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Supplementation with a Polyphenol-Rich Extract, TensLess®, Attenuates Delayed Onset Muscle Soreness and Improves Muscle Recovery from Damages After Eccentric Exercise

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High-intensity exercises are known to provoke delayed onset muscle soreness (DOMS). Delayed onset muscle soreness typically occurs within the first 24 h, peaks between 24 and 72 h, and can last as long as 5–7 days post-exercise. Delayed onset muscle soreness is a multifactorial process involving both mechanical and biochemical components, associated with clinical features that may limit range of motion, and athletes seek for effective recovery strategies to optimize future training sessions. TensLess® is a food supplement developed to help manage post-exercise recovery. The supplement has been investigated on 13 recreationally active athletes of both sex, during a randomized, double-blind, and crossover clinical investigation, including a 3-week washout period. The clinical investigation was based on the study of TensLess® effects for DOMS management and on the reduction of associated muscle damages following an eccentric exercise protocol. Supplementation with TensLess® induced significant decrease in DOMS perception (−33%; $p = 0.008$) as of the first 24 h; this was significantly correlated with a lowered release of muscle damage-associated biomarkers, namely myoglobin, creatinine, and creatine kinase, for the whole length of the recovery period. Taken together, these positive results clearly indicate that post-exercise supplementation with TensLess® may preserve myocytes and reduce soreness following eccentric exercise-induced damages, and, accordingly, significantly shorten muscle recovery. Copyright © 2017 John Wiley & Sons, Ltd.

Keywords: half-squat; athlete; post-workout; DOMS; myocyte biomarker; pain.

INTRODUCTION

The practice of high-intensity exercise involving eccentric muscle contraction, such as resistance training, downhill running, resisted cycling, or stepping, is known to provoke delayed onset muscle soreness (DOMS) (Cleak and Eston, 1992). DOMS typically occurs within the first 24 h, peaks between 24 and 72 h, and can last as long as 5–7 days post-exercise (Howatson and van Someren, 2008). DOMS is classified as a type I muscle strain injury, and its associated clinical features include discomfort, pain, swelling, tenderness, loss of strength, and limited range of motion (Cheung *et al*., 2003). Symptoms associated with DOMS are known to reduce power and overall performance during subsequent bouts of exercise (Clarkson and Hubal, 2002) and may predispose individuals to injury (Cheung *et al*., 2003). Thus, both athletes and recreationally active individuals seek for effective recovery strategies to alleviate discomfort and pain and to help optimize future training sessions.

While the etiology of DOMS is still debated, recent literature suggests that it is a multifactorial process involving both mechanical and biochemical components (Lewis *et al*., 2012). Eccentric contraction induces initial structural damages to the active muscle, namely producing a disruption of the sarcolemma in which it is increased an efflux of cytosolic proteins (Sorichter *et al*., 1999). Therefore, damaged muscle may induce a pro-inflammatory response with the release of chemokines (Tidball, 2011), allowing the recruitment of inflammatory cells at the site of lesions and a concomitant increase in prostaglandins, which are known to activate nociceptors and provoke acute pain and tenderness (Connolly *et al*., 2003). Neutrophils and monocytes/macrophages are then attracted to, and accumulate at, the injured muscle cells. Collectively known as leukocytes, they give rise to cytokines and amplify the inflammatory response by recruiting additional leukocytes (Connolly *et al*., 2003). Collaterally, through an increased oxidative stress, they generate reactive oxygen species (ROS) which also contribute to amplify inflammation and oxidative stress in damaged muscle (Connolly *et al*., 2003). Thus, several factors seem to contribute to DOMS etiology, explaining through corresponding manifestations of muscle damage, the level and occurrence of DOMS.

