Cissus Quadrangularis Reduces Joint Pain in Exercise-Trained Men: A Pilot Study

Richard J. Bloomer, PhD[1]
Tyler M. Farney, MS[1]
Cameron G. McCarthy, MS[1]
Sang-Rok Lee, PhD[1]

[1]Cardiorespiratory/Metabolic Laboratory, Department of Health and Sport Sciences, The University of Memphis, Memphis, TN

DOI: 10.3810/psm.2013.09.2021

Abstract

Background: Strenuous, high-volume exercise is often associated with inflammation and joint pain. *Cissus quadrangularis* (CQ) has been reported to have anti-inflammatory activity. The purpose of our study was to determine the therapeutic effects of CQ supplementation in healthy, exercise-trained men with joint-specific pain. **Methods:** Twenty-nine men between the ages of 20 and 46 years, who reportedly experienced chronic joint pain as a result of strenuous exercise, participated in our pilot study. All men received CQ 3200 mg daily for 8 weeks. Before and after the 8-week intervention period, subjects completed a questionnaire to determine their degree of joint pain (Western Ontario and McMaster Universities Index of Osteoarthritis [WOMAC]). Clinical measures (eg, heart rate, blood pressure, blood biomarkers) were also collected for each subject pre- (baseline) and post-intervention. **Results:** Subject ratings for multiple variables within the WOMAC Index improved (decreased) significantly ($P < 0.05$), with the subject mean total WOMAC score decreasing from 25.4 ± 2.4 to 17.4 ± 2.1 (~31%), pre- to post-intervention. No clinical measure was significantly impacted by use of CQ supplementation. **Conclusion:** An 8-week course of supplementation with CQ reduced joint pain in a sample of 29 young, otherwise healthy, exercise-trained men. Additional study is needed to extend these findings, including comparison with a placebo-controlled cohort, and possibly, examining effects of CQ use in women and older adult subjects.

Keywords: dietary supplements; inflammation; joint pain; WOMAC

Introduction

Strenuous, high-volume exercise is often associated with subject inflammation and joint pain.[1,2] This is particularly true for individuals engaged in weight-bearing exercise, such as running, bodybuilding, and powerlifting, for which the volume and/or loading can be very high.[3,4] In an attempt to lessen joint pain associated with chronic physical activity, certain nutritional supplements[5] and isolated ingredients[6–8] have been used with some success. The two isolated ingredients that have received the most attention in recent years are glucosamine and methylsulfonylmethane (MSM).

Both glucosamine[9–11] and MSM[12–14] have been reported to reduce joint pain in patients with osteoarthritis (OA). To our knowledge, neither ingredient has been studied for purposes of reducing joint pain within a sample of individuals who do not have OA. One previous study using healthy horses[15] reported that MSM supplementation reduced exercise-induced elevations in oxidative stress biomarkers; however, no joint pain-related variables were reported. One additional ingredient beginning to receive attention is *Cissus quadrangularis* (CQ), a perennial plant of the grape family, used for years within Ayurvedic medicine.

Correspondence: Richard J. Bloomer, PhD, Cardiorespiratory/Metabolic Laboratory, Department of Health and Sport Sciences, 106 Roane Field House, The University of Memphis, Memphis, TN 38152.
Phone: 901-678-5638
Fax: 901-678-3591
E-mail: rbloomer@memphis.edu

Cissus quadrangularis has been studied in multiple settings and has been reported to have antioxidant,[16,17] anti-obesity,[18] and anti-inflammatory[19–21] activity. The variation in functional activity may be explained by the wide array of active chemicals known to be found within the CQ plant (eg, polyphenols).[22] The anti-inflammatory activity of CQ may be realized through several different mechanisms. Jainu and Devi[23] found that pretreatment with CQ ameliorated elevation of plasma tumor necrosis factor-α (TNF-α) and interleukin-1 β (IL-1β) in rats with aspirin-induced gastric ulcer, suggesting anti-inflammatory properties of CQ. Their work was supported by a more recent study by Panthong et al,[20] who reported that CQ treatment inhibited edema formation of both the ear and paw in rats, by down-regulating arachidonic acid metabolism. Inflammation is one of the primary features of joint disease and a precipitating factor of patient pain in conditions such as OA[24] and rheumatoid arthritis.[25] It is possible that CQ administration to patients may help relieve such inflammatory-induced joint pain, with the same outcome being possible in those without diagnosed arthritis but who experience joint pain as a result of their exercise program. To our knowledge, no study has evaluated the analgesic properties of CQ in a sample of otherwise healthy men who experience chronic joint pain as a result of their engagement in strenuous exercise. The purpose of our study was to determine the effects of daily (8-week) CQ supplementation on healthy, exercise-trained men with joint-specific pain. A secondary purpose was to determine the safety profile of supplemental CQ use.

