in repeated days cycling and conceivably other sporting scenario's where back-to-back performances are required.	10.3390/nu6020829
Recovery facilitation with Montmorency cherries following high-intensity, metabolically challenging exercise.	[31]	16	Montmorency cherry concentrate can be an efficacious functional food for accelerating recovery and reducing exercise-induced inflammation following strenuous cycling exercise.	10.1139/apnm-2014-0244
Effect of wearing compression stockings on recovery after mild exercise-induced muscle damage.	[96]	11	Perceived muscle soreness was likely to be lower when participants wore CS during trail running compared with the control condition (1 h postrun, 82% chance; 24 h postrun, 80% chance). A likely or possibly beneficial effect of wearing CS during running was also found for isometric peak torque at 1 h postrun (70% chance) and 24 h postrun (60% chance) and throughout the recovery period on countermovement jump, compared with non-CS. Possible, trivial, or unclear differences were observed for CK and IL-6 between all conditions.	10.1123/ijspp.2013-0126
Montmorency tart cherry (Prunus cerasus L.) supplementation accelerates recovery from exercise-induced muscle damage in females.	[32]	20	MC supplementation may be a practical nutritional intervention to help attenuate the symptoms of muscle damage and improve recovery on subsequent days in females.	10.1080/17461391.2018.1502360
Protease supplementation improves muscle function after eccentric exercise.	[79]	29	Protease supplementation seems to attenuate muscle strength losses after eccentric exercise by regulating leukocyte activity and inflammation.	10.1249/MSS.0b013e3181a518f0
Massage therapy attenuates inflammatory signaling after exercise-induced muscle damage.	[58]	11	In summary, when administered to skeletal muscle that has been acutely damaged through exercise, massage therapy appears to be clinically beneficial by reducing inflammation and promoting mitochondrial biogenesis.	10.1126/scitranslmed.3002882
Effects of taurine supplementation following eccentric exercise in young adults.	[91]	21	Taurine supplementation represents an important factor in improving performance and decreasing muscle damage and oxidative stress but does not decrease the inflammatory response after EE	10.1139/apnm-2012-0229
Phlebodium decumanum is a natural supplement that ameliorates the oxidative stress and inflammatory signalling induced by strenuous exercise in adult humans.	[80]	40	These findings provide a basis for similar Phlebodium supplementation for both professional and amateur athletes performing strenuous exercise in order to reduce the undesirable effects of the oxidative stress and inflammation signaling elicited during high-intensity exercise.	10.1007/s00421-011-2295-3
Docosahexaenoic acid affects markers of inflammation and muscle damage after eccentric exercise.	[81]	41	Docosahexaenoic acid supplementation reduced some but not all indicators of muscle damage and inflammation in the 4 days after an acute eccentric exercise bout but did not significantly affect the response to initiation of resistance exercise.	10.1519/JSC.0000000000000617
A single dose of histamine-receptor antagonists before downhill running alters markers of muscle damage and delayed-onset muscle soreness.	[104]	24	Histamine appears to be intimately involved with skeletal muscle during and following exercise. Blocking histamine's actions during muscle-damaging exercise, via common over-the-counter antihistamines, resulted in increased serum creatine kinase, an indirect marker of muscle damage. Paradoxically, blocking histamine's actions attenuated muscle strength loss and reduced perceptions of muscle pain for 72 h following muscle-damaging exercise. These results indicate that exercise-induced histamine release may have a broad impact on protecting muscle from exercise-induced damage.	10.1152/japplphysiol.00518.2016

