

The experimental effect of *Lycium barbarum* on redox homeostasis in physical exercise

Efectul experimental al Lycium barbarum asupra homeostaziei redox în efort fizic

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Abstract

Background. Goji has over 100 potentially beneficial constituents for the human body contained in all parts of the plant, especially in fruit and roots. Data from the literature have suggested beneficial effects on the human body after long-term Goji juice intake.

Aims. We studied the antioxidant effect of *Lycium barbarum* (Goji) natural juice on the body subjected to physical exercise.

Methods. The oxidant-antioxidant balance indicators were determined in 6 groups of male Wistar rats (n = 6 animals/group) which performed physical exercise through the swimming test. Some groups only performed physical exercise, while others were subjected to physical exercise and received an additional daily intake of *Lycium barbarum* natural juice. Nitro-oxidative stress was measured by serum determination of total oxidant status (TOS), total antioxidant capacity (TAC), malondialdehyde (MDA), total thiols, nitrites and nitrates.

Results. Increased TAC and serum thiol levels confirmed the antioxidant potential of *Lycium barbarum* during physical exercise. The daily intake of *Lycium barbarum* natural juice led to the reduction of oxidative stress and, implicitly, of lipid peroxidation, as evidenced by the decrease of serum MDA values.

Conclusions. Under experimental conditions, the administration of natural *Lycium barbarum* juice was beneficial by increasing exercise capacity. Due to its energetic and antioxidant effect, *Lycium barbarum* could represent a natural, non-doping alternative for improving sports performance.

Keywords: *Lycium barbarum* (Goji), oxidant-antioxidant balance, physical exercise.

Rezumat

Premize. Goji are peste 100 de constituenți cu potențial benefic pentru organismul uman conținuți în toate părțile plantei, mai ales la nivelul fructului și al rădăcinii. Date din literatură au sugerat existența unor efecte benefice asupra organismului uman după consumul sucului de Goji pe termen lung.

Obiective. Am studiat efectul antioxidant al sucului natural de fructe *Lycium barbarum* (Goji) asupra organismului în efort fizic.

Metode. Au fost determinați indicatorii balanței oxidanți-antioxidanți la 6 loturi de șobolani masculi rasa Wistar (n = 6 animale/lot) care au efectuat efort fizic prin proba de înot. Unele loturi au fost supuse doar efortului fizic prin proba de înot, iar celelalte au fost supuse efortului și aportului suplimentar de *Lycium barbarum*. Stresul nitro-oxidativ a fost măsurat prin determinarea serică a statusului oxidativ total, a capacității antioxidante totale, a malondialdehidei și a tiolilor totali.

Rezultate. Creșterea valorilor capacității antioxidante totale (TAC), a nivelului seric de tioli a confirmat potențialul antioxidant al *Lycium barbarum* în condiții de efort fizic. Suplimentarea cu suc natural de *Lycium barbarum* a condus la diminuarea stresului oxidativ și, implicit, a peroxidării lipidice, dovedite prin scăderea valorilor malondialdehidei serice.

Concluzii. În condiții experimentale, administrarea sucului natural de *Lycium barbarum* și-a adus aportul benefic la creșterea capacității de efort. Datorită efectului energogen și antioxidant în condiții de efort, *Lycium barbarum* ar putea reprezenta o alternativă naturală, nedopantă, pentru îmbunătățirea performanțelor sportive.

Cuvinte cheie: *Lycium barbarum* (Goji), balanță oxidanți/antioxidanți, efort fizic.

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Introduction

Goji was named *Lycium barba rum* in the botanical nomenclature in 1753 (Carl Linnaeus) (Kulczyński & Gramza-Michałowska, 2016). It belongs to the Solanaceae family, *Lycium* genus (Ma et al., 2009). Although it is known in the literature under many names, the name Goji derived from the Chinese “gouqi” has been widely accepted (Hänsel et al., 1993).

Goji is a shrub with reddish-orange fruits, having a diameter of 1-2 cm² and bitter-sweet taste (Zhang et al., 2001).

Goji has over 100 potentially beneficial constituents for the human body contained in all parts of the plant, especially in fruit and roots. Through these constituents, *Lycium barbarum* exhibits a powerful antioxidant and cytoprotective effect: hypoglycemic (Shaban et al., 1990; Wu et al., 2006), hypolipemic (Zhao et al., 2005; Luo et al., 2004), cardio- (Xu et al., 2005), neuro- (Lin et al., 2003; Yu et al., 2006; Yu et al., 2007), pancreato- and hepatoprotective (Kim et al., 1997; Chin et al., 2003; Slemmer et al., 2008), anti-aging (Zhao et al., 2005; Li et al., 2007b), anti-arterial hypertension (Jia et al., 1998; Chan et al., 2007); it contributes to increasing the body's resistance to physical exercise, etc.