Table 1. Characteristics of Study Subjects (N = 29)

Variable	Value, mean ± SD
Age (y)	27.8 ± 7.5
Height (cm)	177.7 ± 6.3
Body weight (kg)	82.3 ± 13.6
BMI (kg/m^2)	26.1 ± 3.8
Body fat (%)	15.6 ± 6.6
Waist circumference (cm)	87.3 ± 10.4
Hip circumference (cm)	100.9 ± 8.5
Weekly aerobic training (h)	2.7 ± 1.5
Aerobic training history (y)	5.2 ± 4.6
Weekly anaerobic training (h)	4.0 ± 2.4
Anaerobic training history (y)	5.9 ± 5.9

Abbreviation: BMI, body mass index.

Materials and Methods

Subjects

Twenty-nine healthy, exercise-trained men, between the ages of 20 and 46 years, participated in our pilot study. With the exception of 2 subjects, 1 of whom participated solely in aerobic exercise and 1 of whom participated solely in anaerobic exercise, all men participated in both forms of exercise. Aerobic exercise consisted primarily of jogging and running. Anaerobic exercise consisted primarily of free-weight and machine-resistance exercise. Collectively, the 29 men were considered to be recreationally active fitness enthusiasts. Exercise training history data are presented in Table 1. Subjects were instructed to maintain their same exercise training program throughout the study period.

Subjects were not current smokers and did not have any self-reported cardiovascular or metabolic disorders. To our knowledge, subjects were in good health and capable of regularly performing strenuous exercise. To qualify for inclusion in the study, subjects were required to have, at a minimum, mild joint pain as a result of performing their exercise regimen. Health history, medication and dietary supplement usage, and physical activity questionnaires were completed by all subjects and reviewed in detail by an investigator to determine study eligibility. Prior to participation, each subject was informed of all procedures, potential risks, and benefits associated with the study through both verbal and written forms in accordance with the procedures approved by the University Institutional Review Board for Human Subjects Research (approval document number 051311-701). Subjects provided written informed consent.

Supplementation and Testing

All subjects who were enrolled in the study received CQ (SuperCissus), 3200 mg daily. It should be noted that the intent of the investigators was to conduct the study as a placebo-controlled, double-blind, randomized trial; unfortunately, there was miscommunication with the contract manufacturer and all capsules received by investigators were identical and contained CQ. As this was not determined until after the study began, all subjects received capsules containing CQ, despite being informed that they would have a 50% chance of being assigned to placebo. Because all study subjects received the same dose of the same supplement for the duration of the trial, data for all subjects were pooled and presented as pre- and post-intervention. Capsules were provided to subjects by research assistants, with instructions to ingest the capsules as follows: 2 capsules, twice daily, with meals (total of 4 capsules per day [3200 mg]—each capsule

© The Physician and Sportsmedicine, Volume 41, Issue 3, September 2013, ISSN – 0091-3847

providing 800 mg of CQ). Capsule counts upon bottle return (mid-intervention and post-intervention) allowed for calculation of subject compliance.

On each test day (pre- and post-intervention) subjects reported to the lab in a 10-hour fasted state to have blood drawn (fasting blood levels) and to complete questionnaires. Upon arrival at the lab, subjects rested quietly for 10 minutes and the heart rate (60 second palpation) and blood pressure (standard auscultation procedures using a cuff and stethoscope) were measured. Following this, a blood sample was drawn. Subjects then completed 2 short questionnaires regarding their overall joint health and the degree of joint pain experienced during different activities. Specifically, we used the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC),[26,27] as well as a questionnaire developed to assess exercise-specific joint pain. The latter questionnaire asked subjects to rate their joint pain for both upper and lower body pain, during and following exercise (using a scale ranging from 0 to 4, where 0 represented no pain and 4 represented extreme pain).

Venous blood samples (~15 mL) were collected from subjects both pre (baseline) and post the 8-week treatment intervention. Following collection, blood samples were analyzed for CBC, comprehensive metabolic panel, lipid panel, and C-reactive protein (CRP) level.

