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Research Article

Chronic L-Carnitine Supplementation on Exercise Performance, Blood Lactate, and Exercise-Induced Oxidative Stress in Resistance-Trained Males

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Abstract

Background: The purpose of the present study is to investigate the effect of Chronic L-Carnitine Supplementation on Exercise Performance, Blood Lactate, and Exercise-Induced Oxidative Stress in Resistance-Trained Males

Materials and Methods: We examined 35 resistance-trained (1y) male participants (25±2y, 79.8±8.9 kg, 16.1±5.53% body fat) for 9-wk of L-carnitine supplementation in conjunction with resistance training on exercise performance, blood lactate, and exercise-induced oxidative stress. Randomized, placebo-controlled, double-blind treatment of a (1) no intervention, no supplement Control (CON, n=12), (2) maltodextrose Placebo (PLA, 2 g/d, n=11) or (3) L-carnitine (LCR, 2 g/d, n=12). Exercise performance, post-exercise blood lactate (BL) and oxidative stress markers were analyzed at weeks 3, 6, and 9. The PLA and LCR groups followed a specific resistance training program (4 d/w, upper body/lower body split) for a 9-wk. Data were analyzed by GLM and presented as mean (SD) or change (95% CI). Primary outcomes were total lifting volume for the bench (BP) and leg press (LP).

Results: The results a significant increase in BP lifting volume at wk-6 (139 kg, 95% CI 49.1, 230) and wk-9 (238 kg, 95% CI 132, 343) for LCR. Similar results were observed for LP. We also observed a significant increase in Wingate mean power (63.4 W, 95% CI 30.5, 96.3) and peak power (239 W/kg, 95% CI 104, 374) at wk-9 for LCR as well as a significant reduction in post-exercise BL levels and oxidative stress responses. No differences were observed in body composition.

Conclusion: These findings indicate that LCR supplementation improves exercise performance and attenuates the blood lactate and oxidative stress response to resistance training.

Keywords:
Antioxidant, L-Carnitine, lactate, oxidative stress, resistance training

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1. Introduction

L-carnitine (β-hydroxy-c trimethyl amino butyrate) (LCR) is an endogenous compound synthesized in mammals from essential amino acids lysine and methionine with well-established functions in intermediary metabolism (1). Skeletal muscles are known as the primary source of carnitine in the body and possess at least 50 to 200 times higher carnitine concentrations than in blood plasma, where the average concentrations are between 41 (females) and 50 (males) μM/L (1). Carnitine has two major metabolic roles in the skeletal muscle. First, it serves as a substrate for the enzyme carnitine palmitoyl transferase 1. Second, during intense exercise, the synthesis of acetyl carnitine is necessary for the preservation of a feasible pool of free co-enzyme A (CoA), by that means enabling pyruvate dehydrogenase complex (PDC) and tricarboxylic acid cycle to continue (2).

The enhancement of PDC flux during strenuous exercise would be expected to reduce lactic acid formation which could be considered to have a positive impact on exercise performance by lowering muscle acidosis (3). It is generally accepted that the accumulation of hydrogen ions caused by dissociation of lactic acid is a major limiting factor during high intensity exercise. LCR has shown to decrease lactic acid production and the resulting accumulation of hydrogen ions during and after high-intensity exercise (4, 5) and plays an important role in the transportation of long chain fatty acids across the mitochondrial membrane and the buffering of acetyl-CoA (6). It is believed that this buffering mechanism, which decreases the acetyl-CoA/CoA ratio, may also reduce lactic acid production by maintaining the catalytic activity of the PDC. This allows for increased pyruvate oxidation (7).

As a potential anti-inflammatory compound, chronic LCR supplementation has been shown to significantly reduce the levels of inflammation markers such as C-reactive protein, interleukin-6 (IL-6), and tumor necrosis factor-α (TNF- α) (8). In addition, it has been found that the levels of inflammation markers are negatively correlated with the levels of LCR and antioxidant enzymes activities (8). An immune function is temporarily depressed by a single bout of exercise as well as highly associated with an increased incidence of infection in the weeks following strenuous exercise (9). Similarly, plasma levels of cytokines such as interleukin-1β (IL-1β), TNF-α, and IL-6 are increased during and following intense prolonged exercise (10). In particular, resistance exercise/training disrupts the balance between free radical production and the body antioxidant defense system resulting in a condition named an exercise-induced immune dysfunction (11). Gleeson et al. (12) reported that both acute aerobic exercise and chronic resistance training resulted in a decreased monocyte cell-surface expression of Toll-like receptors, a characteristics of the detection and recognition of microbial pathogens.

As a potent antioxidant, LCR is suggested to have protective effects on damaged tissues caused by exercise and diseases. Lee et al. (8) revealed that LCR supplementation reduced the levels of inflammation markers such as CRP, IL-6, and TNF- α from baseline in coronary artery disease patients. In young soccer players, 3 g of acute LCR supplementation increased an antioxidant glutathione and nitrate-nitrite levels after exhaustive exercise (13).

Synergistic LCR supplementations with dietary choline and carnitine for a 21-d period has shown to lower lipid peroxidation and promote conservation of retinol and α-tocopherol in healthy women before and after mild exercise (14). Furthermore, 2 g/d of L-carnitine L-tartrate (LCLT) supplementation for 3-wk attenuated exercise-induced plasma markers of purine catabolism and circulating cytosolic proteins (15). Interestingly, magnetic resonance image scans in this study indicated that muscle disruption was only 41-45% of the placebo area. In another study regarding LCLT, results supported that the LCLT supplementation helped mediate quicker recovery for hypoxic exercise (16). Broad et al. (17) found that 2 g/day of LCLT supplementation for 2-wk suppressed the plasma ammonia response, an indicator of the metabolic stress, to exercise in non-vegetarian active men. Additionally, it was found that LCLT supplementation reduced muscle oxygenation responses to resistance training as well as attenuated plasma malondialdehyde (MDA), a marker of membrane damage (18). The purpose of this study was to investigate the chronic (9-wk) effect of dietary LCR supplementation on exercise performance, BL levels, and exercise-induced oxidative stress in resistance-trained athletes. The primary outcome for the study is total lifting volume for the bench and leg press. Secondary outcomes include Wingate testing indices associated with anaerobic exercise performance and post-exercise BL and oxidative response. We hypothesize that 9-wk of LCR supplementation will improve indices of exercise performance accompanied by reductions in post exercise metabolic responses to exercise.

PARTICIPANTS

Figure1 presents a CONSORT diagram of enrolment to the study. Thirty-five male

2. Materials and Methods

participants (age = 25 ± 2 y; stature = 171 ± 6 cm; body mass = 79.8 ± 8.9 kg; percent body fat = 16.1 ± 5.53%; CON n = 12, PLA n = 11, LCR n = 12) volunteered from Tarbiat Modares University and local surrounding community to participate in this 9-wk study. Inclusion criteria stipulated that all participants to be in good health; age between 18-40; body fat percentage of 10-25% inclusive; and to have at least one-year immediate prior history of regular resistance training including bench press and leg press/squat to be randomized to either PLA or LCR group. To be included in the CON group, participants had to be physically active but not being involved in any type of regular exercise training. Volunteers were excluded from the study if they were current smokers or nutritional supplement users; if they had any metabolic disorders; history of pulmonary disease; hypertension; hypotension; liver or kidney disease; musculoskeletal or neuromuscular disease; neurological disease; autoimmune disease; any cancers; and orthopedic problems that might affect their ability to perform resistance training. Physical activity levels were determined using standardized questionnaires adapted from Stanford usual activity questionnaire, Baecke physical activity questionnaire, Kent State University, and Eastern Michigan University, at baseline and weeks 3, 6, and 9. All participants completed a drug and nutritional-supplement use questionnaire to determine eligibility. In the familiarization session, testing procedures and potential risks and benefits associated with the study were verbally explained in detail. Participants were then provided a written informed consent prior to participation in accordance with the guidelines established by the Institutional Review Board at Tarbiat Modares University.

EXPERIMENTAL DESIGN

The current report represents a study examining chronic supplementation of LCR. This study involved a randomized, placebo-controlled, double-blind design. The study was conducted in exercise physiology laboratory at Tarbiat Modares University. Participants were matched into either PLA or LCR group based on body mass, age, and strength training experience. During familiarization session and following informed consent, a research nutritionist and a professional strength and conditioning specialist met with each participant and explained in detail the strength training regimen as well as nutritional and supplement requirements for the study period.

TESTING SESSIONS

Figure 2 shows the timeline of tests performed. The study included testing at baseline and weeks 3, 6, and 9, at which blood samples were obtained and body composition, exercise performance tests, and a series of BL tests were performed. Participants were instructed to refrain from exercise for 48 hrs and be fasted for at least 12 hrs prior to each testing session.