In an attempt to reduce the symptoms associated with DOMS, non-steroidal anti-inflammatory drugs (NSAIDs) are commonly prescribed post-exercise

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(Schoenfeld, 2012). Their effects on the alleviation of DOMS have been extensively studied, but the results are conflicting. Some authors reported a decrement in the perception of muscle soreness with prophylactically administered NSAIDs (Hasson *et al*., 1993; Sayers *et al*., 2001), while others failed to demonstrate any effect on pain relief of DOMS (Donnelly *et al*., 1990; Barlas *et al*., 2000). Moreover, NSAIDs do not address oxidative stress and the loss of muscle force linked to DOMS (Tokmakidis *et al*., 2003); some authors even suggest that NSAIDs could have detrimental effects on muscle regeneration after injury (Trappe *et al*., 2002). The chronic overuse of NSAIDs has also been related to side effects such as hepatotoxicity, gastrointestinal toxicity, and to renal insufficiency (Feucht and Patel, 2010). In this regard, both elite and novice athletes experiencing exercise-induced muscle discomfort are looking for natural and safe alternatives to address symptoms associated with DOMS.

As a natural alternative to manage DOMS, polyphenolic compounds have recently received growing attention from the scientific community with respect to their well-studied antioxidant and anti-inflammatory benefits. Among them, consumption of phenolic compounds from pomegranate, mangosteen, and berry (Zafra-Stone *et al*., 2007; Xie *et al*., 2015; Ghavipour *et al*., 2017) have demonstrated beneficial effects on human biomarkers of both oxidative stress and inflammation. We hypothesized that such properties ascribed to polyphenolic compounds could be beneficial in reducing muscle soreness and damages as the etiology of DOMS is both inflammatory and oxidative (Connolly *et al*., 2003). Few studies have examined the potential effects of polyphenols in promoting recovery following a bout of intense exercise (Kim and Lee, 2014), and most of the studies have focused on the effect of a single phenolic compound (Laupheimer *et al*., 2014) or a unique fruit source such as juice (Trombold *et al*., 2011) or whole fruit (McLeay *et al*., 2012).

TensLess® is an innovative food supplement produced from a blend of natural bioactive compounds extracted from the fruit of mangosteen, pomegranate, and elderberry, which provide polyphenolic compounds, mainly consisting of xanthones, ellagic acid, and anthocyanins.

Thus, this prospective study aimed to investigate the potential effect of TensLess® on the management of DOMS and muscle damages, following an eccentric exercise protocol in healthy and recreationally active volunteers.

MATERIALS AND METHODS

Ethics statement. The protocol of the study was approved by the Ethics Committee at the Catholic University of Murcia and conducted according to the guidelines laid down in the Declaration of Helsinki (World Medical Association, 2013) and in compliance with Good Clinical Practices defined in ICH Harmonized Tripartite Guidelines (Vijayananthan and Nawawi, 2008). All participants were informed about operating procedures of the clinical trial, and they agreed to sign a written informed consent form before entering the study.

Study population. Eighteen recreationally active volunteers of both sex (12 men and 6 women), in comparable physical condition, with a minimum of 20 years old, were recruited from in Catholic University of Murcia, Spain.

Any individuals usually involved in high-intensity training or with a history of cardiorespiratory problems or chronic illness were not enrolled. In addition, individuals with a history of orthopedic injury or surgery within the last year or having any physical condition considered a contraindication to the type of exercise performed in the study were excluded. Also, those affected by any medical condition or using any medication, nutritional product, dietary supplement, or program which might interfere with the conduct of the study or place the subject at risk were not included. Furthermore, individuals could not participate if they had any food allergy to mangosteen, pomegranate, elderberry, or corn.

Test supplement. TensLess®, supplied by FYTEXIA (France), is principally obtained by alcohol and water extraction of mangosteen (*Garcinia mangostana* L.) and pomegranate (*Punica granatum* L.), by concentration of black elderberry (*Sambucus nigra* L.) juice. TensLess® provides bioactive compounds, especially polyphenols from xanthones, ellagitannins, and anthocyanins family. TensLess® complies with regulations on food contaminants and on banned and prohibited substances. The *placebo* product was 100% maltodextrin, which is polyphenol-free. Both TensLess® and placebo were supplied in 500 mg capsules of identical appearance and flavor.

Supplement was analyzed by means of high-performance liquid chromatography (HPLC). An Agilent HPLC 1260 apparatus (software Openlab CDS chemstation edition) coupled with diode array detector was used. Separation was carried out by mean of a Zorbax Stablebond SB-C18 column (4.6 × 2 mm; 5-µm particle size). To detect different phenolic classes, three different analytical methods were adopted: one for ellagitannins, one for xanthones, and one for anthocyanins.