Dietary Records and Activity

All subjects (N = 29) were instructed to maintain their normal diet throughout the study period and to record food and beverage intake during the 7 days prior to each test day (pre- and post-intervention). Dietary records were reviewed with each subject for accuracy and then analyzed using Food Processor SQL, version 9.9. Although subjects were asked to maintain their usual exercise training program during the entire study period, they were advised to refrain from strenuous physical activity for the 48 hours prior to each test day.

Table 2. Resting Heart Rate and Blood Pressure of Study Subjects (N = 29)

Variable	Pre-Intervention[a]	Post-Intervention[a]
Heart rate (bpm)	63.0 ± 1.7	61.0 ± 1.6
Systolic blood pressure (mm Hg)	118.8 ± 1.7	120.4 ± 1.8
Diastolic blood pressure (mm Hg)	72.9 ± 1.5	75.1 ± 1.8

[a]Values are mean ± SEM.
Abbreviation: SEM, standard error of the mean.

Statistical Analysis

Data were analyzed using a one-way analysis of variance (ANOVA), with comparisons made between pre- and post-intervention data. The data are presented as mean ± standard error of the mean (SEM), except for subject characteristics, which are presented as mean ± standard deviation (SD). All analyses were performed using JMP statistical software.

Results

Of the 29 subjects who completed the study, none reported any adverse event. Subject characteristics are provided in Table 1. The following protocol deviations were noted: 2 subjects received the supplement for 1 additional week (9 weeks total); 2 subjects received the supplement for 2 additional days; 1 subject received the supplement for 1 day < 8 weeks. Subject compliance with capsule intake was 87 ± 2%.

No significant differences were observed in resting heart rate or blood pressure from pre- to post-intervention (Table 2). Data produced from the WOMAC scores are presented in Table 3. Briefly, the subject total WOMAC score decreased approximately 31% from pre- to post-intervention, whereas overall subject pain and physical scores were reduced approximately 33% from pre- to post-intervention (pain, 5.8 ± 0.6 to 3.9 ± 0.5; $P = 0.01$; physical, 16.2 ± 1.8 to 10.8 ± 1.5; $P = 0.03$). The overall subject stiffness score was reduced approximately 23% from pre- to post-intervention (3.5 ± 0.3 to 2.7 ± 0.3; $P = 0.07$).

Subject exercise-related pain was also reduced with CQ treatment ($P < 0.05$; Table 4). No significant differences were noted for CBC and inflammatory marker data (Table 5), comprehensive metabolic panel data (Table 6), or lipid panel data (Table 7). Dietary data are presented in Table 8, with no significant differences from baseline to end of study noted.

Discussion

Findings from our study indicated that 8 weeks of supplementation with CQ in 29 healthy, exercised-trained men resulted in a decrease in certain components of non-exercise pain (Table 3) and exercise-specific pain (Table 4).Our study is the first study that we are aware of to report a treatment effect for CQ in reducing joint pain in human subjects. Of course, our failure to include a true placebo-control group should be considered a limitation of our study. Indeed, future studies using CQ supplementation should seek to include a control group within the design. The total subject WOMAC score decreased from 25.4 ± 2.4 to 17.4 ± 2.1 (~31%) from pre- to post-intervention. Specifically, a significant treatment effect of CQ

Table 3. WOMAC Data: Non-Exercise Pain Measures (N = 29)

Variable	Pre-Intervention[a]	Post-Intervention[a]	*P* value
Walking	1.0 ± 0.1	0.6 ± 0.1	0.049[b]
Stair climbing	1.4 ± 0.2	1.0 ± 0.1	0.057
Nocturnal	0.8 ± 0.2	0.5 ± 0.2	0.241
Rest	0.7 ± 0.1	0.5 ± 0.1	0.298
Weight bearing	1.8 ± 0.2	1.2 ± 0.1	0.012[b]
PAIN Total	5.8 ± 0.6	3.9 ± 0.5	0.012[b]
Morning stiffness	2.1 ± 0.2	1.7 ± 0.2	0.129
Stiffness later in day	1.4 ± 0.2	1.1 ± 0.2	0.157
STIFFNESS Total	3.5 ± 0.3	2.7 ± 0.3	0.078
Descending stairs	1.2 ± 0.2	0.8 ± 0.2	0.128
Ascending stairs	1.4 ± 0.2	1.0 ± 0.1	0.091
Rising from sitting	1.3 ± 0.2	0.8 ± 0.1	0.039[b]
Standing	0.9 ± 0.2	0.8 ± 0.2	0.896
Bending to floor	1.4 ± 0.2	0.9 ± 0.2	0.053
Walking on flat	0.8 ± 0.2	0.4 ± 0.1	0.090
Getting in/out of car	1.0 ± 0.1	0.6 ± 0.1	0.026[b]
Going shopping	0.8 ± 0.2	0.5 ± 0.1	0.196
Putting on socks	0.6 ± 0.2	0.5 ± 0.1	0.547
Rising from bed	1.1 ± 0.2	0.8 ± 0.2	0.214
Taking off socks	0.6 ± 0.2	0.5 ± 0.2	0.643
Lying in bed	0.4 ± 0.1	0.3 ± 0.1	0.525
Sitting	0.6 ± 0.1	0.4 ± 0.1	0.339
Getting on/off toilet	0.6 ± 0.1	0.3 ± 0.1	0.080
Heavy domestic duties	2.1 ± 0.2	1.2 ± 0.2	0.000[b]
Light domestic duties	0.9 ± 0.2	0.6 ± 0.1	0.167
PHYSICAL Total	16.2 ± 1.8	10.8 ± 1.5	0.030[b]
WOMAC Total	25.4 ± 2.4	17.4 ± 2.1	0.017[b]