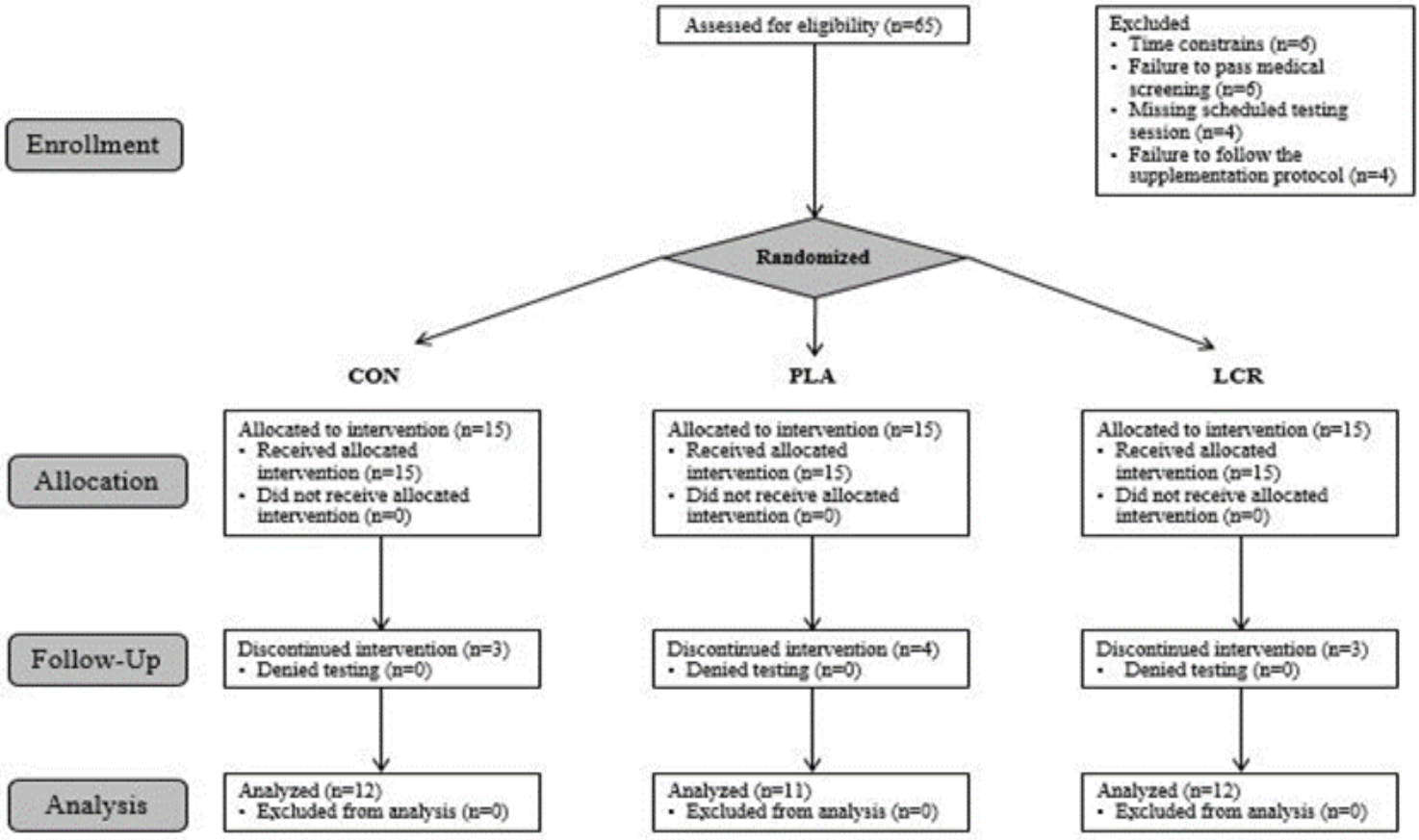

Figure 1. Figure 1. CONSORT Diagram.

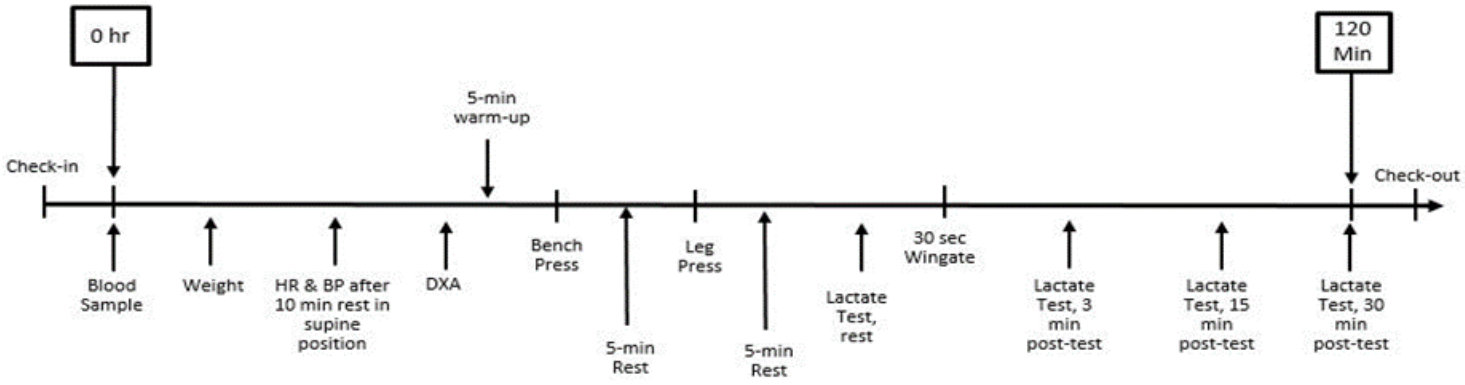

Figure 1. Study Timeline.

STRENGTH ASSESSMENT

In the familiarization session, we assessed the upper and lower body muscular strength using an isotonic bench press and leg press (Pullum Power Sports, Luton, United Kingdom) to determine their one repetition maximum (1RM). The maximal upper and lower body strength was determined following a standard warm-up including 10 repetitions using 50% of participants' estimated 1RM, 5 repetitions using 70% of their estimated 1RM, and 1 repetition using 90% of their estimated 1RM. Participants continued adding weight until their 1RM's were determined. Verbal encouragement was provided during the test to ensure maximal effort. In testing sessions, participants initially performed a general warm-up of ~5 min of light activity involving all muscles to be tested. Next, using 1RM that was determined at the familiarization session, participants performed three sets of bench and leg press test. For the first and second sets, participants performed 10 repetitions at 70% of 1RM on the bench press and leg press interspersed by 2 min of rest between sets and 5 min recovery between each exercise testing modality. During the third set, participants were asked to complete as many repetitions as possible. Total lifting volume was calculated by multiplying the amount of weight lifted times the number of successful repetitions completed.

Test-retest reliability of performing upper and lower body strength assessments on participants in our laboratory on resistance-trained participants show low day-to-day mean coefficients of variation and high reliability for the bench press (5.2%, intraclass, r = 0.98) and leg press (7.4%, intraclass, r = 0.97).

ANAEROBIC CAPACITY ASSESSMENT

Participants performed a Wingate anaerobic capacity test on a computerized Lode Sport Cycle Ergometer (Lode BV, Groningen, The Netherlands) equipped with toe clips at a standardized torque factor 0.7. The torque factor setting was set based on the manufacturer's guidelines relative to the population being tested. The seat position, seat height, handlebar position, and handlebar height were determined during familiarization sessions and repeated for all testing sessions. Participants were instructed to begin sprinting 10 sec prior to application of the workload and continue at an all-out maximal capacity for 30-sec Wingate test. Test-retest reliability of performing Wingate anaerobic capacity test on participants in our laboratory has yielded low day-to-day mean coefficients of variation and high reliability for absolute peak power (9.3%, intraclass, r = 0.95) and mean power (7.6%, intraclass, r = 0.94).

BODY COMPOSITION

Total body mass (kg) was assessed using a standard Siltec® digital scale. Body composition was determined by Dual Energy X-ray Absorptiometry (DXA) (Lunar Prodigy; General Electric, Waukesha, WI). Quality control calibration and scanning procedures were conducted as previously described (19). All participants were scanned in the morning in a fasted state. Test/retest reliability studies performed on male athletes with DXA yielded mean deviation for total bone mineral content and total fat-free/soft tissue mass of 0.31-0.45%, with a mean intra-class correlation of 0.985 (20).

BLOOD LACTATE

BL levels were analyzed from finger prick capillary blood samples (Analox GM7 Lactate Analyzer, Analox, Hammersmith, UK). The analyzer device was calibrated using standard control solution before each testing session. Lactate values were determined at rest and post-exercise at minutes three, fifteen, and thirty. Test to test reliability of conducting BL tests in our laboratory on resistance-trained males indicate low day-to-day mean CV and high reliability (5.2%, intraclass, r = 0.89).

RESTING HEART RATE & BLOOD PRESSURE

Resting heart rate (HR), was measured after 10 min rest in the supine position using standard procedures (21). Then, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were determined using auscultation of the brachial artery and a mercurial sphygmomanometer, based on standard clinical procedures (21).

BLOOD COLLECTION

Participants donated approximately 10 ml of venous blood after being fated for 12 hrs at the beginning of each testing session. Samples were collected from the antecubital vein in two 7.5 ml collection tubes utilizing a standard vacutainer apparatus. Blood samples stood at room temperature for 15 min and then centrifuged at 3500 rpm for 10 min. The serum supernatant was removed and stored at -80 ^{0}C in polypropylene microcentrifuge tubes for later analysis.

SERUM CLINICAL CHEMISTRY ANALYSES

Laboratory measures were conducted at baseline, and weeks 3, 6, and 9. The tests included total antioxidant capacity (TAC), MDA, glutathione peroxidase (GPx), superoxide dismutase (SOD), catalase (CAT), IL-6, and TNF-α. All blood samples were analyzed in biochemistry laboratory located at Tarbiat Modares University. Day-to-day variability in oxidative stress markers in our lab yielded a CV range of 0.06-0.23, and an intraclass correlation coefficient range of 0.67-0.90.

