The Effect of Grape Seed Extract Supplementation on Delayed Onset Muscle Soreness (DOMS) in Young Healthy Female Students

Jilla Raees-Sadati1, Babak Nakhostin-Roohi2, Marethf Siahkouhian2
1 Department of Physical Education, University of Mohaghegh-Ardabili, Ardabil, Iran
2 Department of Physical Education & Sports Science, Ardabil Branch, Islamic Azad University, Ardabil, Iran

Abstract

Background: Delayed onset muscle soreness (DOMS) is a common experience after unusual activities particularly eccentric exercises. The aim of the present study was to investigate the effect of grape seed extract (GSE) on some factors of DOMS on non-athletic female students. Method: Twenty young healthy female students were randomly allocated into two experimental (GSE=10n) and placebo (PLC=10n) groups. T produce DOMS, a forty-five repetition of eccentric elbow curl in three sets was performed. Venous blood samples were obtained before and after supplementation, immediately, 24h, and 48h after exercise for analysis of creatine kinase (CK), lactate dehydrogenase (LDH). The pain was assessed by visual analogue scale (VAS). Results: There was a significant increase in CK activity after exercise compared with before exercise in both groups (P<0.05), but no significant differences between two groups at any time (P>0.05). Furthermore, The VAS scores were significantly lower in GSE compared with PLC group 24h and 48h after exercise (P<0.05). Conclusion: Although GSE supplementation has not been able to affect the CK and LDH activity, it seems that its anti-inflammatory or analgesic effects have been reduced the pain caused by DOMS.

INTRODUCTION

Delayed onset muscle soreness (DOMS) is a disorder that occurs in any individual, depending on his level of physical fitness, and often as a result of eccentric exercises, such as running downhill, stepping, weight lifting [1,2]. This types of exercises lead to damage to the cell membrane and lead to inflammatory responses [3]. One of the symptoms of DOMS is pain, Muscle spasm, swelling, inflammation, decrease of Range of motion (ROM) of the joints and functional activities, as well as biochemical symptoms such as increased creatine kinase (CK), and lactate dehydrogenase (LDH) [4-7]. According to investigations, the intensity of the DOMS follows the reverse U pattern, which peak approximately 24 to 48 hours after activity, and then gradually diminishes and completely disappears 5 to 7 days after the exercise [8,9]. Therefore, prevention and treatment of DOMS have long been considered by sports medicine specialists and physiotherapists, and so far, several studies have been conducted to control the DOMS. Several methods have been used such as warm-up exercises, stretching, ultrasound therapy, interferential currents, massage, ice, vitamin C, E, curcumin, and L-arginine supplementation, as well as non-steroid anti-inflammatory drugs (NSAIDs) [1,4,7,10-15]. Despite the application of different methods, researchers have not reached a consensus on the treatment of this damage.

During intensive exercise, free radicals cause oxidative damage to muscle membranes through fat peroxidation [16]. DOMS, as mentioned, causes damage to the cell membrane. Some researchers believe that one of the reasons for the DOMS may be oxidative stress [17].

Grape seed extract (GSE) is one of the supplements that has been introduced in traditional medicine as an anti-inflammatory agent and is a main source of Oligomeric proanthocyanidine (OPC). This antioxidant appears to help protect cells against damage from free radicals. The OPC in the grape nucleus is the most effective antioxidant compounds [18,19].

Previous studies have shown that proanthocyanidine has significantly decreased oxidative and lipid damage in the brain, liver and also gastrointestinal mucosa in diabetic animals [20].
Another study by Shawo et al. (2003) also showed that the GSE significantly reduced the oxidative stress caused by H₂O₂ and reduced the contractile power of the cultured cardiac cells [21]. Some studies have also shown that GCS has analgesic and anti-inflammatory properties that may be effective in reducing pain and inflammation caused by DOMS [22,23].

Considering the evidence of anti-inflammatory, analgesic and antioxidant effects of GSE on the one hand, and the extent of published research on its use in DOMS in animals and humans, on the other hand, the present study was conducted to determine the effect of GSE on the prevention of DOMS.