[a]Values are mean ± SEM.
[b]Statistically significant change from baseline.
Abbreviations: SEM, standard error of the mean; WOMAC, Western Ontario and McMaster Universities Index of Osteoarthritis.

was seen in reduction of subject joint pain, particularly associated with walking (~40%; $P = 0.049$) and weight bearing (~33%; $P = 0.012$). Also, subject joint pain for stair climbing was decreased (~40%), approaching significance ($P = 0.057$). The overall subject pain score was greatly attenuated (~33%) with 8 weeks of CQ administration. With regard to physical function, we observed subject improvements in various components (such as rising from sitting [~39%], getting in/out of car [~40%], and performing heavy domestic duties [~43%]). The overall subject physical score was improved (~33%) with CQ administration. There was a trend for CQ treatment to ameliorate subject overall stiffness (~23%; $P = 0.078$). Considering the practical nature of the tasks, our findings may have a great deal of relevance. This is particularly true for reductions observed for subject scores in specific exercise-related tasks (Table 4).

Most subjects in our study were cross-trained (participated in both aerobic and anaerobic exercise), and we did not differentiate between the effect of CQ supplementation on subject pain associated with one type of exercise compared with another. Subject exercise-specific data presented in Table 4 are inclusive of pain associated with all forms of exercise and not one form exclusively. Our anecdotal observations support the notion that similar results were observed in subjects engaged in both types of exercise, and findings were not isolated to one exercise mode or another. Additional studies with larger samples may seek to investigate the impact

© The Physician and Sportsmedicine, Volume 41, Issue 3, September 2013, ISSN – 0091-3847

Table 4. Exercise-Specific Pain Data (N = 29)

Variable	Pre-Intervention[a]	Post-Intervention[a]	*P* value
During upper body exercise	1.6 ± 0.2	1.0 ± 0.2	0.019[b]
Following upper body exercise	1.6 ± 0.2	1.1 ± 0.2	0.059
During lower body exercise	2.3 ± 0.1	1.6 ± 0.2	0.002[b]
Following lower body exercise	2.3 ± 0.2	1.5 ± 0.1	0.000[b]
PAIN total	7.8 ± 0.4	5.2 ± 0.5	0.000[b]

[a]Values are mean ± SEM.
[b]Statistically significant change from baseline.
Abbreviation: SEM, standard error of the mean.

of CQ supplementation on subject joint pain specifically associated with aerobic (eg, running) versus anaerobic (eg, weight training) exercise.

The efficacy of CQ supplementation noted in our study specific to joint pain, appears comparable to use of other well-known joint pain supplements (eg, MSM and glucosamine)—at least in terms of WOMAC score outcomes. For example, Kim et al[14] reported a 25.1% reduction in the total WOMAC score in individuals with knee OA following 12 weeks of MSM administration. Mehta et al[28] reported a 60% decrease in total subject WOMAC score following 8 weeks of glucosamine sulfate treatment in humans with mild-to-moderate OA. We note that in both Kim et al's and Mehta et al's studies, subjects had diagnosed OA.

