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# Effect of Muscadine Grape Seed Supplementation on Vascular Function in Subjects with or at Risk for Cardiovascular Disease: A Randomized Crossover Trial

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## Abstract

**Background—**Muscadine grape seeds have high concentrations of polyphenolic compounds with antioxidant and other properties that would be expected to have favorable effects on endothelial function.

**Objectives—**To evaluate the effect of muscadine grape seed supplementation on endothelial function and cardiovascular risk factors in subjects with increased cardiovascular risk.

**Design—**In a randomized, double-blind, placebo-controlled crossover trial, 50 adults with coronary disease or ≥1 cardiac risk factor received muscadine grape seed supplementation (1300 mg daily) and placebo for 4 weeks each, with a 4-week washout. Resting brachial diameter and brachial flow-mediated dilation (FMD) and biomarkers of inflammation, lipid peroxidation, and antioxidant capacity were determined at the beginning and end of each period and compared in mixed linear models.

**Results—**There was no evidence of improved FMD (% change) with muscadine grape seed (muscadine grape seed: pre 5.2% ± 0.3%, post 4.6% ± 0.3%, $p = 0.06$; placebo: pre 5.3% ± 0.4%, post 5.2% ± 0.4%, $p = 0.82$; $p$ for muscadine grape seed vs. placebo = 0.25). However, there was a significant increase in baseline diameter (mm) with muscadine grape seed supplementation (muscadine grape seed: pre 4.05 ± 0.09, post 4.23 ± 0.10, $p = 0.002$; placebo: pre 4.12 ± 0.11, post 4.12 ± 0.10, $p = 0.93$; $p$ for muscadine grape seed vs. placebo = 0.026). All other biomarkers were not significantly altered by muscadine grape seed supplementation.

**Conclusions—**Four weeks of muscadine grape seed supplementation in subjects with increased cardiovascular risk did not produce a statistically significant increase in brachial flow-mediated vasodilation or a significant change in other biomarkers of inflammation, lipid peroxidation, or antioxidant capacity. However, the muscadine grape seed supplement did result in a significant increase in resting brachial diameter. The clinical significance of the effect on resting diameter is not yet established. More research is warranted to fully characterize the vascular effects of this and other grape-derived nutritional supplements and to determine whether these vascular effects translate into important clinical benefits.

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Disclosure: A member of Dr Herrington's family had a significant financial relationship with Le Bleu Corporation. Nature's Pearl Corporation and Le Bleu have the same president and majority shareholder. Accordingly, the Wake Forest University Conflict of Interest Committee developed a conflict management plan to permit participation by Dr Herrington while minimizing the opportunity for results to be compromised by a real or perceived conflict of interest. No other authors report any conflicts of interest.

**Keywords**

endothelial function; cardiovascular disease; dietary supplements; antioxidants

## INTRODUCTION

Dietary flavonoids are a diverse array of polyphenolic phytochemicals present in significant amounts in grapes and other fruits and vegetables. There is an expanding body of evidence that dietary flavonoids in general, and grape-derived flavonoids in particular, have effects on a variety of vascular phenomena [1,2]. Numerous studies have documented favorable effects of dietary supplementation with purple grape–derived products (wine, juice, extracts) on brachial flow-mediated dilation (FMD) [3-10], a generally accepted metric of endothelial function [11]. These data are supported by extensive *in vitro* and animal data documenting that grape-derived polyphenolic compounds can increase the production [12-17] and bioavailability [18] of NO. Some grape polyphenolics, including resveratrol, appear to protect endothelial cells from oxidative damage and reduce inactivation of NO through modulation of pro-oxidative and antioxidative enzymes including NADPH oxidase, superoxide dismutase, and glutathione peroxidase 1 [19]. Collectively, these data provide several biologically plausible mechanisms in support of the frequently cited reductions in heart disease mortality in populations who consume modest amounts of red wine [20] and have generated additional interest in the potential cardiovascular benefits of other grapederived supplements.

The muscadine grape (*Vitis rotundifolia*) is a grape variety that is well adapted to the warm humid climate of the southeast United States. These grapes contain a distinct composition of polyphenols relative to other grape varieties, which is characterized by high concentrations of gallic acid and abundant flavan-3-ols, flavonols, anthocyanins, and ellagic acid [21-24]. Despite the unique biochemical composition of muscadines, relatively little is known about the potential cardiovascular effects of dietary supplements with muscadine grape seeds or other muscadine-derived food supplements.