For ellagitannins, mobile phase A consisted of 6% acetic acid, mobile phase B was 5% acetic acid and 30% acetonitrile and mobile phase C was 100% acetonitrile. The program was as follows: (a) 5 min 100% A; (b) 5 to 10 min linear gradient from 0 to 40% B; (c) 10 to 15 min linear gradient from 40 to 60% B; (d) 15 to 20 min linear gradient from 60 to 75% B; (e) 20 to 25 min linear gradient from 75 to 90% B; (f) 25 to 30 min linear gradient from 90 to 100% B; (g) 30 to 35 min linear gradient from 0 to 100% C; (h) 35 to 40 min 100% C; (i) 40 to 45min linear gradient from 0 to 100% A. Monitoring was performed at 350 nm at a flow rate of 1 mL/min and injection volume of 25 µL. Ellagitannins were expressed as ellagic acid.

For xanthones, mobile phase A consisted of 85% methanol. The program was 15 min 100% A. Monitoring was performed at 250 nm at a flow rate of 1 mL/min and injection volume of 20 µL. Xanthones were expressed as α-mangostin.

For anthocyanins, mobile phase A consisted of 10% formic acid and 3% acetonitrile, and mobile phase B was 10% formic acid and 50% acetonitrile. The program was as follows: (a) 0 to 20 min linear gradient from 6 to

20% B; (b) 20 to 35 min linear gradient from 20 to 40% B; (c) 35 to 40 min linear gradient from 40 to 60% B; (d) 40 to 45 min linear gradient from 60 to 90% B; (e) 45 to 50 min 90% B; (f) 50 to 55 min linear gradient from 90 to 100% B; (g) 55 to 60 min 100% B; (h) 60 to 65 min linear gradient from 0 to 94% A. Monitoring was performed at 520 nm at a flow rate of 0.8 mL/min and injection volume of 10 μL. Anthocyanins were expressed as kuromarin chloride.

Study design. The study consisted on a 5-week, randomized, double-blind, placebo-controlled, crossover pilot clinical trial. Volunteers were randomly assigned using an allocation sequence generated by a computerized random number generator. Once enrolled, subjects received either the test supplement or visually identical placebo for the first supplementation period of 5 days. After this initial period, volunteers were asked to return the container containing remaining capsules, before starting a washout period for 3 weeks. After the washout step, they were enrolled for the second 5-day supplementation period in which they received the opposite supplement.

Volunteers were instructed to take three capsules daily during the supplement periods. On day 1 (D1), they performed the eccentric exercise protocol and took three capsules in the ensuing minute following the training session. On the other days (D2 to D5), they ingested three capsules daily at the end of the working day, which corresponded to a 24-h lag time between two supplementations. Participants reported to the UCAM Research Center for High Performance Sport every day throughout the course of the study, except during the washout period.

Eccentric exercise protocol. At least 7 days prior to the start of the protocol, volunteers participated in a familiarization session in order to determine their individual 8-repetition maximum (RM) for the half-squat exercise. This load was individually determined for each participant using standard multi-RM determination procedures (Baechle and Earle, 2008). On this session, subjects were instructed to perform the half-squat until a 90° knee angle was achieved, following the eccentric phase of the movement (this was practiced extensively).

At D1, volunteers performed eight sets of 8-RM half-squats in order to induce muscle soreness in the knee extensors and flexors. The dynamic eccentric phase of the half-squat lasted 3 s, as set by a digital metronome, and was followed by a rapid knee and hip extension back to the starting point. The eight sets were separated by 2 min of rest. If necessary, during the protocol, the loads were adjusted to ensure that subjects completed the full eight repetitions.

Assessment of perceived muscle soreness—primary outcome. At D1, perceived muscle soreness was recorded before the eccentric exercise (pre-exercise), at the end of the eccentric training (post-exercise), and 1 h after the end of the exercise (post + 1 h). Perceived DOMS were also recorded on days following the exercise (D2 to D5).