In addition to the WOMAC data, we also evaluated the degree by which CQ intervention modulated subject exercise-related joint pain (Table 4). Overall subject exercise-specific joint pain was alleviated (~33%) with 8 weeks of CQ treatment. More specifically, joint pain of both the upper (~38%) and lower (~30%) body was significantly decreased *during* exercise. Following exercise, subject pain scores were substantially reduced in the lower body (~35%). The benefit was also observed in the upper body (~31%), with an approach toward significance ($P = 0.059$). Such findings may have implications for individuals wanting to continue with regular exercise but perhaps being limited by recurring joint pain. Using a supplement such as CQ might allow for regular participation in the desired activity without the same degree of discomfort. Of course, our findings are specific to younger men. It is unknown whether or not CQ supplementation would have similar effects in older adults or in women with joint pain. As joint pain is not only associated with the performance of structured exercise, nor

Table 5. Blood Measures Data of Study Subjects (N = 29)

Variable	Pre-Intervention[a,b]	Post-Intervention[a,b]
WBC ($10^3/\mu L$)	5.1 ± 0.2	5.1 ± 0.2
RBC ($10^6/\mu L$)	5.0 ± 0.1	5.0 ± 0.0
Hemoglobin (g/dL)	15.0 ± 0.2	15.0 ± 0.1
Hematocrit (%)	44.7 ± 0.4	44.8 ± 0.3
MCV (femtoliters)	90.0 ± 0.7	89.8 ± 0.7
MCH (picograms)	30.0 ± 0.3	30.1 ± 0.3
MCHC (g/dL)	33.4 ± 0.1	33.5 ± 0.1
RDW (%)	13.1 ± 0.1	13.0 ± 0.1
Platelets ($10^3/\mu L$)	237.7 ± 7.9	242.5 ± 7.9
Neutrophils (%)	51.2 ± 1.5	53.5 ± 1.5
Lymphocytes (%)	35.0 ± 1.3	33.0 ± 1.2
Monocytes (%)	9.0 ± 0.3	9.0 ± 0.4
Eosinophils (%)	4.3 ± 0.5	3.9 ± 0.5
Basophils (%)	0.6 ± 0.1	0.6 ± 0.1
CRP (mg/L)	1.0 ± 0.3	0.7 ± 0.1

[a]Values are mean ± SEM.
[b]*P* = NS, for all measures.
Abbreviations: CRP, C-reactive protein; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; NS, not significant; RBC, red blood cell; RDW, red cell distribution width; WBC, white blood cell.

Table 6. Comprehensive Metabolic Panel Data of Study Subjects (N = 29)

Variable	Pre-Intervention[a,b]	Post-Intervention[a,b]
Glucose (mg/dL)	88.4 ± 1.2	91.0 ± 1.3
BUN (mg/dL)	17.3 ± 1.1	17.3 ± 1.1
Creatinine (mg/dL)	1.1 ± 0.0	1.1 ± 0.0
BUN: Creatinine	16.3 ± 1.3	16.8 ± 1.2
Sodium (mmol/L)	140.3 ± 0.4	140.7 ± 0.4
Potassium (mmol/L)	4.5 ± 0.1	4.6 ± 0.1
Chloride (mmol/L)	102.2 ± 0.4	102.4 ± 0.3
CO_2 (mmol/L)	27.4 ± 0.3	26.1 ± 0.5
Calcium (mg/dL)	9.5 ± 0.1	9.6 ± 0.1
Protein, Total (g/dL)	6.8 ± 0.1	6.8 ± 0.1
Albumin (g/dL)	4.5 ± 0.0	4.5 ± 0.0
Globulin, Total (g/dL)	2.3 ± 0.1	2.3 ± 0.1
Albumin:Globulin	2.0 ± 0.0	2.0 ± 0.1
Bilirubin, Total (mg/dL)	0.6 ± 0.1	0.6 ± 0.1
ALP (IU/L)	68.3 ± 4.2	69.7 ± 4.1
AST (SGOT) (IU/L)	27.3 ± 2.4	27.1 ± 2.0
ALT (SGPT) (IU/L)	29.6 ± 3.4	27.9 ± 2.3
GGT (IU/L)	21.8 ± 1.9	21.6 ± 2.4

[a]Values are mean ± SEM.
[b]P = NS for all measures.
Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CO^2, carbon dioxide; GGT, γ-glutamyl transpeptidase; NS, not significant; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamic pyruvate transaminase.

