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

Cindy Romain,1 Tomás T. Freitas,2 Francisco J. Martínez-Noguera,2 Caroline Laurent,3 Sylvie Gailliet,3 Linda H. Chung,2 Pedro E. Alcaraz2 and Julien Cases1*
1Innovation and Scientific Affairs, Fytexia, 34350, Vendres, France
2Research Center in High Performance Sport, UCAM Universidad Católica de Murcia, Murcia, Spain
3UMR 204 Nutripass, Institut de Recherche pour le Développement, Université de Montpellier, 34095, Montpellier, France

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. Delayed onset muscle soreness is a multifactoral 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®, a food supplement developed to help manage post-exercise recovery, 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.

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.
The clinical trial, and they agreed to sign a written in-
ticipants were informed about operating procedures of
Guidelines (Vijayananthan and Nawawi, 2008). All par-
cal Association, 2013) and in compliance with Good
Ethics statement. The protocol of the study was ap-
approved by the Ethics Committee at the Catholic Univer-
sity of Murcia and conducted according to the guidelines
headed in the Declaration of Helsinki (World Medi-
health and recreationally active
exercise-induced muscle discomfort are
Looking for natural and safe alternatives to address
symptoms associated with DOMS.
As a natural alternative to manage DOMS, polyphen-
olic compounds have recently received growing atten-
tion 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 poly-
phenolic 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 pheno-
lic 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 pro-
duced from a blend of natural bioactive compounds ex-
ttracted from the fruit of mangosteen, pomegranate, and
erdberry, 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 ex-
ercise protocol in healthy and recreationally active
volunteers.

**MATERIALS AND METHODS**

**Ethics statement.** The protocol of the study was ap-
proved by the Ethics Committee at the Catholic Univer-
sity of Murcia and conducted according to the guidelines
headed in the Declaration of Helsinki (World Medi-

**Study population.** Eighteen recreationally active vol-
unteers 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, individ-
uals 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 sub-
ject 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 concentra-
tion of black elderberry (Sambucus nigra L.) juice.
TensLess® provides bioactive compounds, especially
polyphenols from xanthones, ellagitannins, and antho-
cyanins family. TensLess® complies with regulations on
food contaminants and on banned and prohibited sub-
stances. The placebo product was 100% maltodextrin,
which is polyphenol-free. Both TensLess® and placebo
were supplied in 500 mg capsules of identical appear-
ance 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. Monitor-
ing 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
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, 3500g) 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
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\textsuperscript{®} group (−28%; \(p = 0.002\)); despite at the end of the recovery period (D4 and D5), difference between both groups was not significant.

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

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

Copyright © 2017 John Wiley & Sons, Ltd.
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
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 a-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 (Sami 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 sub-chronic 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 antioxidant 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.

REFERENCES