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Effect of a Single Administration of Focused Extracorporeal Shock Wave in the Relief of Delayed-Onset Muscle Soreness: Results of a Partially Blinded Randomized Controlled Trial.	[101]	46	A single treatment with focused extracorporeal shock wave therapy causes clinically relevant effects in the relief of pain, increase in force, and improvement of pain-associated impairments of daily living. Still, results need to be cautiously interpreted because of the pilot character of this study. Focused extracorporeal shock wave therapy might present an option in the midterm recovery from DOMS (72h) and be an approach to enhance the return to play in athletes.	10.1016/j.apmr.2016.11.013
Effect of Compression Garments on the Development of Delayed-Onset Muscle Soreness: A Multimodal Approach Using Contrast-Enhanced Ultrasound and Acoustic Radiation Force Impulse Elastography.	[98]	14	Continuous wearing of compression garments during the inflammation phase of DOMS may play an important role in regulating muscle stiffness; however, compression garments have no significant effects on intramuscular perfusion or other common clinical assessments.	10.2519/jospt.2018.8038
Influence of tart cherry juice on indices of recovery following marathon running.	[33]	20	The cherry juice appears to provide a viable means to aid recovery following strenuous exercise by increasing total antioxidative capacity, reducing inflammation, lipid peroxidation and so aiding in the recovery of muscle function.	10.1111/j.1600-0838.2009.01005.x
Probiotic Streptococcus thermophilus FP4 and Bifidobacterium breve BR03 Supplementation Attenuates Performance and Range-of-Motion Decrements Following Muscle Damaging Exercise.	[82]	15	Dietary supplementation with probiotic strains S. thermophilus FP4 and B. breve BR03 attenuates performance decrements and muscle tension in the days following muscle-damaging exercise.	10.3390/nu8100642
Effects of Panax ginseng supplementation on muscle damage and inflammation after uphill treadmill running in humans.	[24]	18	RG supplementation could reduce exercise-induced muscle damage and inflammatory responses, resulting in improvements in insulin sensitivity.	10.1142/S0192415X11008944
Effects of powdered Montmorency tart cherry supplementation on an acute bout of intense lower body strength exercise in resistance trained males.	[34]	23	Short-term supplementation of Montmorency powdered tart cherries surrounding a single bout of resistance exercise, appears to be an effective dietary supplement to attenuate muscle soreness, strength decrement during recovery, and markers of muscle catabolism in resistance trained individuals.	10.1186/s12970-015-0102-y
Influence of different types of compression garments on exercise-induced muscle damage markers after a soccer match.	[97]	18	Results showed a positive, but not significant, effect of compression garments on attenuating EIMD biomarkers response, and inflammatory and perceptual responses suggest that compression may improve physiological and psychological recovery.	10.1080/15438627.2017.1393755
Thiol-based antioxidant supplementation alters human skeletal muscle signaling and attenuates its inflammatory response and recovery after intense eccentric exercise.	[26]	10	Although thiol-based antioxidant supplementation enhances GSH availability in skeletal muscle, it disrupts the skeletal muscle inflammatory response and repair capability, potentially because of a blunted activation of redox-sensitive signaling pathways.	10.3945/ajcn.112.049163
Cold-water immersion decreases cerebral oxygenation but improves recovery after intermittent-sprint exercise in the heat.	[29]	9	Improvements in neuromuscular recovery after post-exercise cooling appear to be disassociated with cerebral oxygenation, rather reflecting reductions in thermoregulatory demands to sustain force production.	10.1111/sms.12060
Inflammatory cytokine responses to progressive resistance training and supplementation with fortified milk in men aged 50+ years: an 18-month randomized controlled trial.	[70]	180	Serum IL-6 concentration decreased following PRT, whereas it increased after supplementation with fortified milk concomitant with changes in fat mass. Furthermore, low-grade inflammation at baseline restricted muscle hypertrophy following PRT.	10.1007/s00421-011-1942-z
Protein-leucine ingestion activates a regenerative inflammo-myogenic transcriptome in skeletal muscle following intense endurance exercise.	[83]	12	Protein-leucine ingestion modulates inflammatory-myogenic regenerative processes during skeletal muscle recovery from endurance exercise. Further cellular and translational research is warranted to validate amino acid-mediated myeloid and myocellular mechanisms within skeletal-muscle functional plasticity.	10.1152/ physiolgenomics.00068.2015
Vitamin E supplementation inhibits muscle damage and inflammation after moderate exercise in hypoxia.	[16]	9	250 mg of vitamin E supplementation at 1 h before exercise reduces cell damage markers after exercise in hypoxia and changes the concentration of cytokines, suggesting a possible protective effect against inflammation induced by hypoxia during exercise.	10.1111/jhn.12361
N-acetylcysteine supplementation and oxidative damage and inflammatory response after eccentric exercise.	[17]	29	Treatment with NAC represents an important factor in the defense against muscle soreness and has different effects on oxidative damage and pro- and anti-inflammatory cytokines.	10.1123/ijsnem.18.4.379
Vitamin E supplementation decreases muscular and oxidative damage but not inflammatory response induced by eccentric contraction.	[18]	21	Vitamin E supplementation represents an important factor in the defense against oxidative stress and muscle damage but not against the inflammatory response in humans.	10.1007/s12576-009-0065-3