SUPLEMENTATION PROTOCOL AND DIETARY MONITORING

Using a randomization code in a double-blind, placebo-controlled manner, participants in both LCR and PLA groups were assigned to oral ingestion of either a 2 g/day^{-1} of LCR *(Sina Nutrition, Inc., Tehran, Iran)* or PLA (maltodextrine) for a 9-wk period. Both LCR and PLA supplements were in the form of identical-looking ingestible capsules. Participants were instructed to consume one capsule with breakfast and one capsule with lunch (1g per serving). The use of this dose has shown to be safe and efficacious in previous studies (5, 16, 22). Supplementation began ~30 min after baseline testing session and continued throughout the 9-wk period. In the current study, CON group did not receive the supplement intervention. Compliance to supplementation protocol was monitored by the research dietician who contacted participants on a weekly basis by phone. Participants were asked to bring all empty containers to the testing sessions at weeks 3, 6, and 9, which allowed study personnel to assess compliance with the protocol.

Participants were instructed to maintain their current nutritional regimen throughout the course of the study. In addition, they were given specific instructions on how to record portion sizes and quantities during familiarization session. Participants completed a 3-day food records (two weekdays and one weekend day) a week before all testing sessions. Then, all diet records were analyzed to verify that eating and drinking habits remained consistent throughout the study. Diet records were analyzed for total kilocalories, carbohydrate, protein, and fat using the NutraBase IV Clinical Edition (CyberSoft, Inc., Phoenix, AZ).

RESISTANCE TRAINING PROTOCO

Participants in both PLA and LCR groups completed a modified frequently used 4 day/week resistance training program previously described in detail (23). In the present study, CON group did not receive the training intervention. Briefly, the training program was performed four sessions per week. This protocol involved training the upper and lower body twice per week using a 4-day split (i.e., upper body1, lower body1, upper body2, lower body2) with gradual increases in volume and intensity. The training program was composed of 15 exercises, including bench press, lat pulldown, shoulder press, seated row, dips, pullover, biceps curl, triceps press down, leg press, leg extension, leg curl, back extension, half squat, standing calf raise, and stiff leg deadlift. For each exercise, participants performed 3-6 sets of 8-15 repetitions with as much weight as they could tolerate with proper form (70-85% of the 1RM). As participants' strength and endurance improved, training severity was increased to keep the required repetition range. Rest periods between exercises were 1-3 min, and between sets were 60-120 seconds. Training was performed at three different training facilities, recorded in training logs, and signed off by selected fitness instructors to verify compliance. All three sport clubs used identical training equipment. Furthermore, at each testing session, participants were required to complete a physical activity questionnaire, which described their physical activity during the previous month.

BIOCHEMICAL ANALYSES

TAC was measured as previously described by Erel et al. (24). In this method, the most potent radical, hydroxyl radical, is produced. First, a ferrous ion solution is mixed with hydrogen peroxide (H_2O_2). Next, the antioxidative impact of the sample against the potent free radical reactions was measured. TAC was reported in mmol/L. MDA was measured following the method described by Vassalle et al. (25). In this method, MDA was measured by a colorimetric assay according to the reaction among one MDA molecule and two N-methyl-2-phenylindole molecules at 45°C to produce a stable chromophore compound. Then, turbid samples were centrifuged at 15000 g for 10 min to gain a supernatant with highest absorbance at 586 nm. MDA was expressed in µmol/L. GPx activity was measured by the method described by Bulucu et al. (26). The reaction mixture was 50 mmol/L tris buffer, pH 7.6 containing 1 mmol/L of Na_2EDTA, 2 mmol/L of reduced glutathione, 0.2 mmol/L of NADPH, 4 mmol/L of sodium azide and 1000 U of glutathione reductase. 50 mL of plasma and 950 mL of reaction mixture, or 20 mL of erythrocyte lysate and 980 mL of reaction mixture were mixed and incubated for 5 min at 37°C. Next, the reaction was commenced with 8.8 mmol/L H_2O_2 and the decrease in NADPH absorbance was followed at 340 nm for 3 min. GPx activity was expressed in U/ml. SOD activity was measured as the inhibition of the rate of reduction of cytochrome c by the superoxide radical, observed at 550 nm as previously described by Berzosa et al. (27). SOD was reported in µmol/mL. The CAT activity was measured in hemolysates as described by Aebi et al. (28).

The reaction mixture was 50 mM phosphate buffer pH 7.0, 10 mM H2O2 and erythrocyte lysate. The reduction rate of H2O2 was followed at 240 nm for 30 sec at room temperature. CAT activity was reported in nmol/mL. Serum TNF-α and IL-6 levels were measured by enzyme-linked immunosorbent assay (ELISA) technique as previously described by Arican et al. (29). TNF-α and IL-6 activities were reported in pg/mL.

STATISTICAL ANALYSIS

Data were analyzed using multivariate or univariate general linear models (GLM) examining for between group differences as well as changes from baseline in body composition, HR and BP, exercise performance, and blood markers. Data were considered statistically significant when the probability of error was 0.05. Least significance differences (LSD) post-hoc analyzes were used to compare between group differences when significant group differences were observed. Data are presented as mean ± SD or mean change ± 95% CI as appropriate.

3. Results

PARTICIPANT DEMOGRAPHICS

The demographic characteristics of the three groups are presented in Table 1. Forty-five participants initiated the study; however, seven participants withdrew from the study due to personal reasons and three were excluded due to low compliance (<80%) to the supplement. Therefore, a total of 35 participants completed the study. All participants were male and the age range was 21-28 years. The mean values for age,

Table 1. Baseline characteristics of study participants.

	Group	Mean	p-value
Age (yr)	CON	24.6 ± 2.3	0.33
	PLA	24.5 ± 1.5	
	LCR	25.5 ± 1.5	
Height (cm)	CON	171.5 ± 6.9	0.99
	PLA	171.3 ± 6.7	
	LCR	171.3 ± 3.1	
Weight (kg)	CON	77.1 ± 9.9	0.10
	PLA	77.9 ± 6.8	
	LCR	84.1 ± 8.7	
Body mass index	CON	26.2 ± 3.1	0.16
	PLA	26.6 ± 3.4	
	LCR	28.7 ± 3.4	
Body fat (%)	CON	14.2 ± 4.4	0.24
	PLA	16.1 ± 5.7	
	LCR	18.0 ± 6.0	
Resting HR (b/min)	CON	61.2 ± 6.8	0.31
	PLA	57.0 ± 5.5	
	LCR	60.5 ± 7.8	
Resting SBP (mmHg)	CON	114.8 ± 5.1	0.74
	PLA	116.1 ± 5.9	
	LCR	114.5 ± 5.3	
Resting DBP (mmHg)	CON	74.5 ± 6.3	0.30
	PLA	77.2 ± 3.9	
	LCR	74.0 ± 5.3	

Values are means ± standard deviations. Data were analyzed by one-way ANOVA.

DIETARY ANALYSIS, SUPPLEMENT & TRAINING COMPLIANCE, AND REPORTED SIDE EFFECTS

The food logs were used to measure the average daily caloric and macronutrient intake (Table 2). No significant difference was observed among groups for total calories, protein, fat, and carbohydrate ($p > 0.05$).

All participants in LCR and PLA groups seemed to have exhibited 100% compliance with the supplement and training protocol. Furthermore, subjective assessment of the physical activity evaluations indicated that none of the participants had any prominent changes in their level of physical activity over the course of 9-wk. Participants in LCR group completed the required dosing regimen and testing procedures with no adverse effects for 2 g/day-1 of LCR supplementation ($p > 0.05$).

BODY COMPOSITION

Table 2 presents the results of body composition observed during the study. MANOVA analysis revealed no significant differences among groups in body composition (Wilks' Lambda group $p = 0.43$, time $p = 0.83$, and group x time $p = 0.63$). Univariate analysis did not indicate that LCR supplementation changed body weight ($p = 0.38$), fat mass ($p = 0.70$), fat-free mass ($p = 0.38$), and body fat percentage ($p = 0.50$) compared to PLA and CON groups.

Table 2. Dietary and anthropometric characteristics of study participants.