A 10-cm visual analog rating scale (VAS) was used to evaluate perceived muscle soreness (Lau *et al*., 2013). The anchors at 0 and 10 cm corresponded to 'no soreness' and 'worst possible muscle soreness', respectively. The volunteers drew a line on the VAS corresponding to their level of soreness.

Blood markers of muscle soreness—secondary outcomes. Blood was collected from an antecubital vein on D1 (pre-exercise, immediately post-exercise, and 1 h post-exercise) and from D2 to D5 only one sample daily, using a vacutainer system. One tube of EDTA-treated blood was centrifuged (10 min, 3500*g*) to separate out the plasma. Another tube of blood was clotted and centrifuged (10 min, 5000g) to separate out the serum. Serum myoglobin concentration and plasmatic both, creatinine concentration and total creatine kinase (CK) activity were determined using assay kits obtained from Abcam, Cambridge, UK.

Statistical analysis. Data sets were analyzed using Statview software version 4.51.1 (Abacus Concepts, Berkeley, CA). The data are expressed as mean ± standard deviation (SD). Normality was evaluated by the Shapiro–Wilk test. During the length of the studied exercise inducing DOMS, changes within and between both groups were analyzed using paired and unpaired Student's *t*-test. A minimum value of $p < 0.05$ was selected as the threshold for statistical significance.

RESULTS

Participant characteristics

Twenty volunteers were assessed for eligibility, and two of them did not meet inclusion criteria and were excluded from participation in the study. Among the 18 volunteers recruited in the study, 3 did not report to the Research Center for personal reasons and 2 did not complete the training protocol due to conflict with study schedule. Thirteen participants completed the entire protocol and were included in the analysis (Fig. 1).

Characterization of the phenolic profile of the supplement

The total bioactive content corresponds to 14.61/100 g dry matter. Ellagic acid and derivative contents are measured at 8.64/100 g; xanthone and derivative contents are measured at 5.67/100 g; anthocyanin content measured at 0.3/100 g (Table 1).

Perceived muscle soreness

The mean perceived muscle soreness (DOMS), in response to the eccentric squatting exercise, is illustrated

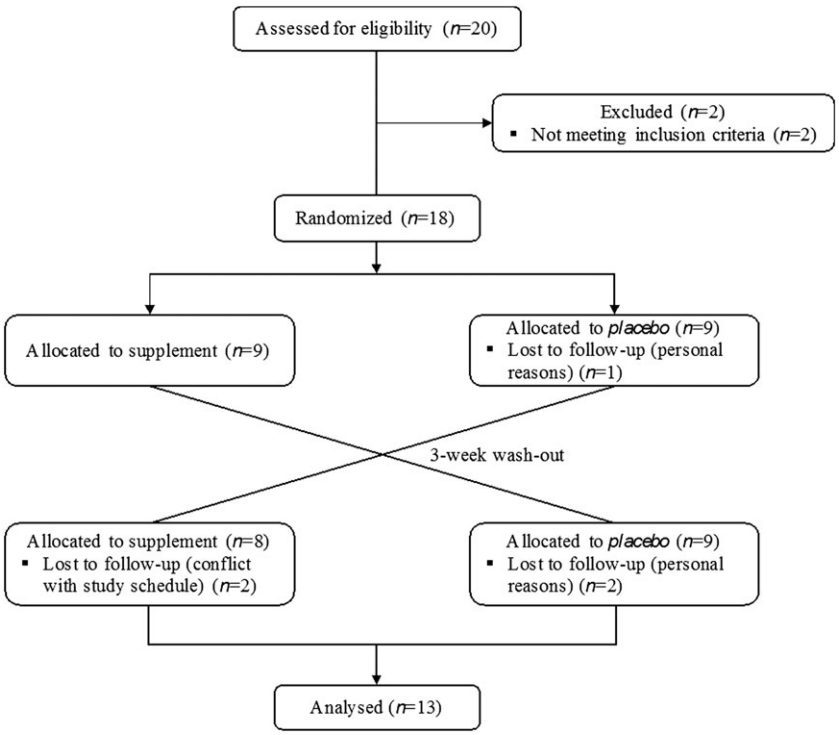

Figure 1. Consolidated Standards of Reporting Trials flow chart of participants during the study intervention.