METHODS & MATERIALS

The present study was designed as a randomized, double-blind, with a control group. Forty young healthy female students of Mohaghegh-Ardabili University (mean age: 20.18 ± 1.6 years, height: 159.64 ± 6.7, and weight: 62.10 ± 10.16 kg) voluntarily participated in this study. They had no regular exercise activity for six months before the study, and had no history of muscular bruising. In the same session, the physiological characteristics of individuals (Table 1) were measured. Inclusion criteria of this research were being in a specific period of menstruation (before this time period), no steroid and non-steroid anti-inflammatory drugs and antioxidant supplements use up to two months before the initiation of the trial. Finally, twenty subjects were randomly allocated into two groups of the grape seed extract (GSE: 10n) and the placebo group (Lactose: 10n). In order to observe ethical considerations, the goals and potential risks of the research were explained verbally and in writing to the subjects and finally written consent were obtained from them. In the GSE group, the extract of the grape seed was received as a capsule of 400 mg and received 1200 mg/day, 7 days prior to exercise for up to 48 hours, and the control group received the same amount of lactose as placebo in the same pattern. Since the subjects lived in a dormitory, their nutritional conditions were almost the same. They were also asked to avoid other supplements, such as antioxidant supplements, that may interfere with their diet. After finishing the supplementation, the subjects conducted the exercise protocols as follows: Before the exercise protocol, the subjects first warmed up for 15 minutes and then sat in the chair for help with the assistant. The selected exercise was elbow curl and it is performed in three sets of 15 repetitions with a rest interval of 3 minutes between sets and 90% of 1RM. The duration of each repetition was 2 seconds concentric contraction and 3 seconds eccentric contraction. It should be noted that the following formula was used to determine the one maximum repetition [19]:

\[
\text{One Maximum Repetition (1RM)} = \frac{\text{Weight (kg)}}{1.02278 - (\text{Number of repetitions} - 0.0278)}
\]

To measure the levels of CK and LDH, before and after taking the supplement (fasting) immediately, 24 and 48 hours after the activity, each time 5ml of blood was taken from the ante cubital vein. CK and LDH were measured using an auto-analyzer (BT3000-Biotechnica Company, Italy). To evaluate the severity of pain, the subjects were asked to express their pain intensity using visual analogue scale (VAS). On this scale, a 10 cm scale between “without pain” and the “most severe pain” was used to evaluate DOMS pain [14]. In order to analyze the research findings, in addition to descriptive statistics, one-factor variance analysis with repeated measurements, and Bonferroni correction were used. If there were significant between group differences, independent t-test was used to compare the results between the two groups at each time step.

Findings

The mean and standard deviation of physical characteristics of the subjects are presented in Table 1. There was no significant difference between the two groups in any of these characteristics (P<0.05).

According to the findings, there was no significant between group differences in the baseline in the CK, LDH and VAS, which emphasized the homogeneity of the subjects (P>0.05). CK significantly increased in both groups 24 and 48 hours after exercise, but there was no significant between group differences in any times (P>0.05) (Figure 1). According to Figure 2, no a significant within or between group differences were observed in the LDL activity (P>0.05).

Moreover, VAS scores showed significant increase in both groups, after exercise compared with before exercise, immediately, 24h and 48h (P<0.05). The results also indicate that VAS scores are significantly low in the GSE group compared with PLC group, 24h and 48h after exercise(P<0.05) (Figure 3).

![Figure 1: CK activity changes in both groups (mean ± SD).](image1)

* indicates a significant increase compared to before activity in both groups (P<0.05).

![Figure 2: LDH activity changes in both groups (mean ± SD).](image2)
and healthy females, the exercise protocol included seven sets of squats with 20 repetition per set that seemed to be heavier than exercise is present [25].

CONCLUSION

According to the results of this study, although GSE did not reduce CK and LDH enzymes activity, its anti-inflammatory and anti-inflammatory properties appear to be effective in reducing pain after DOMS.

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Conflict of interest

The Authors declare no conflict of interest.