Goji fruits are consumed fresh or in the form of juice, tea (infusion) or wine (Zhufan, 2000). They can also be used in combination with conventional products such as yogurt or snacks with seeds, dehydrated fruits and oatmeal (Potterat, 2010) in various culinary preparations (Yin & Dang, 2008) or as seasonings (Jin et al., 2013). The recommended daily dose of dried Goji fruit is 5-12 g, calculated for an adult body (Bensky et al., 2004).

Hypothesis

The beneficial effects of Goji as well as its contribution to increased exercise capacity have led us to study the antioxidant effect of *Lycium barbarum* (Goji) natura l fruit juice on the body subjected to physical exercise through oxidative-antioxidant balance indicators.

Materials and methods

a) Research protocol

The experimental study was performed on 16 weeks old male Wistar rats, with a mean weight of 200 grams, from the Biobase of the “Iuliu Hațieganu” University of Medicine and Pharmacy Cluj-Napoca. The study was approved by the Ethics Board, according to Good Practice Guidelines. The requirements of the Helsinki Declaration, Amsterdam Protocol, Directive 86/609/EEC and the regulations of the Bioethics Commission of the “Iuliu Hațieganu” University of Medicine and Pharmacy Cluj-Napoca were met. All conditions for reducing the suffering of experimental animals and the principles of biodiversity were ensured by observing the provisions of the Government Ordinance no. 37 on the protection of laboratory animals.

The research was carried out in the Experimental Research Laboratory of the Pathophysiology Department of the “Iuliu Hațieganu” University of Medicine and Pharmacy Cluj-Napoca. During the experiment, the animals were maintained under appropriate vivarium

conditions at a controlled temperature of 21-22 °C, 65% humidity, cycle light:dark 12:12 h, standardized feed and water ad libitum.

b) Groups

The measurements were performed in 6 groups of rats (n = 6 animals/group) that were subjected to physical exercise through the swimming test:

- group I - controls + exercise 1 day
- group II - controls + supplement + exercise 1 day
- group III - rats + exercise 7 days
- group IV - rats + daily supplement + exercise 7 days
- group V - rats + exercise 14 days
- group VI - rats + daily supplement + exercise 14 days.

The supplement was represented by 100% natural *Lycium barbarum* fruit juice, imported and distributed by SC Goji Planet SRL. The daily dose of Goji juice of 0.3 ml/animal/day was given by oropharyngeal gavage for 1 day, 1 or 2 weeks.

c) Tests applied

Oxidative stress was induced by physical exercise for 14 days using the swimming test according to the standardized model in the literature (Nayanatara et al., 2005). The aerobic exercise capacity (AEC) was determined by measuring the time, expressed in seconds, from the moment the animals were introduced into the pool until their exhaustion (refusal to swim). The intensity of exercise was changed by loading the animals in groups III-VI with lead weights accounting for 15% of the animal's weight.

The duration of the experiment was 14 days. The studied days were day 1 (T1), day 7 (T2) and day 14 (T3).

Biochemical determinations were performed in the Laboratory of the Pathophysiology Department of “Iuliu Hațieganu” University of Medicine and Pharmacy Cluj-Napoca. For the measurement of the indicators of the O/AO balance in the blood, venous blood samples were taken from the retro-orbital sinus, under general anesthesia with 2:1 10% ketamine and 2% xylazine. From the harvested blood, the serum was separated by centrifugation, in order to measure the indicators. Readings were made on the METERTEK SP-830 spectrophotometer. Animals were sacrificed under general anesthesia by cervical dislocation at the end of the experiment.

The serum indicators determined were total oxidant status (TOS), total antioxidant capacity (TAC), malondialdehyde (MDA) and total thiols. MDA was determined by using the microanalytical method of Pasha and Sadasivadu (Mitev et al., 2010). For the determination of the total oxidant status (TOS) a spectrophotometric method was used (Ozcan, 2005). Determination of thiols was performed by the Ellman method (Mitev et al., 2010) and total antioxidant capacity (TAC) was determined by using the Fenton reaction (Ozcan, 2004).

d) Statistical processing

Descriptive statistics elements were calculated. Data were presented using centrality, location and distribution indicators.