	Group	Time (wks)					
		Week 0	Week 3	Week 6	Week 9		
		Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD		p-level
Diet Characteristics							
Energy Intake (kcals/day)	CON	2449 ± 685	2474 ± 437	2405 ± 516	2289 ± 412	G x T	0.64
	PLA	2116 ± 718	2147 ± 723	2250 ± 546	2000 ± 311		
	LCR	2449 ± 529	2414 ± 490	2457 ± 549	2444 ± 439		
Protein (g)	CON	169.4 ± 94.2	168.7 ± 78.1	173.5 ± 77.7	169.0 ± 71.5	G x T	0.40
	PLA	162.7 ± 101.5	172.3 ± 110.5	178.9 ± 103.0	147.8 ± 57.4		
	LCR	142.9 ± 38.5	150.3 ± 39.1	157.1 ± 38.2	178.4 ± 73.2		
Fat (g)	CON	88.3 ± 34.9	88.0 ± 26.1	85.2 ± 29.8	86.3 ± 21.7	G x T	0.95
	PLA	74.4 ± 36.7	72.2 ± 35.3	73.5 ± 33.1	74.2 ± 26.0		
	LCR	93.4 ± 32.1	98.8 ± 28.3	96.2 ± 22.8	95.0 ± 25.7		
Carbohydrate (g)	CON	244.2 ± 107.8	251.8 ± 78.1	236.0 ± 74.7	209.0 ± 99.8	G x T	0.61
	PLA	198.9 ± 68.1	202.0 ± 50.3	218.2 ± 70.2	185.1 ± 32.1		
	LCR	258.5 ± 106.0	231.2 ± 81.2	240.7 ± 91.0	218.9 ± 61.0		
Anthropometry							
Body Weight (kg)	CON	77.1 ± 10.0	77.2 ± 10.4	77.6 ± 10.5	77.2 ± 10.4	G x T	0.38
	PLA	77.9 ± 7.09	78.1 ± 7.12	77.6 ± 7.26	78.1 ± 7.36		
	LCR	84.3 ± 8.98	84.54 ± 8.78	84.7 ± 8.38	84.5 ± 8.94		
Fat Mass (kg)	CON	10.5 ± 3.41	10.67 ± 3.19	11.0 ± 3.44	11.1 ± 3.22	G x T	0.70
	PLA	12.1 ± 5.05	12.2 ± 5.29	12.0 ± 5.34	12.2 ± 5.14		
	LCR	14.8 ± 5.26	15.1 ± 4.94	15.1 ± 4.81	15.2 ± 4.66		
Fat-Free Mass (kg)	CON	53.9 ± 4.93	54.0 ± 5.0	54.1 ± 2.56	54.0 ± 5.00	G x T	0.38
	PLA	54.1 ± 2.70	54.2 ± 2.70	54.0 ± 2.67	54.2 ± 2.63		
	LCR	56.2 ± 2.78	56.3 ± 2.67	56.4 ± 2.56	56.3 ± 2.70		
Body Fat (%)	CON	13.8 ± 4.25	13.8 ± 3.85	14.3 ± 4.02	14.4 ± 3.94	G x T	0.50
	PLA	15.4 ± 5.47	15.3 ± 5.71	15.2 ± 5.79	15.4 ± 5.57		
	LCR	17.4 ± 5.51	17.9 ± 5.33	17.7 ± 5.00	17.9 ± 4.89		

Values are means ± standard deviations. Dietary intake data were analyzed by MANOVA with repeated measures. Greenhouse-Geisser group (G), time (T), and group x time (G x T) interaction p-levels are reported with univariate treatment p-levels. MANOVA analysis revealed overall Wilks' Lambda group ($p = 0.43$), time ($p = 0.83$), and group x time ($p = 0.63$).

RESTING HEART RATE AND BLOOD PRESSURE

Manova analysis did not show significant differences among groups in hemodynamic responses during the study (Wilks' Lambda group p = 0.98, time p = 0.33, and group x time p = 0.62). Univariate analysis did not reveal that LCR supplementation changed resting HR (p = 0.61), SBP (p = 0.62), and DBP (p = 0.45) compared to PLA and CON groups. All group means remained within 4 beats/min for HR, 2 mmHg for SBP, and 4 mmHg for DBP.

PERFORMANCE ASSESSMENT

MUSCULAR STRENGTH

Bench press. Results for all exercise performance variables are presented in Table 3. MANOVA analysis did not reveal significant interaction effect among groups in bench press performance (p > 0.05). However, MANOVA analysis using baseline values as a covariate and evaluation of mean change and 95% CI's of 1RM upper body strength data indicated that there was a significant increase in bench press performance. The number of reps significantly increased at week 6 only in LCR (2.00 n, 95% CI, 0.59, 3.40), but not in PLA (0.90 n, 95% CI, -0.56, 2.37) or CON (0.75 n, 95% CI, -0.65, 2.15). For week 9, bench press reps assessment was: LCR (3.41 n, 95% CI, 2.19, 4.63), PLA (1.45 n, 95% CI, 0.18, 2.72), and CON (1.25 n, 95% CI, 0.02, 2.47). The significant change in bench press 3rd set lifting volume at week 6 was observed only for LCR (146 kg, 95% CI 38.1, 255), but not in PLA (65.2 kg, 95% CI -48.0, 178), or CON (52.7 kg, 95% CI -55.8, 161). For week 9, bench press 3rd set lifting volume was: LCR (245 kg, 95% CI 147, 343), PLA (117 kg, 95% CI 14.6, 219), and CON (94.8 kg, 95% CI -3.25, 192). There was a significant improvement in total lifting volume (TLV) at week 6 only in LCR (139 kg, 95% CI 49.1, 230), but not in PLA (32.4 kg, 95% CI -62.0, 126), or CON (78.2 kg, 95% CI -12.2, 168). For week 9, bench press TLV was: LCR (238 kg, 95% CI, 132, 343), PLA (84.3 kg, 95% CI, -26.0, 194), and CON (120 kg, 95% CI, 14.7, 226).

The percent change from baseline in bench press reps was higher in LCR (27.5%) compared to PLA (16.4%) and CON (10.9%). The percent change from baseline in bench press 3rd set lifting volume was higher in LCR (27.5%) compared to PLA (16.4%) and CON (10.9%). Lastly, LCR exhibited a higher percent change from baseline in TLV in LCR (10.0%) compared to PLA (3.52%) and CON (5.21%).

Leg press. The measures of leg press reps increased in LCR compared to PLA and CON (p = 0.01). The leg press 3rd set lifting volume increased in LCR compared to CON (p = 0.03). In addition, the leg press TLV was higher in LCR compared to CON (p = 0.03). The analysis of mean changes with 95% CI's demonstrated significant differences in lower body performance among groups. The change in leg press reps from baseline to week 6 was: LCR (5.00 n, 95% CI, 2.19, 7.80), PLA (1.63 n, 95% CI, -1.29, 4.56), and CON (2.33 n, 95% CI, -0.47, 5.13). The change in leg press reps at week 9 was: LCR (8.58 n, 95% CI, 5.30, 11.8), PLA (1.09 n, 95% CI, -2.33, 4.51), and CON (0.83 n, 95% CI, -2.44, 4.11). Comparisons at week 6 demonstrated a significant increase in leg press 3rd lifting volume for LCR (1,483 kg, 95% CI, 543, 2,422) but not in PLA (756 kg, 95% CI, -224, 1,737) or CON (902 kg, 95% CI, -37.4, 1,841). There was a significant mean change from baseline to week 9 in LCR (2,683 kg, 95% CI, 1,568, 3,797), but not in PLA (331 kg, 95% CI, -832, 1,495) or CON (354 kg, 95% CI, -760, 1,468). There was a significant improvement in TLV at week 6 only in LCR (1,483 kg, 95% CI, 543, 2,422) but not in PLA (756 kg, 95% CI, -224, 1,737) or CON (902 kg, 95% CI, -37.4, 1,841). There was a significant mean change from baseline in TLV at week 9 in LCR (2,683 kg, 95% CI, 1,568, 3,797), but not in PLA (331 kg, 95% CI, -832, 1,495) or CON (354 kg, 95% CI, -760, 1,468). The percent change from baseline in leg press reps was higher in LCR (38.1%) compared to PLA (4.68%) and CON (8.94%). The percent change from baseline

Table 3. Exercise performance characteristics of study participants

	Group	Time (wks)					
		Week 0	Week 3	Week 6	Week 9		
		Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD		p-level
Bench Press Repetitions (n)	CON	13.8 ± 4.8	13.5 ± 4.8	14.5 ± 4.6	15.0 ± 4.5	G x T	0.11
	PLA	12.0 ± 3.3	12.3 ± 2.9	12.9 ± 3.4	13.4 ± 3.2		
	LCR	14.1 ± 4.0	14.2 ± 4.2	16.1 ± 3.8	17.5 ± 4.1		
Bench Press 3rd Set Lifting Volume (kg)	CON	997 ± 431	971 ± 419	1,050 ± 405	1,092 ± 431	G x T	0.22
	PLA	1,042 ± 374	1,075 ± 335	1,107 ± 321	1,159 ± 333		
	LCR	1,005 ± 315	1,012 ± 311	1,152 ± 296	1,250 ± 306		
Bench Press Total Lifting Volume (kg)	CON	2,394 ± 579	2,484 ± 505	2,473 ± 578	2,515 ± 619	G x T	0.16
	PLA	2,805 ± 578	2,591 ± 703	2,837 ± 526	2,889 ± 554		
	LCR	2,449 ± 430	2,447 ± 432	2,588 ± 436	2,687 ± 441		
Leg Press Repetitions (n)	CON	22.0 ± 9.77	22.4 ± 9.81	24.3 ± 10.0	22.8 ± 8.6[c]	G x T	0.009
	PLA	22.7 ± 8.32	24.4 ± 9.16	24.3 ± 7.7	23.8 ± 9.0[c]		
	LCR	26.0 ± 6.92	28.4 ± 8.79	31.0 ± 7.4	34.6 ± 7.59[a, b]		
Leg Press 3rd Set Lifting Volume (kg)	CON	7,905 ± 3,497	8,038 ± 3,484	8,807 ± 3,758	8,259 ± 3,276[c]	G x T	0.02
	PLA	9,032 ± 3,556	9,665 ± 3,784	9,788 ± 4,036	9,364 ± 3,733		
	LCR	8,662 ± 3,553	9,440 ± 4,062	10,145 ± 3,210	10,836 ± 3,835[a]		
Leg Press Total Lifting Volume (kg)	CON	15,224 ± 3,936	15,358 ± 3,876	16,126 ± 4,343	15,578 ± 3,885[c]	G x T	0.02
	PLA	17,105 ± 4,971	17,739 ± 5,135	17,862 ± 5,579	17,437 ± 4,970		
	LCR	15,238 ± 4,857	1,6016 ± 5,302	16,721 ± 4,499	17,922 ± 4,717[a]		
Total Body Strength (kg)	CON	8,809 ± 7,107	8,921 ± 7,109	9,299 ± 7,604	9,046 ± 7,205	G x T	0.03
	PLA	9,955 ± 8,092	1,0165 ± 8,537	10,349 ± 8,606	10,163 ± 8,206		
	LCR	8,843 ± 7,351	9,232 ± 7,846	9,655 ± 7,866	10,304 ± 8,442		
Wingate Mean Power (Watt)	CON	600 ± 103	576 ± 112	585 ± 102	575 ± 115	G x T	0.03
	PLA	545 ± 85	524 ± 76	553 ± 75	540 ± 92[c]		
	LCR	561 ± 127	553 ± 133	586 ± 120	624 ± 120[b]		
Wingate Peak Power (Watt/kg)	CON	1,597 ± 362	1,565 ± 435	1,556 ± 408	1,562 ± 357[c]	G x T	0.04
	PLA	1,639 ± 303	1,580 ± 345	1,633 ± 388	1,595 ± 441		
	LCR	1,712 ± 363	1,751 ± 329	1,755 ± 302	1,952 ± 424[a]		
Wingate Total Work (Joules)	CON	17,059 ± 3,100	16,787 ± 2,636	17,158 ± 2,639	17,554 ± 2,647	G x T	0.55
	PLA	17,683 ± 3,118	17,722 ± 2,143	18,030 ± 2,682	17,697 ± 2,640		
	LCR	17,138 ± 3,061	17,293 ± 2,859	17,555 ± 3,015	17,831 ± 3,001		
Wingate Minimum Power (Watt)	CON	194 ± 102	178 ± 84	183 ± 68	193 ± 81	G x T	0.44
	PLA	224 ± 69	199 ± 52	217 ± 71	235 ± 88		
	LCR	220 ± 81	216 ± 75	206 ± 55	211 ± 39		
Wingate Rate of Fatigue (%)	CON	86.2 ± 8.3	88.1 ± 11.3	83.9 ± 10.3	84.6 ± 13.7	G x T	0.64
	PLA	85.3 ± 11.3	86.2 ± 15.0	82.4 ± 11.3	85.6 ± 7.9		
	LCR	89.6 ± 10.3	88.9 ± 10.3	90.5 ± 9.1	88.7 ± 10.1		