Table 1. Characterization of phenolic compounds present in the supplement.

Compounds	Rt (min)	Λ max (nm)	Content (g/100 g)
Xanthone-like 1	3.7	243; 259; 318; 358	0.21
γ-Mangostin	4.7	243; 259; 318; 364	0.58
Xanthone-like 2	5.4	243; 259; 318; 374	0.19
α-Mangostin	7.7	243; 257; 317; 358	4.69
Cyanidin-3-O-glucoside	5.9	265; 516	0.05
Cyanidin-3-O-sambubioside	9.5	280; 518	0.25
Ellagic acid-like 1	13.2	254; 379	0.31
Ellagic acid	16.0	254; 367	8.33

in Fig. 2. Ratings of perceived DOMS were not different pre-exercise and immediately post-exercise between the placebo and the supplemented populations. At 1 h post-exercise, perceived DOMS in the placebo group increased while it stabilized for supplemented subjects; despite this was not significantly different, nevertheless it highlights a noteworthy lower DOMS perception (−31%; $p = 0.121$) when compared with placebo, which is confirmed from D2, the day after (−33%; $p = 0.008$). Indeed, perceived DOMS continued to gradually increase to reach a maximum at 48 h post-exercise (D3) in both groups, but when compared with placebo population, it was significantly lower within the supplemented group (−29%; $p = 0.045$), and even their cumulated perceived soreness (area under the curve) within these first 48 h was as well significantly lower (−31%; $p = 0.005$) when compared with placebo; on the total 5 days with DOMS, the cumulated score was lower in the TensLess® group (−28%; $p = 0.002$); despite at the end of the recovery period (D4 and D5), difference between both groups was not significant.

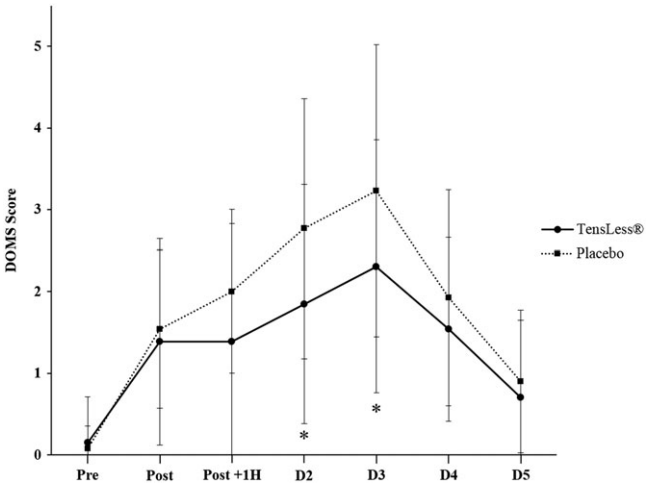

Figure 2. Delayed onset muscle soreness scores in subjects receiving TensLess® or the *placebo*, at baseline (pre), immediately following exercise (post), and during the recovery period (post + 1H, D2, D3, D4, and D5). Values are mean ± SD ($n = 13$). Asterisk superscript indicates an intergroup difference, $p < 0.05$.

Blood markers of muscle damage

Serum myoglobin levels were not significantly different between the two groups at baseline and immediately after the eccentric exercise. Myoglobin values significantly peaked, when compared with baseline, in both groups 1 h following the exercise ($p = 0.0004$ and $p = 0.0127$ for, respectively, placebo and supplemented groups); however, the maximal value was significantly different ($p = 0.044$) between the two groups, with a strong 279% increase compared with baseline in the placebo group and with a weaker 114% increase within the supplemented population. Serum myoglobin returned to baseline values from D2 and remained at baseline levels during the whole recovery period in both groups (Fig. 3A).

At baseline (pre-exercise), both groups exhibited a similar concentration of plasma creatinine. Just after the eccentric exercise, the concentration significantly increased ($p = 0.002$ and $p = 0.003$, respectively, for placebo and supplemented groups) and reached maximal value with a non-significant difference of peak value between the two groups. During the recovery period, the level of plasma creatinine gradually decreased in both groups but with significant differences between the placebo and the supplemented populations as of 1 h after exercise ($p = 0.024$) and also at D2 ($p = 0.015$) (Fig. 3B).