Normal distribution was tested with the Shapiro-Wilk test. ANOVA, Kruskal-Wallis, t (Student), Mann-Whitney (U) and Wilcoxon tests were used for statistical data

processing. The significance threshold was $\alpha = 0.05$, $\alpha = 0.01$ or $\alpha = 0.001$. For the correlation analysis, the Pearson (r) and Spearman (ρ) correlation coefficients were used, and their interpretation was made according to Colton's empirical rules.

Statistical processing was performed using the StatsDirect v.2.7.2 software and the Excel application (Microsoft Office 2010). The results were graphically represented using the Excel application (Microsoft Office 2010).

Results

a) The O/AO balance in the serum

The statistical analysis of total antioxidant capacity (TAC) showed very statistically significant differences between at least two groups ($p < 0.01$) considering all groups, and highly statistically significant differences between at least two groups ($p < 0.001$) considering the three groups with *Lycium barbarum* supplementation.

The statistical analysis of TAC values for unpaired samples evidenced:

- highly statistically significant differences between groups II-VI, V-VI ($p < 0.001$)
- very statistically significant differences between groups IV-V ($p < 0.01$)
- statistically significant differences between groups I-VI, II-IV ($p < 0.05$).

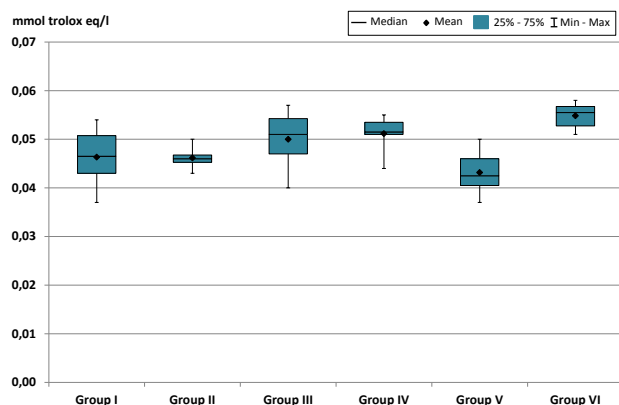


Fig. 1 – Serum TAC in the studied groups.

The statistical analysis of total oxidant status (TOS) showed statistically significant differences between at least two groups ($p < 0.05$) considering all groups, but no statistically significant differences between the groups ($p > 0.05$) considering the three groups with *Lycium barbarum* supplementation or the three groups without *Lycium barbarum* supplementation.

The statistical analysis of TOS values for unpaired samples evidenced:

- very statistically significant differences between groups I-VI ($p < 0.01$)
- statistically significant differences between groups V-VI ($p < 0.05$).

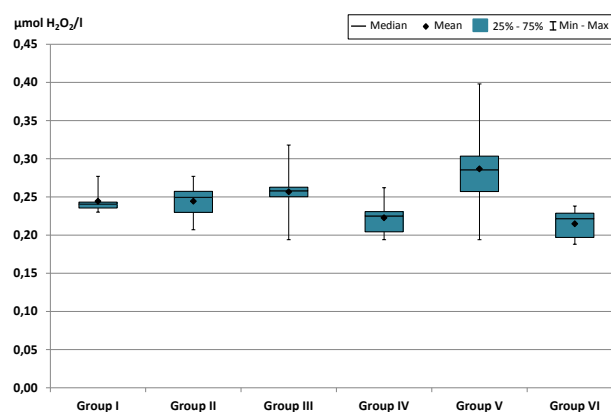


Fig. 2 – Serum TOS in the studied groups

The statistical analysis of thiol values showed no statistically significant differences between the groups ($p > 0.05$) when all the groups, the three groups with *Lycium barbarum* supplementation or the three groups without *Lycium barbarum* supplementation were considered. Contrary to expectations, the statistical analysis of thiol values for unpaired samples evidenced statistically significant differences between groups I-V and V-VI ($p < 0.05$).