The current study was designed to examine the effects of a commercially available muscadine grape seed food supplement (Nature's Pearl) on vascular function and cardiovascular risk factors in subjects with, or at risk for, cardiovascular disease. For the purpose of this study, resting brachial artery diameter and brachial FMD measured using standardized 2-dimensional ultrasound protocols were used as simple noninvasive measures of resting vasomotor tone and endothelial-dependent vasodilator capacity.

## METHODS

### Subjects

The study was designed to examine the effects of the muscadine grape seed supplement in an equal number of men and women with, or at risk for, cardiovascular disease. Among 54 subjects who responded to a general solicitation to participate in the trial, a total of 50 subjects (25 men, 25 women) provided written consent and were enrolled at Wake Forest University Health Sciences. All of the subjects completed the study protocol. The local institutional review board approved the study protocol.

Participants were adult male and nonpregnant female outpatients aged 18–65 years with one or more of the following cardiovascular risk factors: hypertension (blood pressure ≥140/90 mm Hg or current antihypertensive therapy), dyslipidemia (total cholesterol >220 mg/dL + low-density lipoprotein cholesterol >130 mg/dL, or current use of lipid-lowering

medications), or controlled type 2 diabetes mellitus (glycated hemoglobin <8.0% with or without medication). Subjects with a history of coronary artery disease (any history of myocardial infarction or coronary revascularization) were also eligible for participation. Subjects were excluded if they had a history of congestive heart failure (any classification), unstable angina, or acute coronary syndrome within the past 30 days; uncontrolled hypertension (blood pressure ≥170/100 mm Hg); type 1 diabetes mellitus; history of gastrointestinal disease or surgery affecting absorption; peripheral arterial disease; diagnosis of active cancer (excluding non–melanoma cell skin cancer); current use of long-acting nitrates; recent medication change (past 30 days); active plan to change diet or exercise patterns; history of hypersensitivity to any compound in the intervention or placebo; or history of intolerance to nitrates.

## Study Design

The study was a randomized, double-blind, placebo-controlled crossover trial designed to compare the effects of two 650-mg capsules daily of Nature's Pearl muscadine grape seed supplement versus placebo (ClinicalTrials.gov Identifier: NCT01011517). Each muscadine grape seed capsule contained 100% *V. rotundifolia* muscadine grape seed from the Noble variety. After pressing the grape, the seeds were separated from the skin and dried to an approximate 4% moisture content, ground, and encapsulated in a vegetable-based capsule with no fillers or preservatives. The phytochemical profile of the supplement is presented in Table 1. The identically appearing placebo capsules were filled with methylcellulose USP powder. During the 2 treatment periods, the participants were asked to take 2 study capsules each morning, including on the morning of their follow-up clinic visits.

The trial consisted of a screening visit followed 2 weeks later by a sequence of visits at the beginning and end of 2 treatment periods (4 weeks each), separated by a 4-week washout period (total of 5 visits over 14 weeks). During the screening visit, a complete medical history was obtained, a physical examination was performed, and a fasting blood specimen was collected if required to confirm eligibility. On the first and last day of each treatment period, participants returned to the clinic in the fasting state (except for regular medications) for baseline and follow-up measures of blood pressure, FMD (described below), and collection of blood for measures of lipids, inflammatory markers, and markers of antioxidant capacity and oxidative stress. Blood pressure was measured 3 times in the seated position using an automated sphygmomanometer, and the average of the second and third recordings was used for statistical analysis of treatment effects. All measurements were made before 10 AM, <4 hours after the participants took their daily morning dose of study medication. During the entire study period, beginning with the screening visit, participants were asked to abstain from red wine, antioxidant vitamin supplements (including vitamin E, vitamin C, and beta-carotene supplements), >1 cup of black or green tea daily, and other grape seed supplements. Multivitamin supplements were permitted if taken for the study duration.