Between the two groups of volunteers, plasma CK levels were not significantly different at baseline (pre-exercise), neither immediately after the eccentric exercise (post-exercise) nor during the first hour of the recovery period. The eccentric exercise induced a peaked concentration of plasma CK 24 h following muscle-damaging exercise, and compared with baseline, plasma CK levels increased significantly by 139% in the placebo group ($p = 0.006$) and 103% within the supplemented population ($p = 0.005$). Compared with this D2 peak, the supplemented group displayed significant decrease at D3 ($p = 0.018$), D4 ($p = 0.004$), and D5 ($p = 0.032$), and concentrations returned to baseline values. Conversely, any decreases in CK levels in the placebo group during the recovery period were not significant compared with the peak at D2 and continued to be significantly different to the baseline concentration (Fig. 3C).

DISCUSSION

This prospective study highlights the beneficial, both acute and sub-chronic effects of the supplementation with TensLess®, a polyphenol-rich extract-based food supplement, on adverse symptoms associated with DOMS, namely eccentric exercise-related markers of muscle impairment.

The eccentric exercise, that is, weighted half-squats, successfully induced DOMS, as evidenced by the reported scores of perceived muscle soreness, which is in

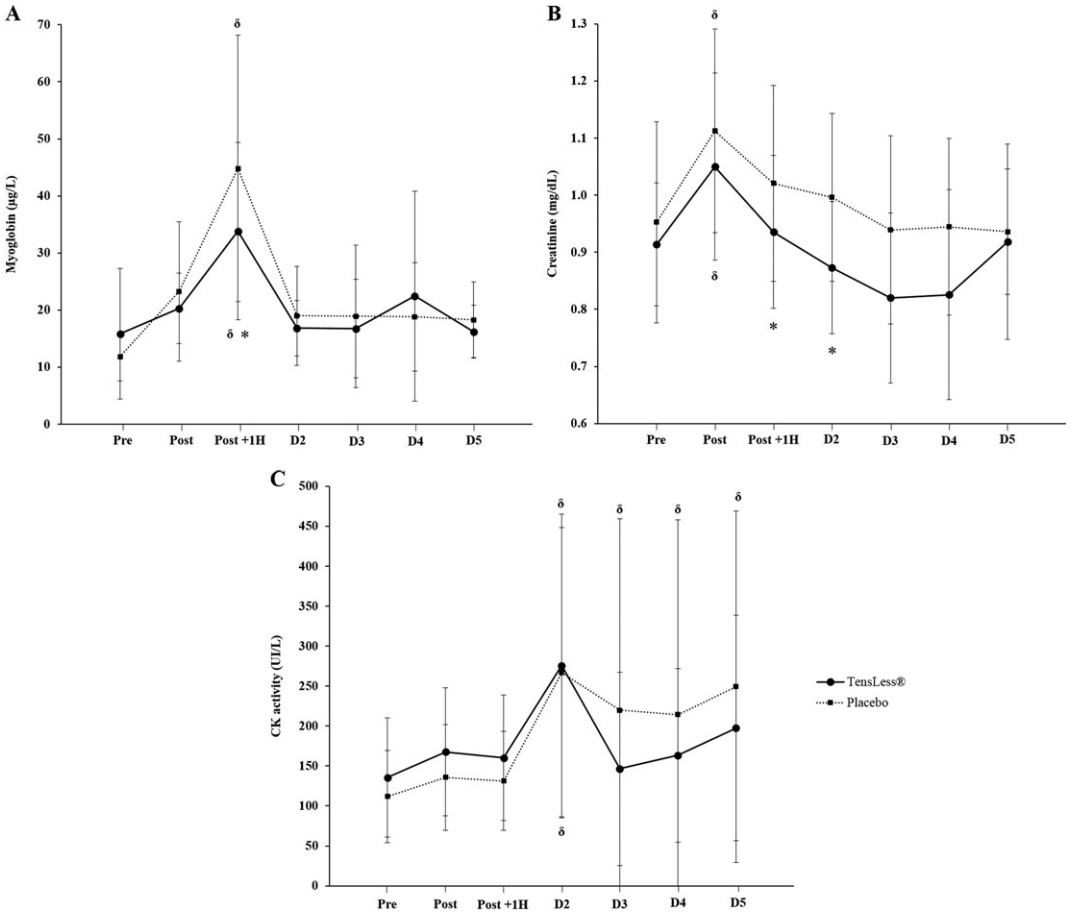

Figure 3. Serum myoglobin concentration (A), plasmatic creatinine concentration (B), and plasmatic CK activity (C) in subjects receiving TensLess® or the *placebo*, at baseline (pre), immediately following exercise (post), and during the recovery period (post + 1H, D2, D3, D4, and D5). Values are mean ± SD ($n = 13$). Delta superscript indicates a difference as compared with baseline, $p < 0.05$. Asterisk superscript indicates an intergroup difference, $p < 0.05$.

line with previous studies (Shimomura *et al*., 2010; Pearcey *et al*., 2015) where DOMS peaked at 48 h (D3) following similar protocol. Also, the increased levels of skeletal muscle enzymes and proteins in blood circulation, such as myoglobin, creatinine, and CK, confirmed the induction of muscle damages following the squat exercise, given that they are the most valuable and direct markers of muscle injury (Brancaccio *et al*., 2010). Accordingly, the protocol used to induce muscle damages was appropriate for evaluating the potential effect of a dietary food supplement in managing DOMS.