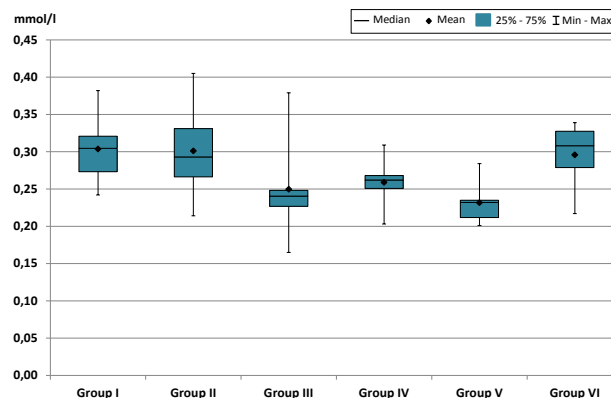


Fig. 3 – Serum thiols in the studied groups

The statistical analysis of MDA values showed statistically significant differences between at least two groups ($p < 0.05$) considering all groups, and statistically significant differences between at least two groups ($p < 0.05$) considering the three groups with *Lycium barbarum* supplementation.

The statistical analysis of MDA values for unpaired samples evidenced:

- highly statistically significant differences between groups II-VI, V-VI ($p < 0.001$)
- very statistically significant differences between groups I-VI ($p < 0.01$)
- statistically significant differences between groups I-V, III-VI ($p < 0.05$).

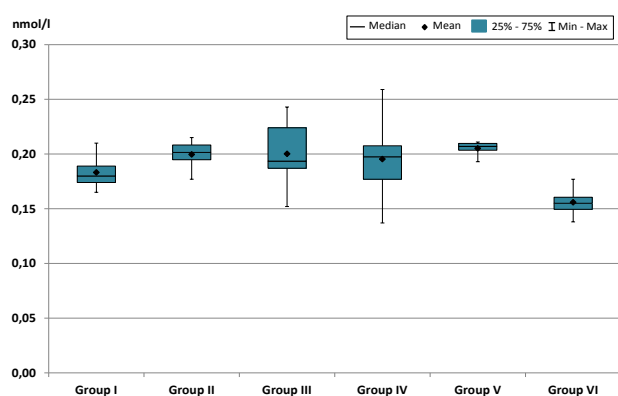


Fig. 4 – Serum MDA in the studied groups

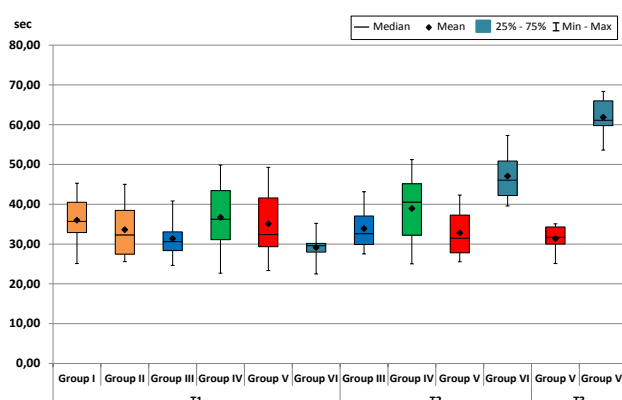


Fig. 5 – Aerobic exercise capacity in the studied groups

b) *Aerobic exercise capacity (AEC)*

The statistical analysis of AEC values at time T1 showed no statistically significant differences between the groups ($p > 0.05$) when all the groups, the three groups with *Lycium barbarum* supplementation or the three groups without *Lycium barbarum* supplementation were considered. The statistical analysis for unpaired samples at time T1 showed no statistically significant differences between the groups ($p > 0.05$).

The statistical analysis of AEC values at time T2 showed statistically significant differences between at least two groups ($p < 0.05$) considering all groups. The statistical analysis for unpaired samples at time T2 evidenced very statistically significant differences between groups III-VI, V-VI ($p < 0.01$).

The statistical analysis for unpaired samples of aerobic exercise capacity values at time T3 showed highly statistically significant differences between groups V-VI ($p < 0.001$).

The statistical analysis of AEC values, considering all three time points, evidenced highly statistically significant differences between at least two of the studied time points in group VI ($p < 0.001$), but no statistically significant differences were found between any of the three time points in group V ($p > 0.05$).

The statistical analysis for paired samples of aerobic exercise capacity values showed:

- in group III - very statistically significant differences between times T1-T2 ($p < 0.01$)
- in group VI - highly statistically significant differences between times T1-T2, T1-T3 and T2-T3 ($p < 0.001$).

c) *Correlations between the values of O/AO balance indicators*

For the groups without *Lycium barbarum* supplementation (I, III, V), the statistical analysis of correlation between the values of the studied indicators showed:

- in group I – very good positive correlations between thiols-MDA, very good negative correlations between TAC-TOS, and acceptable positive correlations between TAC-thiols, TOS-MDA
- in group III – very good positive correlations between TAC-MDA, very good negative correlations between TAC-thiols, good negative correlations between TOS-thiols, thiols-MDA, and acceptable positive correlations between TAC-TOS, TOS-MDA
- in group V – very good positive correlations between TAC, thiols, TAC-MDA, good negative correlations between TAC-TOS, TOS-thiols, acceptable negative correlations between TOS-MDA, and acceptable positive correlations between thiols-MDA.