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Multiple Cold-Water Immersions Attenuate Muscle Damage but not Alter Systemic Inflammation and Muscle Function Recovery: A Parallel Randomized Controlled Trial.	[53]	30	Multiple CWIs attenuated muscle damage, but not altered systemic inflammation and muscle function recovery.	10.1038/s41598-018-28942-5
Resistance Training Alone or Combined With N-3 PUFA-Rich Diet in Older Women: Effects on Muscle Fiber Hypertrophy.	[84]	63	Resistance training combined to an N-3 PUFA-rich healthy diet but not alone triggers local anti-inflammatory and growth responses, favoring skeletal muscle hypertrophy in already recreationally active older women.	10.1093/gerona/gly130
Effects of oral curcumin ingested before or after eccentric exercise on markers of muscle damage and inflammation.	[85]	20	CUR ingestion before exercise could attenuate acute inflammation, and after exercise could attenuate muscle damage and facilitate faster recovery.	10.1111/sms.13373
Pomegranate Extract Improves Maximal Performance of Trained Cyclists after an Exhausting Endurance Trial: A Randomised Controlled Trial.	[86]	26	PE, after a prolonged submaximal effort, may be effective in improving performance outcomes at maximal effort and might help to restore force in the damaged muscles.	10.3390/nu11040721
Potential ergogenic activity of grape juice in runners.	[22]	28	Supplementation with purple grape juice shows an ergogenic effect in recreational runners by promoting increased time-to-exhaustion, accompanied by increased antioxidant activity and a possible reduction in inflammatory markers.	10.1139/apnm-2015-0152
Skeletal muscle PGF(2)(alpha) and PGE(2) in response to eccentric resistance exercise: influence of ibuprofen acetaminophen.	[42]	24	Ibuprofen and acetaminophen have a comparable effect on suppressing the normal increase in PGF(2alpha) in human skeletal muscle after eccentric resistance exercise, which may profoundly influence the anabolic response of muscle to this form of exercise.	10.1210/jcem.86.10.7928
Ellagitannin consumption improves strength recovery 2-3 d after eccentric exercise.	[106]	16	Supplementation with Ellagitannins from pomegranate extract significantly improves recovery of isometric strength 2-3 d after a damaging eccentric exercise.	10.1249/MSS.0b013e3181b64edd
The effect of various cold-water immersion protocols on exercise-induced inflammatory response and functional recovery from high-intensity sprint exercise.	[54]	8	Cold-water immersion appears to facilitate restoration of muscle performance in a stretch-shortening cycle, but not concentric power. These changes do not appear to be related to inflammatory modulation. CWI protocols of excessive duration may actually exacerbate the concentration of cytokines in circulation post-exercise; however, the origin of the circulating cytokines is not necessarily skeletal muscle.	10.1007/s00421-014-2954-2
Role of vitamin C and E supplementation on IL-6 in response to training.	[20]	21	Although vitamin C and E supplementation may attenuate exercise-induced increases in plasma IL-6 there is no clear additive effect when combined with endurance training.	10.1152/japplphysiol.01027.2010

Table 3: Not effective means in reducing muscle inflammation and muscle damage (48 articles).

Article	Author(S)	N	Results	DOI
Oxidative stress, inflammation and recovery of muscle function after damaging exercise: effect of 6-week mixed antioxidant supplementation.	[11]	38	Combined vitamin C & E supplementation neither reduced markers of oxidative stress or inflammation nor did it facilitate recovery of muscle function after exercise-induced muscle damage.	10.1007/s00421-010-1718-x
Contraction-induced muscle damage is unaffected by vitamin E supplementation.	[12]	16	Vitamin E supplementation (30 d at 1200 IU.d-1), which resulted in a 2.8-fold higher serum vitamin E concentration ($P < 0.01$), had no effect on indices of contraction-induced muscle damage nor inflammation (macrophage infiltration) as a result of eccentrically biased muscle contractions.	10.1097/00005768-200205000-00012
Effects of lymphatic drainage and cryotherapy on indirect markers of muscle damage.	[44]	30	Large and small damage markers were not affected differently by MLD, CRY, or RST, when applied for 30 min and no beneficial effects on inflammation or muscle soreness could be found for MLD and CRY when compared to RST. This information is particularly important for those sports physicians and conditioning specialists who use biochemical muscle damage markers to adjust the training load and volume of athletes.	10.23736/S0022-4707.17.07261-9
The Effects of Montmorency Tart Cherry Concentrate Supplementation on Recovery Following Prolonged, Intermittent Exercise.	[31]	16	MC is efficacious in accelerating recovery following prolonged, repeat sprint activity, such as soccer and rugby, and lends further evidence that polyphenol-rich foods like MC are effective in accelerating recovery following various types of strenuous exercise.	10.3390/nu8070441
Naproxen does not alter indices of muscle damage in resistance-exercise trained men.	[36]	8	NSAID administration did not alter CK rise, muscle force deficit at 24 h postexercise, nor perceived muscle pain. In addition, the increased CK at 24 h postexercise was not associated with an acute myofibrillar inflammatory cell infiltrate in moderately trained men after resistance exercise.	10.1097/00005768-199901000-00002