Values are means ± standard deviations. Bench press and leg press performance were analyzed by MANOVA with repeated measures. Greenhouse-Geisser group (G), time (T), and group x time (G x T) interaction p-levels are reported with univariate treatment p-levels. MANOVA analysis revealed overall Wilks' Lambda group ($p = 0.72$), time ($p < 0.0001$), and group x time ($p = 0.03$). [a] denotes a significant difference from CON. [b] denotes a significant difference from PLA. [c] denotes a significant difference from LCR.

in leg press 3rd set lifting volume was higher in LCR (30.2%) compared to PLA (4.68%) and CON (8.94%). Lastly, LCR demonstrated a higher percent change from baseline in TLV in LCR (19.9%) compared to PLA (2.47%) and CON (3.23%).

Total body strength. MANOVA revealed a significant interaction effect among groups in total body strength ($p = 0.03$). Post-hoc analysis demonstrated that total strength was significantly higher in LCR compared to CON. The analysis of mean changes with 95% CI's indicated significant changes in total body strength performance among groups. There was a significant mean change from baseline to week 6 in LCR (811 kg, 95% CI, 313, 1,309), but not in PLA (394 kg, 95% CI, -126, 914) or CON (490 kg, 95% CI, -8.17, 988). In addition, there was a significant improvement in total strength at week 9 only in LCR (1,460 kg, 95% CI, 845, 2,075) but not in PLA (207 kg, 95% CI, -434, 850) or CON (237 kg, 95% CI, -377, 851). The percent change from baseline in total strength performance was higher in LCR (15.0%) compared to PLA (3.00%) and CON (4.22%)

ANAEROBIC POWER

MANOVA revealed significant interaction effects for Wingate mean power ($p = 0.03$) and peak power ($p = 0.04$) among groups. Post-hoc analysis indicated that the mean power was significantly higher in LCR compared to PLA. In addition, peak power was significantly increased in LCR compared to CON group. MANOVA analysis did not reveal significant interaction effect among groups in Wingate total work, minimum power, and rate of fatigue ($p > 0.05$). The analysis of mean changes with 95% CI's indicated significant differences in Wingate anaerobic performance among groups. There was a significant improvement in Wingate mean power at week 9 only in LCR (63.4-Watt, 95% CI, 30.5, 96.3), but not in PLA (-5.24 Watt, 95% CI, -39.6, 29.1), or CON (-24.9 Watt, 95% CI, -57.8, 7.94). The significant change in Wingate peak power at week 9 was observed only in LCR (239 Watt/kg, 95% CI 104, 374), but not in PLA (-43.5 Watt/kg, 95% CI -184, 97.3), or CON (-34.9 Watt/kg, 95% CI -169, 99.9). The percent change from baseline in Wingate mean power was improved only in LCR (12.8%), but not in PLA (-0.95%) or CON (-3.99%). Finally, there was a significant improvement in percent change from baseline in Wingate mean power only in LCR (14.4%), but not in PLA(-2.95%) or CON (-1.66%).

BLOOD LACTATE ASSESSMENT

Table 4 presents pre- and post-exercise BL assessment. MANOVA analysis revealed significant interaction effects for 3-min ($p = 0.04$), 15-min ($p = 0.03$), and 30-min ($p = 0.04$) post-exercise BL levels. Post-hoc analysis demonstrated that BL level at 3-min and 30-min post-exercise was significantly lower in LCR compared to CON. In addition, BL level at 15-min post-exercise was significantly lower in LCR compared to PLA and CON. The analysis of mean changes with 95% CI's demonstrated significant changes in post-exercise BL levels among groups. The significant decrease in 3-min post-exercise BL at week 9 was observed only in LCR (-1.84 mmol/l, 95% CI -2.95, -0.73), but not in PLA (-0.17 mmol/l, 95% CI -1.32, 0.98), or CON (0.61 mmol/l, 95% CI -.05, 1.71). The significant mean change from baseline in 15-min post-exercise BL at week 9 was seen in LCR (-1.60 mmol/l, 95% CI -2.63, -0.57), but not in PLA (0.04 mmol/l, 95% CI -1.03, 1.12), or CON (0.32 mmol/l, 95% CI -.70, 1.35). The mean change in 30-min post-exercise BL from baseline to week 9 was: LCR (-0.64 mmol/l, 95% CI, -1.07, -0.21), PLA (0.50 mmol/l, 95% CI, 0.05, 0.96), and CON (-0.41 mmol/l, 95% CI, -0.84, 0.02).

The percent change from baseline at 3-min post-exercise BL level was: LCR (-17.2%), PLA (-1.46%), and CON (8.11%); at min-15: LCR (-14.8%), PLA (0.89%), and CON (4.27%); and at min-30: LCR (-13.6%), PLA (9.54%), and CON (-5.64%).

OXIDATIVE STRESS ASSESSMENT

Results for all oxidative stress biomarkers are presented in Table 4. MANOVA revealed a significant interaction effect among groups in serum TAC ($p = 0.01$), MDA ($p = 0.02$), and GPx ($p = 0.03$). Post-hoc analysis exhibited that TAC was significantly higher and MDA was significantly lower in LCR compared to PLA and CON. In addition, GPx was significantly higher in LCR compared to PLA. We did not observe any significant difference at serum SOD, CAT, IL-6, and TNF-α levels among groups. The analysis of mean changes with 95% CI's demonstrated significant differences in oxidative stress biomarkers among groups. There was a significant increase in serum TAC at week 9 in LCR (0.18 mmol/L, 95% CI, 0.07, 0.28), but not in PLA (-0.02 mmol/L, 95% CI, -0.12, 0.08), or CON (-0.03 mmol/L, 95% CI, -0.13, 0.06). A significant increase was observed in serum GPx at week 9 in LCR (1.75 U/ml, 95% CI, 0.61, 2.90), but not in PLA (-0.54 U/ml, 95% CI, -1.73, 0.65), or CON (0.19 U/ml, 95% CI, -0.95, 1.33). There was a significant decrease in serum IL-6 at week 9 in LCR (-0.53 pg/mL, 95% CI, -1.00, -0.06), but not in PLA (0.17 pg/mL, 95% CI, -0.31, 0.66), or CON (-0.13 pg/mL, 95% CI, -0.60, 0.33). The percent change from baseline in serum TAC was increased only in LCR (11.5%), but not in PLA (-0.02%), or CON (-1.94%). There was a significant decrease in percent change from baseline in serum MDA only in LCR (-31.1%), but not in CON (14.5%). A significant increase was seen in serum GPx only in LCR (17.4%), nut not in PLA (-3.26).

4. Discussion

The primary aim of our study was to examine LCR supplementation on anaerobic type exercise performance including of indices of muscle strength and Wingate testing (i.e., 30-sec). The results of our study demonstrated a significant increase in BP and LP lifting volume at wk-6 and wk-9 for the LCR group. We also observed a significant increase in our secondary outcomes, which included an improvement in Wingate mean power and peak power. Thus, we accept our research hypothesis that oral supplementation with LCR at 2 g/d improves anaerobic based exercise performance in young, resistance-trained individuals. We further examined the effects of LCR on the metabolic response to exercise finding a significant attenuation in BL and markers of post-exercise inflammation. Therefore, we accept the hypothesis that LCR supplementation reduces these metabolic responses to exercise. Interestingly, the observed changes in resistance training findings became manifest at 6-wk, while the Wingate and metabolic responses did not become significant at wk-9. Our results add to the known body of literature as LCR has been well studied in endurance athletes, but less is known regarding its effects in those involved in resistance training.