For the groups with *Lycium barbarum* supplementation (II, IV, VI), the statistical analysis of correlation between the values of the studied indicators showed:

- in group II – good positive correlations between TAC-thiols, TAC-MDA, good negative correlations between TOS-MDA, and acceptable negative correlations between TAC-TOS
- in group IV – very good negative correlations between TOS-MDA and acceptable positive correlations between TOS-thiols
- in group VI – good positive correlations between TOS-MDA, good negative correlations between TAC-TOS, TOS-thiols, thiols-MDA, and acceptable negative correlations between TAC-thiols.

Table I

Statistical analysis of correlation between the values of the serum indicators of the O/AO balance.

Indicators	Group I	Group III	Group V	Group II	Group IV	Group VI
TOS	-0.9429 ****	0.3198 **	-0.6821 ***	-0.4838 **	-0.1804 *	-0.5618 ***
TAC - Thiols	0.3144 **	-0.8322 ****	0.6270 ***	0.7106 ***	0.2066 *	-0.3362 **
MDA	0.0315 *	0.8044 ****	0.5564 ***	0.6288 ***	0.0783 *	0.1352 *
TOS - Thiols	-0.1429 *	-0.5693 ***	-0.5557 ***	0.0128 *	0.4140 **	-0.5786 ***
MDA	0.3143 **	0.4131 **	-0.3219 **	-0.6237 ***	-0.8989 ****	0.5114 ***
Thiols - MDA	0.8690 ****	-0.5453 ***	0.2896 **	0.0139 *	-0.1504 *	-0.5966 ***

Correlations: **** very good, *** good, ** acceptable, * weak

d) Correlations between the values of the aerobic exercise capacity and those of the O/AO balance indicators

For the groups without *Lycium barbarum* supplementation (I, III, V), the statistical analysis of correlation between the values of the aerobic exercise capacity and the O/AO balance indicators showed:

- in group I – acceptable positive correlations with TOS
- in group III – acceptable positive correlations with TOS and acceptable negative correlations with thiols
- in group V – very good positive correlations with TAC and MDA, good positive correlations with thiols, and good negative correlations with TOS.

For the groups with *Lycium barbarum* supplementation (II, IV, VI), the statistical analysis of correlation between the values of the aerobic exercise capacity and the O/AO balance indicators showed:

- in group II – very good positive correlations with thiols, acceptable positive correlations with TAC, and acceptable negative correlations with MDA
- in group IV – very good positive correlations with MDA, good negative correlations with TOS, and acceptable positive correlations with thiols
- in group VI – acceptable negative correlations with MDA.

Discussions

Supplements with an antioxidant role have been promoted by manufacturers as means of improving the body's resistance to oxidative stress, of preventing and repairing oxidative lesions caused by excessive physical strain. Due to the fact that *L. barbarum* (Goji) is considered a remarkable antioxidant (Zhang, 2013), it has become an active substance with antioxidant role frequently incorporated in food supplements. A 30-day study on humans who consumed Goji juice demonstrated its increased antioxidant effect and suggested beneficial effects on the body in case of long-term consumption (Amagase et al., 2009).

Our results have shown that the administration of *Lycium barbarum* improves the total antioxidant capacity (TAC) after a period of physical exercise. Antioxidant effects were significantly improved under physical exercise conditions after antioxidant administration, both at half-time and at 14 days.

Significant differences were also observed in the total oxidant status (TOS). In animals that received Goji juice, TOS decreased after 14 days of exercise compared to the control group. Increased oxidative stress was evident in animals that performed physical exercise compared to those that received *Lycium barbarum* juice for 14 days and

performed physical exercise under the same conditions as the first ones. Thus, *Lycium barbarum* had a beneficial effect on combating oxidative stress produced under exercise.

Thiols decreased significantly during the study period in animals that performed only physical exercise, the values being lower both at half-time and at the end of the study period compared to exercise-trained animals that received Goji supplements. Determination of serum thiols also highlighted the beneficial antioxidant effect of *Lycium barbarum* administered for 14 days during physical exercise, the values being significantly increased in comparison to those of animals subjected to the same conditions, without Goji supplementation.