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Supplementation with vitamin C and N-acetyl-cysteine increases oxidative stress in humans after an acute muscle injury induced by eccentric exercise.	[13]	14	The acute human inflammatory model strongly suggests that vitamin C and NAC supplementation immediately post-injury, transiently increases tissue damage and oxidative stress.	10.1016/s0891-5849(01)00640-2
Antioxidant-rich beetroot juice does not adversely affect acute neuromuscular adaptation following eccentric exercise.	[14]	29	Supplementation with antioxidant-rich beetroot juice does not adversely affect acute adaptations to a bout of eccentric exercise.	10.1080/02640414.2016.1192670
Minimal muscle damage after a marathon and no influence of beetroot juice on inflammation and recovery.	[14]	34	Beetroot juice did not attenuate inflammation or reduce muscle damage following a marathon, possibly because most of these indices were not markedly different from baseline values in the days after the marathon.	10.1139/apnm-2016-0525
The effects of collagen peptides on muscle damage, inflammation and bone turnover following exercise: a randomized, controlled trial.	[60]	24	CP had moderate benefits for the recovery of CMJ and muscle soreness but had no influence on inflammation and bone collagen synthesis.	10.1007/s00726-019-02706-5
Omega-3 supplementation with resistance training does not improve body composition or lower biomarkers of inflammation more so than resistance training alone in older men.	[61]	23	Omega-3 supplementation did nothing to enhance these parameters or influence inflammatory biomarkers.	10.1016/j.nutres.2018.09.005
Effect of cryotherapy on muscle recovery and inflammation following a bout of damaging exercise.	[45]	20	20 min of cryotherapy was ineffective in attenuating the strength decrement and soreness seen after muscle-damaging exercise, but may have mitigated the rise in plasma CCL2 concentration. These results do not support the use of cryotherapy during recovery.	10.1007/s00421-013-2693-9
Effects of taurine on markers of muscle damage, inflammatory response and physical performance in triathletes.	[62]	9	Taurine supplementation did not provide benefits on performance and muscle damage in triathletes.	10.23736/S0022-4707.17.07497-7
Amino acids intake and physical fitness among adolescents.	[63]	1481	Lower limbs muscular fitness seems to be positively associated with tryptophan, histidine and methionine intake in boys, regardless of centre, age, socioeconomic status, physical activity and total energy intake (model 1). However, these associations disappeared once carbohydrates intake was controlled for (model 2). In girls, only proline intake seems to be positively associated with lower limbs muscular fitness (model 2) while cardiorespiratory fitness seems to be positively associated with leucine (model 1) and proline intake (models 1 and 2). None of the observed significant associations remained significant once multiple testing was controlled for. In conclusion, we failed to detect any associations between any of the evaluated AAs and physical fitness after taking into account the effect of multiple testing.	10.1007/s00726-017-2393-6
Influence of compression garments on recovery after marathon running.	[95]	24	The use of a lower limb compression garment improved subjective perceptions of recovery; however, there was neither a significant improvement in muscular strength nor a significant attenuation in markers of exercise-induced muscle damage and inflammation.	10.1519/JSC.0000000000000469
Tart cherry concentrate does not enhance muscle protein synthesis response to exercise and protein in healthy older men.	[28]	16	Short-term MCC ingestion does not affect the anabolic response to protein and exercise in healthy, relatively active, older men, despite MCC ingestion attenuating expression of proteins involved in the muscle inflammatory response to exercise, which may influence the chronic training response.	10.1016/j.exger.2018.06.007
Effects of anatabine and unilateral maximal eccentric isokinetic muscle actions on serum markers of muscle damage and inflammation.	[64]	17	The primary findings of this study were two-fold: (a) anatabine had no beneficial effects on traditional markers of muscle damage (creatine kinase, lactate dehydrogenase, and myoglobin) compared to placebo after the eccentric exercise protocol, and (b) the eccentric exercise protocol did not elicit increase in the pro-inflammatory cytokines (c-reactive protein and TNF-α). Future studies are needed to examine the effects of anatabine on naturally-occurring inflammation that is common with aging or obesity. Furthermore, additional research is needed to examine the relationship between muscle damage and inflammation after eccentric exercises of different modes, durations, and intensities.	10.1016/j.ejphar.2014.01.054