The main symptom related to DOMS and for which scientific researches are converging is pain, which is known to limit both recovery and subsequent athletic performances (Twist and Eston, 2005). The origin of pain linked with DOMS is hypothesized to be induced by the release of prostaglandin E2 (PGE-2), which sensitizes types III and IV afferent nerve fibers through nociceptors. Furthermore, inflammatory responses to eccentric exercise would contribute to the sensation of pain (Connolly *et al*., 2003). The post-exercise supplementation significantly decreased cumulated perceived soreness (DOMS) as evidenced with a 31% reduction within the first 2 days post-exercise when compared with the placebo group; similar result was obtained regarding perceived pain (data not shown). Mechanisms supposed to be linked to the beneficial effects of the supplement on the alleviation of muscle soreness and associated pain could be attributed to both direct antinociceptive and indirect anti-inflammatory activities of phenolic compounds. Indeed, beyond previously demonstrated anti-inflammatory effects of α-mangostin (Chen *et al*., 2008; Romain and Cases, 2015), a xanthone from polyphenol family naturally occurring in mangosteen, it has recently been shown that this compound is able to inhibit both central and peripheral nociception in a rodent model of induced pain through interaction with at least three different physiological pathways linked to pain perception (Sani *et al*., 2015). Apart from mangosteen bioactive, phenolic compounds from pomegranate extract, and particularly ellagic acid, could also contribute to decrease eccentric exercise-induced muscle soreness. As with mangosteen, pomegranate extracts display anti-inflammatory and, both central and peripheral, antinociceptive properties in animal models (González-Trujano *et al*., 2015). Trombold *et al*. (2010) reported that an intake of 500 mg of ellagitannins twice a day during a 5-day period preceding eccentric exercise was able to reduce DOMS by 15% as of 2 h after muscle damage induction. However, in the aforementioned study, no significant differences between the placebo group and the ellagitannin-supplemented population were found within the 24 to 96 h post-exercise period (Trombold *et al*., 2010). TensLess® also displays anthocyanins from elderberry concentrate, which could potentiate the beneficial effects of the supplement on eccentric exercise-induced soreness and pain. Indeed, this was demonstrated by previous researches in which an intake of tart cherry juice, a fruit source of similar anthocyanins, was found to be effective in reducing pain following long-distance running (Kuehl *et al*., 2010). In the present study, the supplement induced 29% reduction in perceived soreness during the first 48 h corresponding to the DOMS and pain peak period. This important soreness and pain-alleviating benefit might be elicited by a synergistic action of bioactive polyphenols that are at the basis of TensLess® formulation and which are altogether capable to provide both an acute and a subchronic beneficial effect.