The primary difference between our study and that of Jacobs is that the latter study examined the acute effects of LCR ingestion on repeated, short (10-sec) bouts of anaerobic performance testing, whereas we examined the chronic effects of LCR on longer bouts (30-sec). The reduction in BL in both studies has also been observed in endurance athletes and those undertaking in high intensity exercise (30, 2).

Table 3. Post-exercise blood lactate and oxidative stress characteristics of the study participants

	Group	Time (wks)					
		Week 0	Week 3	Week 6	Week 9		
		Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD		p-level
Blood Lactate							
Pre-exercise (mmol/L^{-1})	CON	2.20 ± 0.52	2.31 ± 0.51	2.34 ± 0.39	2.26 ± 0.45	G x T	0.84
	PLA	2.17 ± 0.35	2.31 ± 0.33	2.22 ± 0.25	2.32 ± 0.43		
	LCR	2.05 ± 0.20	2.12 ± 0.26	2.08 ± 0.25	2.15 ± 0.29		
3-min post exercise (mmol/L^{-1})	CON	10.9 ± 1.75	11.0 ± 1.25	10.6 ± 1.31	11.5 ± 1.75[c]	G x T	0.04
	PLA	10.7 ± 1.19	10.4 ± 1.47	10.2 ± 1.93	10.5 ± 2.04[c]		
	LCR	10.1 ± 0.99	9.8 ± 0.91	9.34 ± 1.46	8.29 ± 0.56[a, c]		
15-min post exercise (mmol/L^{-1})	CON	11.3 ± 1.32	11.3 ± 1.24	10.9 ± 0.92	11.6 ± 1.77[c]	G x T	0.03
	PLA	10.7 ± 1.06	10.5 ± 1.64	10.3 ± 1.25	10.8 ± 1.24		
	LCR	9.87 ± 1.49	9.70 ± 0.89	9.03 ± 0.92	8.27 ± 0.71[a]		
30-min post exercise (mmol/L^{-1})	CON	6.61 ± 1.29	6.13 ± 1.31	6.17 ± 1.09	5.90 ± 1.26[c]	G x T	0.04
	PLA	5.73 ± 1.14	6.69 ± 0.98	5.75 ± 1.14	6.24 ± 1.25		
	LCR	4.60 ± 0.97	4.51 ± 0.96	4.22 ± 1.27	3.96 ± 0.99[a]		
Oxidative Stress							
TAC (mmol/L)	CON	1.40 ± 0.15	1.35 ± 0.11	1.34 ± 0.15	1.37 ± 0.18[c]	G x T	0.01
	PLA	1.45 ± 0.22	1.41 ± 0.16	1.46 ± 0.19	1.43 ± 0.16[c]		
	LCR	1.59 ± 0.13	1.60 ± 0.10	1.66 ± 0.15	1.77 ± 0.14[a,b]		
MDA (µmol/L)	CON	0.58 ± 0.16	0.63 ± 0.16	0.60 ± 0.16	0.63 ± 0.15[c]	G x T	0.02
	PLA	0.64 ± 0.13	0.63 ± 0.18	0.62 ± 0.10	0.46 ± 0.14[a]		
	LCR	0.56 ± 0.15	0.47 ± 0.09	0.48 ± 0.16	0.37 ± 0.18[a,b]		
GPx (U/ml)	CON	11.3 ± 2.42	11.2 ± 2.04	11.4 ± 1.56	11.5 ± 1.85	G x T	0.03
	PLA	11.9 ± 2.15	12.1 ± 2.21	11.9 ± 1.81	11.4 ± 2.05[c]		
	LCR	11.7 ± 2.23	12.1 ± 1.92	12.2 ± 1.50	13.5 ± 1.73[b]		
SOD (µmol/mL)	CON	319 ± 91.8	310 ± 91.6	327 ± 81.9	330 ± 66.9	G x T	0.83
	PLA	317 ± 83.1	317 ± 62.6	314 ± 49.6	320 ± 60.8		
	LCR	319 ± 65.0	331 ± 50.9	332 ± 65.7	315 ± 61.2		
CAT (nmol/mL)	CON	109 ± 13.5	109 ± 12.1	110 ± 13.3	110 ± 12.4	G x T	0.96
	PLA	116 ± 12.6	119 ± 21.6	117 ± 10.9	117 ± 12.3		
	LCR	114 ± 13.4	116 ± 9.5	119 ± 9.0	114 ± 26.9		
IL-6 (pg/mL)	CON	4.27 ± 0.86	4.52 ± 1.19	4.53 ± 0.95	4.13 ± 0.62	G x T	0.28
	PLA	4.73 ± 0.52	4.47 ± 1.21	4.82 ± 0.60	4.90 ± 0.43		
	LCR	4.75 ± 0.93	4.42 ± 1.25	4.37 ± 0.86	4.22 ± 0.63		
TNF-α (pg/mL)	CON	4.76 ± 1.08	4.83 ± 0.85	4.73 ± 0.75	4.83 ± 1.11	G x T	0.43
	PLA	5.55 ± 0.83	5.49 ± 0.81	5.47 ± 1.39	6.03 ± 0.92		
	LCR	4.76 ± 1.02	4.45 ± 0.86	4.55 ± 0.74	4.35 ± 0.87		

Values are means ± standard deviations. Oxidative stress data were analyzed by MANOVA with repeated measures. Greenhouse-Geisser group (G), time (T), and group x time (G x T) interaction p-levels are reported with univariate treatment p-levels. MANOVA analysis revealed overall Wilks' Lambda group ($p < 0.0001$), time ($p = 0.44$), and group x time ($p = 0.12$). [a] denotes a significant difference from CON. [b] denotes a significant difference from PLA. [c] denotes a significant difference from LCR.

An interesting point of difference between the two studies is that Jacobs et al. used 4.5 g of glycine propionyl-L-carnitine, while we used 2 g/d of LCR in the form of L-Carnitine. These observations bring up potential issues regarding dosage amount and LCR chemical form that need further research regarding the efficacy of either. For example, Siliprandi et al. (1990) administered the effects of 2 g of LCR before high intensity exercise and found a decrease plasma lactate following exercise (31).

Not all studies agree with ours regarding high intensity exercise. In an early study performed by Barnett et al., participants supplemented for 14-d with LCR and were subsequently tested for high-intensity cycling performance by riding for 4-min at 90% VO2max, followed 20-min of rest, then five 1-min rides at 115% VO2max, interspersed by 2-min rest (7). Despite a significant increase in plasma free carnitine concentrations during the supplementation protocol, the LCR treatment had no significant effect on muscle carnitine concentration or lactate accumulation during exercise. The attenuation in BL concentrations after severe exercise accompanying chronic LCR supplementation appear to be primarily due to carnitine-mediated enhancement in PDC activation and flux observed at intense exercise. During exercise of this nature, when the use of acetyl group via Krebs cycle is exceeding its production by the PDC reaction, carnitine buffers against acetyl-CoA accumulation by making acetylcarnitine in an enzymatic reaction, thereby ensuring a feasible supply of free CoASH to maintain Krebs cycle flux (32).

L-carnitine transports activated long-chain fatty acids from the cytosol into the mitochondrion and is therefore essential for mitochondrial beta oxidation (33). During beta oxidation, acyl-CoA increase in the mitochondria. Acyl-CoA, is used as an intermediate in lipid metabolism and is involved in lipid biosynthesis and fatty acid transport. Excessive amount of acyl-CoA inhibits several enzymes such as acetyl-CoA carboxylase, pyruvate dehydrogenase complex, and pyruvate carboxylase. Some mechanisms contribute to modulation of acyl-CoA levels. First, high levels of acyl-COA can cause inhibiting various enzymes synthesizing them. Second, further metabolism of acyl-CoA occurs in energy pathways. Third, toxic acyl-CoA can be converted to non-toxic acylcarnitine and transferred to cytoplasm (34, 35). These conditions explain the impact of carnitine in lactic acid metabolism. Lactic acid is continuously synthesized from pyruvate by the enzyme lactate dehydrogenase during rest and exercise. It does not increase in concentration until the rate of lactate production exceeds the rate of lactate removal, which is governed by a number of factors such as monocarboxylate transporters, concentration of lactate dehydrogenase, and oxidative capacity of tissues (36). The findings of our study also demonstrate that chronic LCR supplementation (2 g/day) is effective at increasing TAC and GPx markers and decreasing MDA levels. Since no significant changes were observed in dietary intake during the study period, the changes in these markers can be attributed to antioxidant capacity of LCR supplementation. These findings support our hypotheses in demonstrating that dietary LCR supplementation improves exercise-induced oxidative stress condition. Recent studies have indicated that LCR administration prevents exercise-induced oxidative stress by decreasing lipid peroxidation, scavenging oxygen radicals, and regulating the activities of the enzymes involved in defense against oxidative damage such as GPx, SOD, and CAT (13, 37, 38, 39). Lee et al. (8) indicated that LCR might have antioxidant properties for exercise-induced oxidative stress.