## Endothelial Function Study Protocol

Details of the brachial FMD protocol, automated analysis, and reproducibility have been published previously [25]. Briefly, subjects rested in a quiet, temperature-controlled room for 15 minutes. A standard (pediatric) cuff was placed on the right forearm 5 cm below the antecubital fossa. The ultrasound transducer was placed longitudinally over the brachial artery 2–4 cm above the anticubital fossa, where continuous scanning of the brachial artery was obtained for 2 minutes before the cuff occlusion, 4 minutes of cuff occlusion, and 2 minutes immediately after cuff release. Data were analyzed with an automated analysis system that determines changes in brachial artery diameter for 2 minutes after cuff release. Artery diameter was defined as the average distance between the medial-adventitial boundaries for the segment of interest. Baseline and maximum diameters were automatically

determined and stored in a database. These diameters were used to calculate the absolute and the percentage change of the brachial artery diameter in response to the flow stimulus. Using an identical protocol, intrareader reproducibility for baseline diameter, maximum diameter, and % FMD have been previously evaluated by comparing an original and a blinded quality control reread of ultrasounds from 40 subjects [26]. The intraclass correlation coefficients were 0.99, 0.99, and 0.93, respectively. Intrasubject variability was evaluated by comparing results from repeated examinations of 19 subjects on 2 days 1 week apart. The intraclass correlation coefficients for baseline diameter, maximum diameter, and % FMD were 0.90, 0.90, and 0.54, respectively.

## Measurement of Markers of Inflammation, Lipid Peroxidation, and Antioxidant Capacity

C-reactive protein (CRP) was measured using an enzyme-linked immunosorbent assay (ELISA; high sensitivity) kit from the American Laboratory Products Company (ALPCO, Windham, NH 03087). The intra-assay coefficient of variability is 6.7% and the interassay coefficient of variation is 8% for a mean 1.37 and 12% for a mean of 2.23 mg/dL. The sensitivity is 0.002 mg/dL. Interleukin-6 was measured using a human UltraSensitive ELISA (Invitrogen, Camarillo, CA). The intraassay coefficient of variability is 6.2% and the interassay coefficient of variation is 6.7% for a mean of 5.2 and 7.3 pg/mL, respectively. The sensitivity is 20 ng/mL.

The plasma concentration of malondialdehyde (MDA) was measured using a colorimetric microplate assay (Oxford Biomedical Research Inc., Oxford, MI). The limit of detection of the MDA assay in a purified system is 0.5 nmol/mL, and the standard error of the measurement (SEM) is less than 5%. 8-isoprostance was measured by EIA (Cayman Chemical Company, Ann Arbor, MI) following a multistage methanol and SepPak extraction process. All samples were corrected for recovery, which averaged 79%. The sensitivity of the assay is 2.7 pg/mL. The intra-assay and interassay coefficients of variation are 7.2% and 15.5% at a concentration 12.8 pg/mL, respectively. There is no cross-reactivity with prostaglandin $F_{1\alpha}$, prostanglandin $E_1$, 6-keto prostanglandin $F_{1\alpha}$, or thromboxane $B_2$. There is 20% cross-reactivity with 8-iso prostaglandin $F_{3\alpha}$. MDA and 8-isoprostane are indicators of lipid peroxidation [27,28].

Total antioxidant power was determined using a competition assay with bathocuproine (BC) in a copper sulphate solution (Oxford Biomedical Research, Inc.). BC forms stable complexes with monovalent, but not divalent, Cu. These complexes have a typical spectrum of absorption with a maximum at 480–490 nm. The reduction of $Cu^{++}$ with liposoluble and water-soluble nonenzymatic antioxidants is quantified by spectrophotometry at 480 nm and standardized using known concentrations of uric acid.

## Statistical Analysis

The effects of supplementation with muscadine grape seed and placebo were compared with mixed linear models using the residual maximum likelihood method to take into account repeated measures and to test for potential treatment order or period effects. The addition of treatment × period or treatment × order interaction terms in the models were used to test for presence of a carryover effect. In exploratory analyses, there were no significant period or order effects or interactions noted. Accordingly, the least-squares means and standard errors from the mix-linear model without order or period terms were used to summarize and compare the pretreatment and posttreatment period measurements within each treatment type (muscadine grape seed or placebo) and to test for an overall treatment effect (muscadine grape seed vs. placebo). Stratified analyses were performed to look for evidence of differential effects by age, gender, prevalent heart disease, or heart disease risk factors. Comparisons of pretreatment versus posttreatment period measurements and tests of the

effect of treatment for CRP were performed on the log scale. Although triglyceride concentration was also nonnormally distributed, exploratory analyses demonstrated that log transformation of triglycerides was not required to conform to the assumptions of the mixed linear model and did not change the qualitative inferences; therefore, the triglycerides were analyzed and are presented in the original scale. Nominal 2-tailed *p* values are presented for the primary outcome (percentage change in brachial diameter) and for all secondary outcomes. All analyses were performed using SAS version 9.1 (Cary, NC).