The half-squat protocol used in the present study, successfully induced skeletal muscle injury, as exemplified by the significant increase in typical blood markers of damaged myocytes (Brancaccio *et al*., 2010), for which both oxidative stress and inflammatory responses to exercise are suspected to be the principal culprits (Baird *et al*., 2012). Even though no statistical difference was found between the two groups with regards to CK peak values, nevertheless the supplement significantly induced a shorter return to baseline level at 48 h (from D3), while in the placebo group, it remained not statistically different than peak level during the recovery period.

Creatinine, although generally used as an indicator of renal health, has also been shown to significantly increase following high-intensity exercise (Levers *et al*., 2015). In the present study, post-exercise levels of creatinine were in the normal range (0.7 to 1.2 mg/dL), indicating no alteration of renal function but a normal response to eccentric exercise with a significant time effect occurring in both groups just after the completion of the squats protocol. While creatinine rapidly decreased with a significant reduction from D2 and a return to baseline value at D3 in the supplemented group, it significantly remained at peak level for the placebo population; this confirms a faster recovery with TensLess®. Finally, this beneficial effect is confirmed with serum myoglobin, another sensitive marker of muscle injury. While the concentration peaked 1 h following the exercise in both groups, a significant 25% lower increase in the supplemented group was experienced when compared with placebo.

Taken together, these positive results on direct biomarkers of muscle damages clearly indicate that post-exercise supplementation with TensLess® may preserve myocytes from eccentric exercise-induced damages which significantly enhance muscle recovery. The literature shows that eccentric exercise-induced oxidative stress with increased reactive oxygen species release would be among main contributory mechanisms of both the initiation and progression of muscle damages (Stagos *et al*., 2015). This may occur through an enhanced peroxidation of lipid membranes inducing then after the disruption of muscle cells with a concomitant efflux of cytosolic proteins (Jówko *et al*., 2015). In accordance with the proposed biochemical mechanisms underlying muscle damages, it may be hypothesized that phenolic compounds from TensLess®, for which antioxidative properties have been extensively studied and demonstrated in humans (Zafra-Stone *et al*., 2007; Kondo *et al*., 2009; Matthaiou *et al*., 2014), effectively may combine with their anti-inflammatory activities to limit eccentric exercise-induced muscle damages (Clarkson and Hubal, 2002; Sureda *et al.,* 2014), thereby explaining the decreased efflux of cytosolic proteins and enzymes from the skeletal muscle into the bloodstream.

Thus, post-exercise supplementation with TensLess® demonstrates a positive effect on both exercise-induced DOMS and muscle damages, which explains the significant faster recovery.

Nevertheless, further investigations need to be conducted in order to validate the biochemical mechanisms of action of phenolic compounds in relation to the

amelioration of muscle injury by both their anti-inflammatory and antioxidative properties. Additionally, a pivotal study involving a larger sample of volunteers and incorporating high-profile athletes for which athletic performance measurements during the recovery period, namely strength and range of motion, would have to be performed; this would let us allow to clearly demonstrate the hypothesized mechanism implicated during functional improvement following dietary supplementation with TensLess®.

Author Contributions

J.C. and C.R. furnished the supplement and the placebo and assisted with study conception and design and manuscript preparation. L.H.C. and P.A. conceived and designed the study, recruited subjects, performed exercise training, data collection and analysis, and manuscript preparation. T.T.F. and F.J.M.N. assisted with study coordination, subject recruitment, exercise training, data collection, and analysis. C.L. and S.G. performed measurements of biochemical activities.

Conflict of Interest

Fytexia is involved in the research and development and marketing and sales of polyphenol extracts from various fruit and vegetables regularly consumed within the Mediterranean diet for food and nutraceutical industries. Therefore, Fytexia has a commercial interest in this publication. UCAM and UMR 204 Nutripass were paid by Fytexia to perform and report the scientific work that formed the basis of this publication. Fytexia, UCAM, UMR 204 Nutripass, and all authors declare that the data in this report represent a true and faithful representation of the work that has been performed. The financial assistance of Fytexia is gratefully acknowledged.

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