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Post-exercise branched chain amino acid supplementation does not affect recovery markers following three consecutive high intensity resistance training bouts compared to carbohydrate supplementation.	[65]	30	BCAA-CHO supplementation did not reduce decrements in lower body strength or improve select markers of muscle damage/ soreness compared to CHO supplementation over three consecutive days of intense lower-body training.	10.1186/s12970-016-0142-y
Phosphatidylserine supplementation and recovery following downhill running.	[66]	8	Supplementation with 750 mg x d(-1) S-PtdSer for 10 d does not afford additional protection against delayed onset of muscle soreness and markers of muscle damage, inflammation, and oxidative stress that follow prolonged downhill running.	10.1249/01.mss.0000229459.11452.a0
Whole-body cryotherapy (-110 °C) following high-intensity intermittent exercise does not alter hormonal, inflammatory or muscle damage biomarkers in trained males.	[46]	11	The postulated physiological mechanisms by which WBC is proposed to improve recovery, i.e. reductions in inflammation and muscle damage, may not be accurate.	10.1016/j.cyto.2018.07.018
Rhodiola/Cordyceps-Based Herbal Supplement Promotes Endurance Training-Improved Body Composition But Not Oxidative Stress and Metabolic Biomarkers: A Preliminary Randomized Controlled Study.	[67]	14	Improvement in body composition profiles were significantly greater in the RC group (body weight: p = 0.044, BMI: p = 0.003, upper extremity fat mass: p = 0.032, lower extremity muscle mass: p = 0.029, trunk fat mass: p = 0.011) compared to the PLA group after training. The blood lipid profile and systemic oxidative stress makers (thiobarbituric reactive substanceand total antioxidant capacity) did not differ between groups. Although endurance training markedly improved endurance capacity and glycemic control ability (i.e., fast blood glucose, insulin, and HOMA index), there were no differences in these variables between treatments.	10.3390/nu11102357
High doses of anti-inflammatory drugs compromise muscle strength and hypertrophic adaptations to resistance training in young adults.	[37]	31	Maximal over-the-counter doses of ibuprofen attenuate strength and muscle hypertrophic adaptations to 8 weeks of resistance training in young adults. Thus, young individuals using resistance training to maximize muscle growth or strength should avoid excessive intake of anti-inflammatory drugs.	10.1111/apha.12948
Arachidonic acid supplementation transiently augments the acute inflammatory response to resistance exercise in trained men.	[68]	19	These data show that ARA supplementation transiently increased the inflammatory response to acute resistance exercise but did not impair recovery.	10.1152/japplphysiol.00169.2018
Influence of cold-water immersion on limb blood flow after resistance exercise.	[48]	12	Cold and cool water similarly reduce femoral artery and cutaneous blood flow responses but not muscle temperature following resistance exercise.	10.1080/17461391.2017.1279222
Effect of tart cherry juice on recovery and next day performance in well-trained Water Polo players.	[29]	9	The lack of difference observed in the blood markers between groups may reflect the intermittent, non-weight bearing demands of Water Polo, with such activity possibly unable to create a substantial inflammatory response or oxidative stress (over 7 days) to impede performance; thereby negating any potential beneficial effects associated with CJ supplementation.	10.1186/s12970-016-0151-x
Sensory level electrical muscle stimulation: effect on markers of muscle injury.	[99]	14	MHVS treatment may not enhance recovery after muscle injury because of lack of improvements in strength and active range of motion.	10.1136/bjsm.2003.007401
Effect of carbohydrate intake during recovery from eccentric exercise on interleukin-6 and muscle-damage markers.	[69]	8	Carbohydrate supplementation during recovery from soreness-inducing exercise does not influence the delayed IL-6 response temporally linked to inflammation or indications of muscle damage. Thus, increased carbohydrate consumption at levels consistent with recommendations for replenishing glycogen stores does not impair or promote the immune and muscle responses.	10.1123/ijsnem.17.6.507
Ibuprofen use, endotoxemia, inflammation, and plasma cytokines during ultramarathon competition.	[38]	29	Ibuprofen use compared to nonuse by athletes competing in a 160-km race did not alter muscle damage or soreness, and was related to elevated indicators of endotoxemia and inflammation.	10.1016/j.bbi.2006.02.001
Grape consumption's effects on fitness, muscle injury, mood, and perceived health.	[15]	40	Mixed-model ANOVA showed no significant effect of grape consumption on any of the outcomes. Six weeks of supplemental grape consumption by recreationally active young adults has no effect on VO(2max), work capacity, mood, perceived health status, inflammation, pain, or physical-function responses to a mild injury induced by eccentric exercise.	10.1123/ijsnem.23.1.57
A COX-2 inhibitor reduces muscle soreness, but does not influence recovery and adaptation after eccentric exercise.	[39]	70	In summary, celecoxib, a COX-2 inhibitor, did not detectably affect recovery of muscle function or markers of inflammation and regeneration after unaccustomed eccentric exercise, nor did the drug influence the repeated-bout effect. However, it alleviated muscle soreness.	10.1111/j.1600-0838.2009.00947.x
The effects of cold water immersion and active recovery on inflammation and cell stress responses in human skeletal muscle after resistance exercise.	[47]	9	Cold water immersion is no more effective than active recovery for reducing inflammation or cellular stress in muscle after a bout of resistance exercise.	10.1113/JP272881