is it limited to younger men, future studies should seek to include both men and women of varying age in order to more fully elucidate the impact of CQ supplementation on relief of joint pain. From a mechanistic perspective, CQ may exert its effects in a number of ways—and though all individuals experiencing joint pain may not have arthritis, using OA as a model to better understand the discreet nature of joint pain may be helpful. The etiology of OA is not fully understood, however, inflammation is considered a key component in the process of idiopathic joint disease. The degenerative cartilage seen in patients with OA is attributable to an imbalanced matrix component characterized by impaired anabolic capacity with progressive catabolic breakdown by inflammatory-specific chemicals.[29,30] For example, inflammatory cytokines (eg, IL-1β and TNF-α) promote the process of cartilage degradation and chondrocyte apoptosis, accelerating the progression of OA.[30,31] The relationship between joint disorders and inflammation is well supported by data from a study by van de Loo et al.[32] They observed that IL-1 injection attenuated chondrocyte proteoglycan (PG) synthesis in the patellar cartilage of arthritic mice. However, the impaired PG anabolism was attenuated by inhibiting IL-1 (α+β) activation, resulting in a substantial decrease in cartilage damage.

We observed a significant decrease in subject joint pain in our study, but the reduction in subject CRP levels (a marker of systemic inflammation) did not reach statistical significance, despite a ~30% decrease in CRP levels. It is possible that a larger sample size would have allowed for statistical significance to be achieved in this marker, as our power would have been increased. Related to this, Oben et al[18] reported that serum CRP levels were significantly decreased in overweight (16.8%) and obese (20.8%) individuals following 8 weeks of CQ intake with no decreases in CRP levels seen in the placebo group. A more recent study[19] also noted an anti-inflammatory effect of CQ supplementation, with subjects showing decreased protein expression in TNF-α, cyclooxygenase (COX)-2, and inducible nitric oxide synthase with CQ extract treatment.[19] When the combined data are considered, it can be speculated that the alleviation of subject joint pain was possibly driven by enhancement of anti-inflammatory capabilities provided with regular and therapeutic CQ administration.

Supplementation with CQ did not result in any statistically significant change in subjects' resting heart rate or blood pressure, or a change in any factor within the CBC, metabolic panel, or lipid panel—suggesting the safety of CQ use, in agreement with prior reports.[18,33] The safety profile of CQ use appears positive, however, additional long-term studies, including a placebo arm, are needed to determine the potential impact of CQ supplementation on measures of clinical safety.

Conclusion

Data from our initial pilot study, using a sample of 29 exercise-trained men, indicated the efficacy of CQ supplementation to alleviate joint pain related and unrelated to exercise. Reduction in subject pain may be associated with a reduction in inflammation, as noted by the 30% decrease in CRP levels (Table 5). Use of CQ appears to be safe and well tolerated, at least based on our initial assessment, which monitored subject heart rate, blood pressure, and common blood-borne factors over the 8-week intervention period. Larger scale studies, possibly including women and older adult subjects, with a

Table 7. Lipid Panel Data of Study Subjects (N = 29)

Variable	Pre-Intervention[a,b]	Post-Intervention[a,b]
Cholesterol (mg/dL)	162.9 ± 5.1	163.1 ± 5.8
Triglycerides (mg/dL)	93.4 ± 9.4	86.7 ± 8.9
HDL-C (mg/dL)	54.2 ± 2.6	56.4 ± 3.1
VLDL-C (mg/dL)	18.6 ± 1.9	17.3 ± 1.8
LDL-C (mg/dL)	90.1 ± 4.5	89.3 ± 5.2
LDL-C/HDL-C	1.8 ± 0.1	1.7 ± 0.2
Total/HDL-C	3.1 ± 0.1	3.1 ± 0.2

[a]Values are mean ± SEM.
[b]*P* = NS for all measures.
Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NS, not significant; VLDL-C, very low-density lipoprotein cholesterol.

Table 8. Dietary Intake of Study Subjects (N = 29)

Variable	Pre-Intervention[a,b]	Post-Intervention[a,b]
Kilocalories	2470.6 ± 133.2	2556.3 ± 148.3
Protein (g)	139.6 ± 13.7	146.2 ± 12.4
Carbohydrate (g)	259.7 ± 12.8	262.4 ± 18.5
Fiber (g)	23.1 ± 2.0	23.0 ± 2.1
Sugar (g)	87.4 ± 7.2	89.1 ± 8.2
Fat (g)	91.2 ± 8.2	98.1 ± 11.4
Saturated Fat (g)	28.9 ± 2.8	30.8 ± 3.6
Vitamin C (mg)	92.4 ± 15.1	72.3 ± 8.8
Vitamin E (mg)	10.9 ± 1.5	10.4 ± 1.8
Vitamin A (RE)	462.3 ± 69.9	536.0 ± 78.6
Selenium (μg)	85.2 ± 10.4	95.1 ± 9.7

[a]Values are mean ± SEM.
[b]P = NS for all values.
Abbreviation: RE, retinol equivalent.