An experimental study on rats looked at the oxidative stress caused by excessive exercise, by increasing MDA levels and serum creatine kinase activity and lowering glycogen levels and SOD and GPx activity. Lipid peroxidation causes increased membrane permeability, resulting in loss of cytosolic proteins. The administration of *L. barbarum* with a high content of polysaccharides improved muscle antioxidant activity (Niu et al., 2008).

Our data showed that MDA values after administration of *Lycium barbarum* natural juice and after 14 days of training were significantly lower compared to day 1 (regardless of whether or not Goji juice was administered), as well as to days 7 and 14 in the absence of Goji juice. Our results are in agreement with other studies, showing that high levels of MDA, which is one of the final degradation products in lipid peroxidation and is an important indicator of oxidative stress in cells and tissues, are associated with severe oxidative stress and increased lipid peroxidation, respectively (You et al., 2011).

In the literature, the effectiveness of *L. barbarum* was demonstrated in free radical uptake, in the inhibition of lipid peroxidation (Gao et al., 2010; Cheng & Kong, 2011; Yi et al., 2013), in the improvement of muscle fatigue and mitochondrial dysfunction. The protective effect of Goji was also revealed by the limitation of the increase of lipid peroxidation and the decrease of SOD and GSH-Px enzymes at muscle level (Kerr, 2010).

Pharmacological investigations on the antioxidant effect of *L. barbarum* mainly attributed this capacity to *L. barbarum* polysaccharides (LBP) (Li et al., 2007a; Li & Zhou, 2007), but also to other components such as flavonoids or carotenoids (Le et al., 2007; Jiang, 2014). The mechanism of action of both classes of compounds includes metal reducing and chelating capabilities, as well as the ability to clean free radicals (Li & Zhou, 2007).

A study conducted on mice trained for swimming

Table II

Statistical analysis of correlation between the values of the serum indicators of the O/AO balance and the aerobic exercise capacity in the studied groups.

Indicators	Group I	Group III	Group V	Group II	Group IV	Group VI
TAC	-0.1612 *	-0.0605 *	0.9410 ****	0.3541 **	-0.1300 *	0.1723 *
TOS	0.3714 **	0.4630 **	-0.5676 ***	-0.1547 *	-0.6336 ***	-0.2344 *
Thiols	0.2129 *	-0.2728 **	0.5217 ***	0.7618 ****	0.2737 **	0.0137 *
MDA	-0.0542 *	0.2227 *	0.7758 ****	-0.3736 **	0.8579 ****	-0.3553 **

Correlations: **** very good, *** good, ** acceptable, * weak

revealed the beneficial effect of *Lycium barbarum* polysaccharide content on muscle fatigue, by lowering lactate concentration and increasing glycogen concentration (Yao & Li, 2010).

Our data on exercise capacity showed that this increased significantly on day 7 in animals that swam and received Goji compared to those that were only subjected to physical exercise by swimming. The same situation was maintained at the end of the study period. Exercise capacity decreased in animals that swam for 14 days without Goji supplementation, but the differences were not significant between the three studied time moments. In animals that swam for 14 days and received Goji supplements, the exercise capacity increased, the differences being significant between the studied times.

Finally, the results of the correlation analysis between the studied O/AO balance indicators suggest that Goji administration improves the ability to combat oxidative stress under exercise. Also, the correlation of the O/AO balance with the aerobic exercise capacity demonstrated that in the Goji supplemented group, with the increase of the exercise capacity, the values of oxidative stress indicators decreased at the end of the experimental study.

Conclusions

1. The increase in the total antioxidant capacity (TAC) confirmed the antioxidant potential of *Lycium barbarum* under physical exercise conditions.

2. The increase in serum thiol levels after supplementation with *Lycium barbarum* natural juice demonstrates the increase in the antioxidant capacity of the body under physical exercise conditions.

3. Supplementation with *Lycium barbarum* natural juice led to the reduction of oxidative stress and, implicitly, of lipid peroxidation, evidenced by the decrease of serum malondialdehyde values.

4. Administration of *Lycium barbarum* natural juice made a positive contribution to increasing exercise capacity.

5. Due to its energetic and antioxidant effect under physical exercise conditions, *Lycium barbarum* could be a natural, non-doping alternative for improving sports performance and post-exercise recovery.

Conflicts of interest

Nothing to declare.

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