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Ibuprofen and acetaminophen: effect on muscle inflammation after eccentric exercise.	[40]	24	Maximal over-the-counter doses of ibuprofen or acetaminophen, when administered therapeutically, do not affect muscle concentrations of neutrophils or macrophages 24 h after a novel bout of eccentric contractions.	10.1249/01.MSS.0000069917.51742.98
The effects of Lyprinol(®) on delayed onset muscle soreness and muscle damage in well trained athletes: a double-blind randomised controlled trial.	[41]	20	After 2 months ingestion of Lyprinol(®) at the currently recommended dosage (200mg/day) and a demanding eccentric exercise intervention, Lyprinol(®) did not convincingly affect DOMS and indicators of muscle damage.	10.1016/j.ctim.2011.08.004
The effects of topical Arnica on performance, pain and muscle damage after intense eccentric exercise.	[56]	20	The application of topical Arnica did not affect any performance assessments or markers of muscle damage or inflammation. Topical Arnica used immediately after intense eccentric exercise and for the following 96 hours did not have an effect on performance or blood markers. It did however demonstrate the possibility of providing pain relief three days post-eccentric exercise.	10.1080/17461391.2013.829126
The effect of milk on recovery from repeat-sprint cycling in female team-sport athletes.	[71]	10	Consumption of 500 mL of milk after repeat sprint cycling had little to no benefit in minimising losses in peak torque or minimising increases in soreness and tiredness and had no effect on serum markers of muscle damage and inflammation.	10.1139/apnm-2017-0275
Creatine supplementation does not reduce muscle damage or enhance recovery from resistance exercise.	[72]	22	Oral creatine supplementation does not reduce skeletal muscle damage or enhance recovery following a hypoxic resistance exercise challenge.	10.1519/R-21076.1
Effect of dietary protein content during recovery from high-intensity cycling on subsequent performance and markers of stress, inflammation, and muscle damage in well-trained men.	[73]	12	Sprint mean power was not clearly different on day 2 (0.0%; 95%CL: +/-3.9%), but on day 4 it was 4.1% higher (+/-4.1%) in the protein-enriched condition relative to control. Reduced creatine kinase was possible (26%; +/-30%) but effects on oxidative stress, inflammatory markers, and cortisol were inconclusive or trivial. Overnight nitrogen balance was positive in the protein-enriched condition on day 1 (249+/-70 mg N.kg FFM(-1); mean+/-SD), but negative (-48+/-26 mg N.kg FFM(-1)) in the control condition. A nutritive effect of post-exercise protein content was not discernible short term (15 h), but a delayed performance benefit (60 h) was observed following protein-enriched high-carbohydrate ingestion.	10.1139/H07-136
Blood flow after exercise-induced muscle damage.	[50]	18	Ice does not seem to decrease muscle perfusion when blood flow is elevated, as it would be during inflammation.	10.4085/1062-6050-49.6.01
Evaluation of Rhodiola rosea supplementation on skeletal muscle damage and inflammation in runners following a competitive marathon.	[74]	24	RR supplementation (600mg/day) for 30days before running a marathon did not attenuate the post-marathon decrease in muscle function, or increases in muscle damage, DOMS, eHSP72, or plasma cytokines in experienced runners.	10.1016/j.bbi.2013.09.005
Leucine metabolites do not attenuate training-induced inflammation in young resistance trained men.	[75]	40	Using leucine metabolites to modulate inflammation cannot be recommended from the results obtained herein. Furthermore, increases in inflammatory markers, from training, do not correlate with any outcome variable and are likely the result of training adaptations.	10.1080/02640414.2019.1617503
Antioxidants do not prevent postexercise peroxidation and may delay muscle recovery.	[10]	20	AOX supplementation does not offer protection against exercise-induced lipid peroxidation and inflammation and may hinder the recovery of muscle damage.	10.1249/MSS.0b013e31819fe8e3
No effect of short-term 17beta-estradiol supplementation in healthy men on systemic inflammatory responses to exercise.	[76]	11	8 days of ES in healthy men did not influence systemic inflammation-related responses to acute exercise. Future studies should investigate 17beta-estradiol effects on IL-6 production and neutrophil infiltration within skeletal muscle during and after exercise.	10.1152/ajpregu.00605.2005
Relationship of vitamin E metabolism and oxidation in exercising human subjects.	[19]	22	We found that supplementation with both vitamins E and C only prevented increases in lipid peroxidation, but had no apparent effect on DNA damage, inflammation or muscle damage. These results suggest that the mechanism of oxidative damage is operating independently of the inflammatory and muscle damage responses.	10.1079/bjn20061697
Topical cooling (icing) delays recovery from eccentric exercise-induced muscle damage.	[51]	11	Topical cooling, a commonly used clinical intervention, seems to not improve but rather delay recovery from eccentric exercise-induced muscle damage.	10.1519/JSC.0b013e318267a22c
Short-Wave Diathermy Pretreatment and Inflammatory Myokine Response After High-Intensity Eccentric Exercise.	[55]	15	The SWD preheating treatment provided a treatment effect for intramuscular inflammatory myokines induced through high-intensity eccentric exercise but did not affect other factors associated with intense exercise and inflammation.	10.4085/1062-6050-50.1.12