© The Physician and Sportsmedicine, Volume 41, Issue 3, September 2013, ISSN – 0091-3847

placebo-control group—using a double-blind, randomized design—are warranted to extend these initial findings.

Acknowledgments

Funding for this work was provided in part by USPlabs, LLC, and the University of Memphis, Memphis, TN.

Conflict of Interest Statement

Richard J. Bloomer, PhD, has received research funding from or has acted as a consultant to Bergstrom Nutrition and USP Labs. Tyler M. Farney, MS, Cameron G. McCarthy, MS, and Sang-Rok Lee, PhD, declare no conflicts of interest.

References

1. Behrens M, Mau-Moeller A, Bruhn S. Effect of exercise-induced muscle damage on neuromuscular function of the quadriceps muscle. *Int J Sports Med*. 2012;33(8):600-606.
2. Miranda H, Viikari-Juntura E, Martikainen R, Takala EP, Riihimaki H. Physical exercise and musculoskeletal pain among forest industry workers. *Scand J Med Sci Sports*. 2001;11(4):239-246.
3. Kujala UM, Kettunen J, Paananen H, et al. Knee osteoarthritis in former runners, soccer players, weight lifters, and shooters. *Arthritis Rheum*. 1995;38(4):539-546.
4. Saxon L, Finch C, Bass S. Sports participation, sports injuries and osteoarthritis: Implications for prevention. *Sports Med*. 1999;28(2):123-135.
5. Clark KL, Sebastianelli W, Flechsenhar KR, et al. 24-week study on the use of collagen hydrolysate as a dietary supplement in athletes with activity-related joint pain. *Curr Med Res Opin*. 2008;24(5):1485-1496.
6. Dunn-Lewis C, Kraemer WJ, Kupchak BR, et al. A multi-nutrient supplement reduced markers of inflammation and improved physical performance in active individuals of middle to older age: A randomized, double-blind, placebo-controlled study. *Nutr J*. 2011;10:90.
7. Magrans-Courtney T, Wilborn C, Rasmussen C, et al. Effects of diet type and supplementation of glucosamine, chondroitin, and MSM on body composition, functional status, and markers of health in women with knee osteoarthritis initiating a resistance-based exercise and weight loss program. *J Int Soc Sports Nutr*. 2011;8(1):8.
8. Ostojic SM, Arsic M, Prodanovic S, Vukovic J, Zlatanovic M. Glucosamine administration in athletes: Effects on recovery of acute knee injury. *Res Sports Med*. 2007;15(2):113-124.
9. Bruyere O, Pavelka K, Rovati LC, et al. Glucosamine sulfate reduces osteoarthritis progression in postmenopausal women with knee osteoarthritis: Evidence from two 3-year studies. *Menopause*. 2004;11(2):138-143.
10. Gruenwald J, Petzold E, Busch R, Petzold HP, Graubaum HJ. Effect of glucosamine sulfate with or without omega-3 fatty acids in patients with osteoarthritis. *Adv Ther*. 2009;26(9):858-871.
11. Matsuno H, Nakamura H, Katayama K, et al. Effects of an oral administration of glucosamine-chondroitin-quercetin glucoside on the synovial fluid properties in patients with osteoarthritis and rheumatoid arthritis. *Biosci Biotechnol Biochem*. 2009;73(2):288-292.
12. Debbi EM, Agar G, Fichman G, et al. Efficacy of methylsulfonylmethane supplementation on osteoarthritis of the knee: A randomized controlled study. *BMC Complement Altern Med*. 2011;11:50.
13. Ezaki J, Hashimoto M, Hosokawa Y, Ishimi Y. Assessment of safety and efficacy of methylsulfonylmethane on bone and knee joints in osteoarthritis animal model. *J Bone Miner Metab*. 2012.
14. Kim LS, Axelrod LJ, Howard P, Buratovich N, Waters RF. Efficacy of methylsulfonylmethane (MSM) in osteoarthritis pain of the knee: A pilot clinical trial. *Osteoarthritis Cartilage*. 2006;14(3):286-294.
15. Maranon G, Munoz-Escassi B, Manley W, et al. The effect of methyl sulphonyl methane supplementation on biomarkers of oxidative stress in sport horses following jumping exercise. *Acta Vet Scand*. 2008;50:45.