After 3 wk of LCLT supplementation (2 g LCR per day), plasma MDA returned to resting values by 15 min post-exercise during LCLT, whereas MDA remained significantly elevated above pre-exercise throughout 24 h of recovery during PLA. Another study assessed the effect of 2 wk supplementation with LCR (2 g/day) on oxidative stress in active healthy young men. Results indicated that TAC increased and serum MDA decreased in LCR compared to PLA (38). Inflammatory reactions induce the production of reactive oxygen species (ROS) that regulates the expression of proinflammatory cytokines such as IL-1, IL-6 and TNF-α, and then activates nuclear transcription factor-κB (NF-κB) pathway (40, 41). NF-κB, as a transcriptional regulator of DNA, has a crucial role in the expression of more than 200 genes involved in immune and inflammatory responses (42, 43). Some studies identified exercise as a strong stimulus for NF-κB activation in response to both continuous and high-intensity intermittent exercise protocols (44, 45, 46). Studies have shown that supplementation with antioxidants such as LCR, glutathione, and astaxanthin may reduce the formation of ROS, resulting in inhibition of the NF-κB activating cascade (47, 48, 49, 50).

5. Conclusion

A strength of our study is that it was performed over a nine-week period. The benefit to supplementing for this length of time helped to delineate treatment effects, where strength performance improved by wk-6; yet, longer periods of supplementation were necessary to observe an effect for Wingate test determinants anaerobic performance. A limitation of our study is that we did not perform muscle biopsies, which would have provided better information regarding LCR supplementation within muscle tissue. Examining different dosages of LCR or similar compounds could also enhance our study and future research efforts. Our findings are further strengthened by the fact that we recruited participants with one year of training experiencing, thus minimizing any neurological training effects and enhancing the generalizability of our study to individuals engaged in resistance training across various sporting disciplines. Our results indicate that LCR supplementation at the dose of 2 g/day increases muscle strength, improves 30-sec anaerobic performance, decreases post-exercise BL levels, and attenuates exercise-induced oxidative stress markers in resistance-trained athletes, but is not associated with any change in body composition or hemodynamic parameters.

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Compliance with ethical standards

Conflict of interest None

Ethical approval the research was conducted with regard to the ethical principles Tarbiat Modares University.

Informed consent Informed consent was obtained from all participants.

Author contributions

Conceptualization: E.F.; Methodology: E.F.; Software: E.F.; Validation: E.F.; Formal analysis: E.F.; Investigation: E.F.; Resources: E.F.; Data curation: E.F.; Writing - original draft: E.F.; Writing - review & editing: E.F.; Visualization: E.F.; Supervision: E.F.; Project administration: E.F.; Funding acquisition: E.F.

References

1. Karlic H, Lohninger A. Supplementation of L-carnitine in athletes: does it make sense? Nutrition. 2004 Jul-Aug;20(7-8):709-15. doi: 10.1016/j.nut.2004.04.003. PMID: 15212755.

2. Wall BT, Stephens FB, Constantin-Teodosiu D, Marimuthu K, Macdonald IA, Greenhaff PL. Chronic oral ingestion of L-carnitine and carbohydrate increases muscle carnitine content and alters muscle fuel metabolism during exercise in humans. J Physiol. 2011 Feb 15;589(Pt 4):963-73. doi: 10.1113/jphysiol.2010.201343. Epub 2011 Jan 4. PMID: 21224234; PMCID: PMC3060373.

3. Sahlin K. Metabolic factors in fatigue. Sports Med. 1992 Feb;13(2):99-107. doi: 10.2165/00007256-199213020-00005. PMID: 1561513.

4. Jacobs PL, Goldstein ER, Blackburn W, Orem I, Hughes JJ. Glycine propionyl-L-carnitine produces enhanced anaerobic work capacity with reduced lactate accumulation in resistance trained males. J Int Soc Sports Nutr. 2009 Apr 2;6:9. doi: 10.1186/1550-2783-6-9. PMID: 19341458; PMCID: PMC2674410.

5. Mitchell JB, Rogers MM, Basset JT, Hubing KA. Fatigue during high-intensity endurance exercise: the interaction between metabolic factors and thermal stress. J Strength Cond Res. 2014 Jul;28(7):1906-14. doi: 10.1519/JSC.0000000000000319. PMID: 24276293.

6. Sharma S, Black SM. CARNITINE HOMEOSTASIS, MITOCHONDRIAL FUNCTION, AND CARDIOVASCULAR DISEASE. Drug Discov Today Dis Mech. 2009;6(1-4):e31-e39. doi: 10.1016/j.ddmec.2009.02.001. PMID: 20648231; PMCID: PMC2905823.

7. Barnett C, Costill DL, Vukovich MD, Cole KJ, Goodpaster BH, Trappe SW, Fink WJ. Effect of L-carnitine supplementation on muscle and blood carnitine content and lactate accumulation during high-intensity sprint cycling. Int J Sport Nutr. 1994 Sep;4(3):280-8. doi: 10.1123/ijsn.4.3.280. PMID: 7987362.

8. Lee BJ, Lin JS, Lin YC, Lin PT. Antiinflammatory effects of L-carnitine supplementation (1000 mg/d) in coronary artery disease patients. Nutrition. 2015 Mar;31(3):475-9. doi: 10.1016/j.nut.2014.10.001. Epub 2014 Oct 16. PMID: 25701337.

9. Gleeson M. Immune function in sport and exercise. J Appl Physiol (1985). 2007 Aug;103(2):693-9. doi: 10.1152/japplphysiol.00008.2007. Epub 2007 Feb 15. PMID: 17303714.

10. Starkie RL, Rolland J, Angus DJ, Anderson MJ, Febbraio MA. Circulating monocytes are not the source of elevations in plasma IL-6 and TNF-alpha levels after prolonged running. Am J Physiol Cell Physiol. 2001 Apr;280(4):C769-74. doi: 10.1152/ajpcell.2001.280.4.C769. PMID: 11245592.

11. McBride JM, Kraemer WJ, Triplett-McBride T, Sebastianelli W. Effect of resistance exercise on free radical production. Med Sci Sports Exerc. 1998 Jan;30(1):67-72. doi: 10.1097/00005768-199801000-00010. PMID: 9475646.

12. Gleeson M, McFarlin B, Flynn M. Exercise and Toll-like receptors. Exerc Immunol Rev. 2006; 12:34-53. PMID: 17201071.

13. Atalay Guzel N, Erikoglu Orer G, Sezen Bircan F, Coskun Cevher S. Effects of acute L-carnitine supplementation on nitric oxide production and oxidative stress after exhaustive exercise in young soccer players. J Sports Med Phys Fitness. 2015 Jan-Feb;55(1-2):9-15. Epub 2014 Oct 7. PMID: 25289711.

14. Sachan DS, Hongu N, Johnsen M. Decreasing oxidative stress with choline and carnitine in women. J Am Coll Nutr. 2005 Jun;24(3):172-6. doi: 10.1080/07315724.2005.10719462. PMID: 15930482.

15. Volek JS, Kraemer WJ, Rubin MR, Gómez AL, Ratamess NA, Gaynor P. L-Carnitine L-tartrate supplementation favorably affects markers of recovery from exercise stress. Am J Physiol Endocrinol Metab. 2002 Feb;282(2):E474-82. doi: 10.1152/ajpendo.00277.2001. PMID: 11788381.

16. Kraemer WJ, Volek JS, French DN, Rubin MR, Sharman MJ, Gómez AL, Ratamess NA, Newton RU, Jemiolo B, Craig BW, Häkkinen K. The effects of L-carnitine L-tartrate supplementation on hormonal responses to resistance exercise and recovery. J Strength Cond Res. 2003 Aug;17(3):455-62. doi: 10.1519/1533-4287(2003)017<0455: teolls>2.0.co;2. PMID: 12930169.

17. Broad EM, Maughan RJ, Galloway SD. Carbohydrate, protein, and fat metabolism during exercise after oral carnitine supplementation in humans. Int J Sport Nutr Exerc Metab. 2008 Dec;18(6):567-84. doi: 10.1123/ijsnem.18.6.567. PMID: 19164828.

18. Spiering BA, Kraemer WJ, Hatfield DL, Vingren JL, Fragala MS, Ho JY, Thomas GA, Häkkinen K, Volek JS. Effects of L-carnitine L-tartrate supplementation on muscle oxygenation responses to resistance exercise. J Strength Cond Res. 2008 Jul;22(4):1130-5. doi: 10.1519/JSC.0b013e31817d48d9. PMID: 18545197.

19. Cribb PJ, Williams AD, Carey MF, Hayes A. The effect of whey isolate and resistance training on strength, body composition, and plasma glutamine. Int J Sport Nutr Exerc Metab. 2006 Oct;16(5):494-509. doi: 10.1123/ijsnem.16.5.494. PMID: 17240782.

20. Jagim, A.R., Oliver, J.M., Sanchez, A. et al. A buffered form of creatine does not promote greater changes in muscle creatine content, body composition, or training adaptations than creatine monohydrate. J Int Soc Sports Nutr 9, 43 (2012). https://doi.org/10.1186/1550-2783-9-43

21. Ferguson B. ACSM's Guidelines for Exercise Testing and Prescription 9th Ed. 2014. J Can Chiropr Assoc. 2014 Sep;58(3):328. PMCID: PMC4139760.

22. Kraemer WJ, Spiering BA, Volek JS, Ratamess NA, Sharman MJ, Rubin MR, French DN, Silvestre R, Hatfield DL, Van Heest JL, Vingren JL, Judelson DA, Deschenes MR, Maresh CM. Androgenic responses to resistance exercise: effects of feeding and L-carnitine. Med Sci Sports Exerc. 2006 Jul;38(7):1288-96. doi: 10.1249/01.mss.0000227314.85728.35. Erratum in: Med Sci Sports Exerc. 2006 Oct;38(10):1861. PMID: 16826026.