REFERENCES

1. Heiss R, Lutter C, Freiwald J, Hoppe MW, Grim C, Poetgen K, et al. Advances in Delayed-Onset Muscle Soreness (DOMS)—Part II: Treatment and Prevention. Sportverletzung. Sportschaden. 2019;33(01):21-9.
2. Kim J, Lee J. A review of nutritional intervention on delayed onset muscle soreness. Part I. Journal of exercise rehabilitation. 2014;10(6):349-.
3. Fridén J, Sfakianos PN, Hargens AR, Åkeson WH. Residual muscular swelling after repetitive eccentric contractions. Journal of orthopaedic research. 1988;6(4):493-8.
4. Nahkhostin-Roohi B, Mohammadiaghdam Z. The effect of L-Arginine supplementation on Delayed Onset Muscle Soreness (DOMS) after eccentric heavy exercise. Hormozgan Medical Journal. 2017;21(3):169-77.
5. Chang W-D, Wu J-H, Chang N-J, Lee C-L, Chen S. Effects of Laser Acupuncture on Delayed Onset Muscle Soreness of the Biceps Brachii Muscle: A Randomized Controlled Trial. Evidence-Based Complementary and Alternative Medicine. 2019;2019.
6. Lee J, Goldfarb AH, Rescino MH, Hegde S, Patrick S, Apperson K. Eccentric exercise effect on blood oxidative-stress markers and delayed onset of muscle soreness. Medicine & Science in Sports & Exercise. 2002;34(3):443-8.
7. Nahkhostin-Roohi B, Nasivand Moradlou A, Mahmoodi Hamidabad S, Ghanivand B. The effect of curcumin supplementation on selected markers of delayed onset muscle soreness (DOMS). Annals of Applied Sport Science. 2016;4(2):25-31.
8. Tartibian B, AZIZ BBK. The effect of taking naroxen drug on the level of perceived pain and changes of CPK serum after eccentric exercise. 2008.
9. Tiidus P. Can oestrogen influence skeletal muscle damage, inflammation, and repair? British journal of sports medicine. 2005;39(5):251-3.
10. Isabell WK, Durrant E, Myer W, Anderson S. The effects of ice massage, ice massage with exercise, and exercise on the prevention and treatment of delayed onset muscle soreness. Journal of Athletic Training. 1992;27(3):208.
11. Rodenburg J, Steenbeek D, Schiereck P, Bär P. Warm-up, stretching and massage diminish harmful effects of eccentric exercise. International Journal of Sports medicine. 1994;15(07):414-9.
12. Ketcham A. A Comparison Between Pulsed Ultrasound and Self-Myofascial Release on Delayed-Onset Muscle Soreness. 2018.
13. Simmons G, Cooper S, Muse D. Enhancing methods for the delayed onset muscle soreness (DOMS) pain model. The Journal of Pain. 2018;19(3):581.
14. Ellis L, Yates BA, McKenzie AL, Muñoz CX, Casa DJ, Armstrong LE. Oral Nutritional Supplement Effects on Urine Color: 908 Board# 224 June 1, 330 PM-500 PM. Medicine & Science in Sports & Exercise. 2016;48(5S):256.

**DISCUSSION**

The aim of this study was to investigate the effects of GSE on CK, LDH, and pain following eccentric exercise in healthy young female students. Considering the significant increase in serum CK, it can be concluded that the protocol used in this study has been effective in the producing DOMS. Most studies have shown increased serum CK after eccentric exercise [6,7,25-27]. The results of this study also indicate that supplementation of GSE was not affected on CK activity after extrinsic exercise (Figure 1). According to Theodorou et al. (2011) the vitamin C and E as antioxidant, were not suppressed after eccentric exercise that the result was consistent our study [28]. Contrary to the current study, our recent research showed that curcumin use as an antioxidant can reduce the CK activity compared with the control group [7]. Curcumin seems to have been able to reduce the leakage of CK from the myocytes to the blood by increasing the antioxidant power and consequently lowering the lipid peroxidation of the cell [29-31]. The reason for the lack of the same results is not clear, but the difference in the type, the amount, and duration of antioxidant supplementation, the type of eccentric exercise protocol were the causes of the difference in outcome.

Unlike CK, LDH activity did not show any significant increase after exercise compared with before exercise (P>0.05). Moreover, no difference was observed between the groups (P>0.05) (Figure 3). Since LDH, as an indicator of muscle damage, is less sensitive to CK, it is possible that heavier or longer eccentric exercise was required to significantly increase its activity [32]. Contrary to the results of current research, our recent researches have shown that eccentric exercise is able to increase the LDL activity [7,25]. Probably the intensity and duration of activity in our previous studies have been enough to stimulate the increase of this enzyme activity and then its leakage into the bloodstream.

For example, in one of these studies, which was conducted in 2017 with the aim of evaluating the effect of L-arginine on DOMS in young

**Figure 3: VAS scores in both groups (mean ± SD).**

† indicates a significant between groups differences (P<0.05).

**Table 1: Mean and standard deviation of subjects’ demographic characteristics (mean ± SD)**

|                      | Age (year) | Height (cm) | Weight (kg) | BMI (kg.m$^{-2}$) |
|----------------------|------------|-------------|-------------|-------------------|
| PLC group (n=10)     | 20.2 ± 4.6 | 161.4 ± 10.5 | 61.6 ± 1.4  | 22.3 ± 1.9        |
| GSE group (n=10)     | 20.1 ± 2.4 | 157.8 ± 11.1 | 63.5 ± 1.3  | 22.5 ± 1.2        |
15. Connolly D, Lauzon C, Agnew J, Dunn M, Reed B. The effects of vitamin C supplementation on symptoms of delayed onset muscle soreness. Journal of sports medicine and physical fitness. 2006;46(3):462.