16. Chidambaram J, Carani Venkatraman A. Cissus quadrangularis stem alleviates insulin resistance, oxidative injury and fatty liver disease in rats fed high fat plus fructose diet. *Food Chem Toxicol*. 2010;48(8-9):2021-2029.
17. Sapsrithong T, Kaewprem W, Tongumpai S, Nusuetrong P, Meksuriyen D. Cissus quadrangularis ethanol extract upregulates superoxide dismutase, glutathione peroxidase and endothelial nitric oxide synthase expression in hydrogen peroxide-injured human ECV304 cells. *J Ethnopharmacol*. 2012;143(2):664-672.
18. Oben J, Kuate D, Agbor G, Momo C, Talla X. The use of a Cissus quadrangularis formulation in the management of weight loss and metabolic syndrome. *Lipids Health Dis*. 2006;5:24.
19. Bhujade AM, Talmale S, Kumar N, et al. Evaluation of Cissus quadrangularis extracts as an inhibitor of COX, 5-LOX, and proinflammatory mediators. *J Ethnopharmacol*. 2012;141(3):989-996.
20. Panthong A, Supraditaporn W, Kanjanapothi D, Taesotikul T, Reutrakul V. Analgesic, anti-inflammatory and venotonic effects of Cissus quadrangularis Linn. *J Ethnopharmacol*. 2007;110(2):264-270.
21. Srisook K, Palachot M, Mongkol N, Srisook E, Sarapusit S. Anti-inflammatory effect of ethyl acetate extract from cissus quadrangularis linn may be involved with induction of heme oxygenase-1 and suppression of NF-kappaB activation. J Ethnopharmacol. 2011;133(3):1008-1014.
22. Singh G, Rawat P, Maurya R. Constituents of Cissus quadrangularis. *Nat Prod Res*. 2007;21(6):522-528.
23. Jainu M, Devi CS. Gastroprotective action of cissus quadrangularis extract against NSAID induced gastric ulcer: Role of proinflammatory cytokines and oxidative damage. *Chem Biol Interact*. 2006;161(3):262-270.
24. Goldring MB, Otero M. Inflammation in osteoarthritis. Curr Opin Rheumatol. 2011;23(5):471-478.
25. Bardwell WA, Nicassio PM, Weisman MH, Gevirtz R, Bazzo D. Rheumatoid arthritis severity scale: A brief, physician-completed scale not confounded by patient self-report of psychological functioning. *Rheumatology* (Oxford). 2002;41(1):38-45.
26. Davies GM, Watson DJ, Bellamy N. Comparison of the responsiveness and relative effect size of the Western Ontario and McMaster Universities Osteoarthritis index and the short-form medical outcomes study survey in a randomized, clinical trial of osteoarthritis patients. *Arthritis Care Res*. 1999;12(3):172-179.
27. Salaffi F, Leardini G, Canesi B, et al. Reliability and validity of the western ontario and McMaster universities (WOMAC) osteoarthritis index in Italian patients with osteoarthritis of the knee. *Osteoarthritis Cartilage*. 2003;11(8):551-560.
28. Mehta K, Gala J, Bhasale S, et al. Comparison of glucosamine sulfate and a polyherbal supplement for the relief of osteoarthritis of the knee: A randomized controlled trial [ISRCTN25438351]. *BMC Complement Altern Med*. 2007;7:34.
29. Martel-Pelletier J, Boileau C, Pelletier JP, Roughley PJ. Cartilage in normal and osteoarthritis conditions. *Best Pract Res Clin Rheumatol*. 2008;22(2):351-384.
30. Shen CL, Smith BJ, Lo DF, et al. Dietary polyphenols and mechanisms of osteoarthritis. *J Nutr Biochem*. 2012.
31. Krasnokutsky S, Attur M, Palmer G, Samuels J, Abramson SB. Current concepts in the pathogenesis of osteoarthritis. *Osteoarthritis Cartilage*. 2008;16 Suppl 3:S1-3.
32. van de Loo FA, Joosten LA, van Lent PL, Arntz OJ, van den Berg WB. Role of interleukin-1, tumor necrosis factor alpha, and interleukin-6 in cartilage proteoglycan metabolism and destruction. effect of in situ blocking in murine antigen- and zymosan-induced arthritis. *Arthritis Rheum*. 1995;38(2):164-172.
33. Kothari SC, Shivarudraiah P, Venkataramaiah SB, et al. Safety assessment of Cissus quadrangularis extract (CQR-300): Subchronic toxicity and mutagenicity studies. *Food Chem Toxicol*. 2011;49(12):3343-3357.