23. Schmitz SM, Hofheins JE, Lemieux R. Nine weeks of supplementation with a multi-nutrient product augments gains in lean mass, strength, and muscular performance in resistance trained men. J Int Soc Sports Nutr. 2010 Dec 16;7:40. doi: 10.1186/1550-2783-7-40. PMID: 21162744; PMCID: PMC3016253.

24. Erel O. A novel automated direct measurement method for total antioxidant capacity using a new generation, more stable ABTS radical cation. Clin Biochem. 2004 Apr;37(4):277-85. doi: 10.1016/j.clinbiochem.2003.11.015. PMID: 15003729.

25. Vassalle C, Lubrano V, L'Abbate A, Clerico A. Determination of nitrite plus nitrate and malondialdehyde in human plasma: analytical performance and the effect of smoking and exercise. Clin Chem Lab Med. 2002 Aug;40(8):802-9. doi: 10.1515/CCLM.2002.139. PMID: 12392309.

26. Bulucu F, Vural A, Aydin A, Sayal A. Oxidative stress status in adults with nephrotic syndrome. Clin Nephrol. 2000 Mar;53(3):169-73. PMID: 10749294.

27. Berzosa C, Cebrián I, Fuentes-Broto L, Gómez-Trullén E, Piedrafita E, Martínez-Ballarín E, López-Pingarrón L, Reiter RJ, García JJ. Acute exercise increases plasma total antioxidant status and antioxidant enzyme activities in untrained men. J Biomed Biotechnol. 2011; 2011:540458. doi: 10.1155/2011/540458. Epub 2011 Mar 9. PMID: 21436993; PMCID: PMC3062968.

28. Aebi H. Catalase in vitro. Methods Enzymol. 1984; 105:121-6. doi: 10.1016/s0076-6879(84)05016-3. PMID: 6727660.

29. Arican O, Aral M, Sasmaz S, Ciragil P. Serum levels of TNF-alpha, IFN-gamma, IL-6, IL-8, IL-12, IL-17, and IL-18 in patients with active psoriasis and correlation with disease severity. Mediators Inflamm. 2005 Oct 24;2005(5):273-9. doi: 10.1155/MI.2005.273. PMID: 16258194; PMCID: PMC1533889.

30. Vecchiet L, Di Lisa F, Pieralisi G, Ripari P, Menabò R, Giamberardino MA, Siliprandi N. Influence of L-carnitine administration on maximal physical exercise. Eur J Appl Physiol Occup Physiol. 1990;61(5-6):486-90. doi: 10.1007/BF00236072. PMID: 2127744.

31. Siliprandi N, Di Lisa F, Pieralisi G, Ripari P, Maccari F, Menabo R, Giamberardino MA, Vecchiet L. Metabolic changes induced by maximal exercise in human subjects following L-carnitine administration. Biochim Biophys Acta. 1990 Apr 23;1034(1):17-21. doi: 10.1016/0304-4165(90)90147-o. PMID: 2328258.

32. Constantin-Teodosiu D, Carlin JI, Cederblad G, Harris RC, Hultman E. Acetyl group accumulation and pyruvate dehydrogenase activity in human muscle during incremental exercise. Acta Physiol Scand. 1991 Dec;143(4):367-72. doi: 10.1111/j.1748-1716. 1991.tb09247. x. PMID: 1815472.

33. Schooneman MG, Vaz FM, Houten SM, Soeters MR. Acylcarnitines: reflecting or inflicting insulin resistance? Diabetes. 2013 Jan;62(1):1-8. doi: 10.2337/db12-0466. PMID: 23258903; PMCID: PMC3526046.

34. Gönen MS, Kısakol G, Güngör K, and Kaya ODA. The Effect of L-Carnitine Treatment on Lactic Acid Levels in Normal Subjects and Patients with IGT. Turkish Journal of Endocrinology and Metabolism 1: 13-16, 2005. https://www.turkjem.org/current-issue/the-effect-of-l-carnitine-treatment-on-lactic-acid-levels-in-normal-subjects-and-patients-with-igt-14706

35. Stumpf DA, Parker WD Jr, Angelini C. Carnitine deficiency, organic acidemias, and Reye's syndrome. Neurology. 1985 Jul;35(7):1041-5. doi: 10.1212/wnl.35.7.1041. PMID: 3892364.

36. Williamson JR, Arrigoni-Martelli E. The roles of glucose-induced metabolic hypoxia and imbalances in carnitine metabolism in mediating diabetes-induced vascular dysfunction. Int J Clin Pharmacol Res. 1992;12(5-6):247-52. PMID: 1301405.

37. Bloomer RJ, Tschume LC, Smith WA. Glycine propionyl-L-carnitine modulates lipid peroxidation and nitric oxide in human subjects. Int J Vitam Nutr Res. 2009 May;79(3):131-41. doi: 10.1024/0300-9831.79.3.131. PMID: 20209464.

38. Lee BJ, Lin JS, Lin YC, Lin PT. Effects of L-carnitine supplementation on oxidative stress and antioxidant enzymes activities in patients with coronary artery disease: a randomized, placebo-controlled trial. Nutr J. 2014 Aug 4;13:79. doi: 10.1186/1475-2891-13-79. PMID: 25092108; PMCID: PMC4125592.

39. Síktar E, Ekinci D, Síktar E, Beydemir S, Gülçin I, Günay M. Protective role of L-carnitine supplementation against exhaustive exercise induced oxidative stress in rats. Eur J Pharmacol. 2011 Oct 15;668(3):407-13. doi: 10.1016/j.ejphar.2011.07.032. Epub 2011 Aug 5. PMID: 21839078.

40. Hakim J. Formes réactives de l'oxygène et inflammation [Reactive oxygen species and inflammation]. C R Seances Soc Biol Fil. 1993;187(3):286-95. French. PMID: 8019908.

41. Morgan MJ, Liu ZG. Crosstalk of reactive oxygen species and NF-κB signaling. Cell Res. 2011 Jan;21(1):103-15. doi: 10.1038/cr.2010.178. Epub 2010 Dec 28. PMID: 21187859; PMCID: PMC3193400.

42. Koc A, Ozkan T, Karabay AZ, Sunguroglu A, Aktan F. Effect of L-carnitine on the synthesis of nitric oxide in RAW 264·7 murine macrophage cell line. Cell Biochem Funct. 2011 Dec;29(8):679-85. doi: 10.1002/cbf.1807. Epub 2011 Oct 19. PMID: 22012571.

43. Setia S, Sanyal SN. Nuclear factor kappa B: a pro-inflammatory, transcription factor-mediated signalling pathway in lung carcinogenesis and its inhibition by nonsteroidal anti-inflammatory drugs. J Environ Pathol Toxicol Oncol. 2012;31(1):27-37. doi: 10.1615/jenvironpatholtoxicoloncol. v31.i1.40. PMID: 22591282.

44. Cuevas MJ, Almar M, García-Glez JC, García-López D, De Paz JA, Alvear-Ordenes I, González-Gallego J. Changes in oxidative stress markers and NF-kappaB activation induced by sprint exercise. Free Radic Res. 2005 Apr;39(4):431-9. doi: 10.1080/10715760500072149. PMID: 16028368.

45. García-López D, Cuevas MJ, Almar M, Lima E, De Paz JA, González-Gallego J. Effects of eccentric exercise on NF-kappaB activation in blood mononuclear cells. Med Sci Sports Exerc. 2007 Apr;39(4):653-64. doi: 10.1249/mss.0b013e31802f04f6. PMID: 17414803.

46. Vider J, Laaksonen DE, Kilk A, Atalay M, Lehtmaa J, Zilmer M, Sen CK. Physical exercise induces activation of NF-kappaB in human peripheral blood lymphocytes. Antioxid Redox Signal. 2001 Dec;3(6):1131-7. doi: 10.1089/152308601317203639. PMID: 11813986.

47. Birben E, Sahiner UM, Sackesen C, Erzurum S, Kalayci O. Oxidative stress and antioxidant defense. World Allergy Organ J. 2012 Jan;5(1):9-19. doi: 10.1097/WOX.0b013e3182439613. Epub 2012 Jan 13. PMID: 23268465; PMCID: PMC3488923.

48. Conner EM, Grisham MB. Inflammation, free radicals, and antioxidants. Nutrition. 1996 Apr;12(4):274-7. doi: 10.1016/s0899-9007(96)00000-8. PMID: 8862535.

49. Farruggia C, Kim MB, Bae M, Lee Y, Pham TX, Yang Y, Han MJ, Park YK, Lee JY. Astaxanthin exerts anti-inflammatory and antioxidant effects in macrophages in NRF2-dependent and independent manners. J Nutr Biochem. 2018 Dec;62:202-209. doi: 10.1016/j.jnutbio.2018.09.005. Epub 2018 Sep 19. PMID: 30308382.

50. Kurutas EB, Cetinkaya A, Bulbuloglu E, Kantarceken B. Effects of antioxidant therapy on leukocyte myeloperoxidase and Cu/Zn-superoxide dismutase and plasma malondialdehyde levels in experimental colitis. Mediators Inflamm. 2005 Dec 14;2005(6):390-4. doi: 10.1155/MI.2005.390. PMID: 16489261; PMCID: PMC1533903.