16. Nakhostin-Roohi B, Babaei P, Rahmani-Nia F, Bohlooli S. Effect of vitamin C supplementation on lipid peroxidation, muscle damage and inflammation after 30-min exercise at 75% VO2 submax. Journal of Sports Medicine and Physical Fitness. 2008;48(2):217.

17. Jamurtas A. Exercise-Induced Muscle Damage and Oxidative Stress. Multidisciplinary Digital Publishing Institute; 2018.

18. Zülli F, Belser E, Neuschwander M, Muggli R. Antioxidants from grape seeds protect hairagainst reactive oxygen species. PersonalCare, October. 2001:65-7.

19. Bagchi D, Garg A, Krohn R, Bagchi M, Tran M, Stohs S. Oxygen free radical scavenging abilities of vitamins C and E, and a grape seed proanthocyanidin extract in vitro. Research communications in molecular pathology and pharmacology. 1997;95(2):179-89.

20. El-Alfy AT, Ahmed AA, Fatani AJ. Protective effect of red grape seeds proanthocyanidins against induction of diabetes by alloxan in rats. Pharmacological research. 2005;52(3):264-70.

21. Shao Z-H, Becker LB, Hoek TLV, Schumacker PT, Li C-Q, Zhao D, et al. Grape seed proanthocyanidin extract attenuates oxidant injury in cardiomyocytes. Pharmacological research. 2003;47(6):463-9.

22. Terra X, Valls J, Vitrac X, Mérrillon J-M, Arola L, Ardévol A, et al. Grape seed procyanidins act as antiinflammatory agents in endotoxin-stimulated RAW 264.7 macrophages by inhibiting NFKB signaling pathway. Journal of agricultural and food chemistry. 2007;55(11):4357-65.

23. Shi J, Yu J, Pohorly JE, Kakuda Y. Polyphenolics in grape seeds—biochemistry and functionality. Journal of medicinal food. 2003;6(4):291-9.

24. Price DD, Bush FM, Long S, Harkins SW. A comparison of pain measurement characteristics of mechanical visual analogue and simple numerical rating scales. Pain. 1994;56(2):217-26.

25. Nakhostin-Roohi B, Mohammadi-Aghdam Z. The effect of L-Arginine supplementation on Delayed Onset Muscle Soreness (DOMS) after eccentric heavy exercise. Bimonthly Journal of Hormozgan University of Medical Sciences. 2017;21(3):169-77.

26. Bakhtiyari AH, Safavi-Farokhi Z, Aminian-Far A. Influence of vibration on delayed onset of muscle soreness following eccentric exercise. British journal of sports medicine. 2007;41(3):145-8.

27. Close GL, Ashton T, Cable T, Doran D, MacLaren DP. Eccentric exercise, isokinetic muscle torque and delayed onset muscle soreness: the role of reactive oxygen species. European journal of applied physiology. 2004;91(5-6):615-21.

28. Theodorou AA, Nikolaidis MG, Paschalis V, Koutsias S, Panayiotou G, Fatouros IG, et al. No effect of antioxidant supplementation on muscle performance and blood redox status adaptations to eccentric training. The American journal of clinical nutrition. 2011;93(6):1373-83.

29. Bohlooli S, Barmaki S, Khoshkhahehes F, Nakhostin-Roohi B. The effect of spinach supplementation on exercise-induced oxidative stress. The Journal of sports medicine and physical fitness. 2015;55(6):609-14.

30. Nakhostin-Roohi B, Khoshkhahehes F, Parandak K, Ramazanazadeh R. Influence of L-carnitine supplementation on exercise-induced muscle damage. Medicina Dello Sport. 2014;67(2):251-9.

31. Khoshkhahehes F, Siahkuhain M, Fisher G, Nakhostin-Roohi B. Influence of a low-dose cox-2 inhibitor drug on exercise-induced inflammation, muscle damage and lipid peroxidation. Biology of sport. 2013;30(1):61.

32. Connolly DA, Sayers SP, McHugh MP. Treatment and prevention of delayed onset muscle soreness. Journal of strength and conditioning research. 2003;17(1):197-208.