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Instrument-assisted soft tissue mobilization: effects on the properties of human plantar flexors.	[55]	11	There were no significant differences in MTS, PROM, PASTQ, MVCPT, IL-6 and TNF-α between the TL or CL. A significant decrease in the perception of function and a significant increase in pain for the TL were found following IASTM.	10.1055/s-0034-1384543
Effect of supplemental oxygen on post-exercise inflammatory response and oxidative stress.	[54]	10	Supplemental oxygen provided during the recovery periods of interval based exercise improves the recovery time of SPO(2) but has no effect on post-exercise ROS or inflammatory responses.	10.1007/s00421-012-2521-7
Effects of Methylsulfonylmethane (MSM) on exercise-induced oxidative stress, muscle damage, and pain following a half-marathon: a double-blind, randomized, placebo-controlled trial.	[77]	22	MSM supplementation was not associated with a decrease from pre-training levels of oxidative stress or muscle damage associated with an acute bout of exercise. MSM supplementation attenuated post-exercise muscle and joint pain at clinically, but not statistically significant levels.	10.1186/s12970-017-0181-z
Comparison of carbohydrate and milk-based beverages on muscle damage and glycogen following exercise.	[78]	17	In summary, there were no influences of any post-exercise beverage on muscle glycogen replacement, inflammation, or muscle function.	10.1123/ijsnem.11.4.406

for accelerating recovery after strenuous exercises, and not effective to reduce muscle inflammatory response or inflammatory/muscle damage biomarkers [27-29].

Despite of the findings above, five studies from years 2010-2019, may present different results that in some corroborate and in some disagree. The Polyphenol-rich foods can be effective for combating post exercise oxidative and inflammatory cascades, be effective for accelerating recovery and reduce exercise inflammatory responses, attenuate muscle soreness and muscle catabolism [30-34].

In 2016, Levers, et al. had strong evidences, with short-term supplementation of Montmorency powdered tart cherries, as attenuated markers of muscle catabolism, reduced immune and inflammatory stress, better maintained redox balance, and increased performance in aerobically trained individuals [35].

Non-steroidal anti-inflammatory drugs (Nsaid's)

NSAID's type of drug is one of the most consumed in the world, mainly among athletes [37]. The use of NSAID's by athletes is, mainly, to reduce the muscular soreness, muscle damage, and muscle inflammation.

The literature findings, do not support the use of Naproxen, Ibuprofen, COX-2 inhibitor, Acetaminophen, and Lyprinol(®) for the above cited parameters [36-42]. Also, the findings of Lija M, et. al. 2018, evidence that the excessive use of anti-inflammatory drugs may reduce and compromise muscle strength and muscle adaptation capacity in young adults [37].

O'Grady M, et al. 2000, findings demonstrate pre administration of diclofenac significantly reduces indices of exercise-induced skeletal muscle damage [43].

Cryotherapy

Most of all amateur and professional athletes use cooling (ice bags), cold water immersion, and/or whole body cryotherapy to reduce muscle pain, muscle soreness and muscle damages. It is an ancient practice that has been passed forward, but it really has efficacy or clinical significance?

Seven studies report non-significant results for cryotherapy (20 minutes; 30 minutes of cryotherapy; intermittent whole body (-110ºC) cryotherapy; cold water limb immersion; topical cooling) in reducing biochemical muscle damage markers, attenuating strength decrement, and soreness, showing that maybe the mechanism of cryotherapy recovery is not accurate and not supporting the use of cryotherapy on recovery [44-47]. Findings, also show that cryotherapy reduces arterial and cutaneous blood flow, and cerebral oxygenation, but not muscle temperature after resistance training [48-50].

In addition, topical cooling (icing) show to delay muscle recovery after muscle damage, therefore is not recommended as therapy intervention [51].

The protocol of multiple cold-water immersions attenuated muscle damage, but had no/small effects on muscle function recovery [52-54].

Massage therapy/soft tissue therapies

Instrument-Assisted Soft Tissue Mobilization of plantar fascia had no effects on biochemical markers of muscle damage or inflammation and had a negative result at perception of function (reduced) and pain (increased) [55].

The use of topical Arnica after exercise did not changed any of the markers of inflammation or tissue damage. Regardless of these findings, the use of topical Arnica showed to be effective as pain relief three days post exercise [56].

Vibration Therapy reduces muscle soreness and biochemical markers of muscle damage and inflammation. It may stimulate lymphocyte and neutrophil responses and may be a useful modality in treating muscle inflammation. Also, massage therapy appears to be clinically beneficial by reducing inflammation and promoting mitochondrial biogenesis. When choosing between Vibration or Massage Therapy, the professional should take into account the patients preference, the experience with the technique and previous clinical outcomes, because both therapies promote muscle recovery after the performance of muscle-damaging exercise [57-59].

Supplementation

The evidence for Collagen Peptides; Omega-3; Taurine; Amino acids; Anatabine; Phosphatidylserine; Rhodiola/ Cordyceps; Arachidonic acid; Creatine; Methylsulfonylmethane;

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17beta-estradiol; Leucine Metabolites; Carbohydrate, Milk and Protein intake; supplementation has not or non-significant effect on muscle damage recovery and muscle inflammation biochemical markers [60-78].

The evidence for Protease; Phlebodium decumanum; Docosahexaenoic acid; Probiotic Streptococcus thermophilus FP4 and Bifidobacterium breve BR03; Protein-leucine; N-3 PUFA; Curcumin; Pomegranate Extract; Ellagitannin; supplementation is low/moderate on muscle damage recovery and muscle inflammation biochemical markers [79-86].

There was a moderate/strong evidence for Electrokinetically Modified Water; lemon verbena extract (Recoverben®); Iron; Black Currant Nectar; supplementation in recovering from muscle damage and reducing biochemical markers of muscle damage and inflammation [87-90].

Although the evidence above, there was moderate effect for Collagen Peptides on recovery [60], moderate to strong evidence that Rhodiola/Cordyceps improved endurance capacity and glycemic control [67], low (clinically) evidence for Methylsulfonylmethane in reduction of muscle and joint pain, low evidence for Taurine supplementation in improvement of performance and decrease of muscle damage [91].

Milk Protein concentrate supplementation is effective to reduce muscle strength loss after exercise-induced muscle damage [92].

Combined Bacillus coagulans GBI-30, 6086 and HMB, supplementation were effective to maintain muscle integrity and attenuate muscle inflammation biochemical markers in intense military training [93].

The increased consumption of carbohydrates in order to replenish the glycogen stores had no effect (positive or negative) in immune and muscular responses [69]. But increased consumption of carbohydrates and protein (as shake) and after exercise-induced damage seems to be effective to reduce muscle damage and increase recovery [94].

Compression garments

There is not a common sense for the compression garments. When we think about inflammation and tissue damage, should be used before, during or after physical activities?

In 2014, Hill JA, et al. carried a research with 24 marathon athletes and found that the use of compression garments for recovery (after physical activity) do no attenuate the biochemical markers of pain and muscle damage, but does improve the athlete perception of recovery [95].

The use of compression stockings after physical activity recovery may also be beneficial for reduce perceived muscle soreness, and had no benefits for biochemical markers [96,97].

If the athlete is already in delayed onset muscle soreness or at an inflammation phase of muscle damage, compression garments can be effective to reduce muscle stiffness [98].

Other means

Not effective for improvement of muscle damage and inflammation biochemical markers

- Electrical Muscle Stimulation (Sensory Level) – but may be effective for improvement of range of motion and provide relief for muscle soreness [99].
- Short-Wave Diathermy [55].
- Supplemental Oxygen [100].
- Focused Extracorporeal Shock Wave – May be effective for delayed on set muscle soreness [101].

Effective for improvement of muscle damage and inflammation biochemical markers

- Infrared Low-Level Laser Therapy (810nm) – 50 J dose, pre exercise, may increase performance [102].
- Infrared Photobiomodulation Therapy (810nm) - 100 mW power output per diode, pre exercise, increased muscular performance and post exercise recovery [103].
- Exercise-induced histamine release may have a broad impact on protecting muscle from exercise-induced damage – Therefore the use of anti-histamine drugs before exercise may induce to increased perception of muscle pain and strength loss, also may impair muscle damage [104-107].

Conclusion

This article evidences the most effective treatments or prevention techniques for improvement of muscle damage, inflammation biochemical markers and muscle recovery.

In our knowledge it is the first in PubMed database that assemble diverse health care subjects, and it may serve as an easy guideline for clinical decision making.

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