## RESULTS

The mean age (SD) of the participants was 52.3 (8.1) years, with a mean body mass index of 29.8 (6.0) $kg/m^2$. Mean (SD) systolic and diastolic blood pressures were 123.8 (13.0) and 73.5 (8.5) mm Hg, respectively. Thirteen participants (26%) had prevalent heart disease, and most had hypertension (58%). Additional details concerning the baseline characteristics of the study population are presented in Table 2.

There was no significant improvement in brachial FMD with the muscadine grape seed intervention (Table 3). In fact, there was a nonsignificant trend toward a reduction in percentage change after 1 month of muscadine grape seed supplementation (−0.65% ± 0.36% mean ± SEM, $p = 0.06$) compared with only a −0.09% ± 0.36% mean ± SEM change with placebo treatment. However, careful examination of the data revealed that the reason for the nonsignificant reduction in percentage change was not due to a drop in brachial response to the flow stimulus (the absolute increase in diameter was similar during both treatment periods) but rather a statistically significant 4.4% increase in resting brachial diameter (baseline: 4.05 ± 0.09 vs. follow-up: 4.23 ± 0.10, $p = 0.002$; Table 3). In a similar fashion, the muscadine grape seed supplement also produced a significant increase in maximum diameter (baseline: 4.25 ± 0.10 vs. follow-up: 4.43 ± 0.10, $p = 0.004$). The overall treatment effect (muscadine grape seed vs. placebo) on baseline and maximum diameter was significant ($p = 0.03$ and 0.05, respectively).

Based on the variance in the observed measures of FMD, there was 80% power to detect a 13% or larger treatment effect with a 2-sided alpha level of 0.05. Consistent patterns of no effect on FMD but increased resting brachial diameter following muscadine grape seed supplementation were observed after stratification by age (< or ≥53.5 years), gender, prior myocardial infarction, current smoking, hypertension, or use of cholesterol or antihypertensive medications; however, the differences were not statistically significant in all subgroups, probably because of reduced sample sizes (data not shown).

The muscadine grape seed supplement did not result in significant changes in blood pressure, lipid parameters, glucose, or inflammatory markers (Table 4). Similarly, there were no differences between the grape seed supplement and placebo with respect to changes in MDA, 8-isoprostane, or total antioxidant capacity (Table 5). There was an increase in plasma 8-isoprostane levels from baseline to follow-up when the subjects were taking placebo ($p = 0.002$) that was not observed when the same subjects were taking the muscadine grape seed supplement; however, the overall test for an effect of treatment on isoprostane was not significant ($p = 0.08$).

## DISCUSSION

In this double-blind randomized crossover trial, there was no evidence that 1 month of daily supplementation with muscadine grape seed improved endothelial function measured by brachial FMD. However, there was clear evidence that this supplement produced an increase in resting brachial diameter. This increase in resting diameter was not accompanied by a

reduction in blood pressure or changes in other plasma markers of cardiovascular risk, including plasma lipids and CRP.

The finding of no effect on FMD is unexpected based on the antioxidant and other properties of the muscadine seed polyphenolics [29] and the generally consistent evidence from prior studies that dietary anitoxidants improve FMD [2,30]. It is possible that the differences between the vascular effects of muscadine grape seed observed in the current study and those documented in previous studies of other grape-derived supplements [3-10] are related to differences in study design, including the time between the last dose and the measurement of endothelial function (up to 4 hours in the current study), dose and duration of supplementation, preparation of the grape-derived supplements, and so forth. Alternatively, it is also possible that the composition of phenolics in muscadines produces a different type of vascular effect characterized by a vasodilator effect at rest rather than an augmented vasodilator response to a flow stimulus. Previous studies have documented that brachial FMD is inversely related to the diameter of the brachial artery at rest [25], a pattern that was also recapitulated in the current study ($r^2 = -0.18$). Thus, it may not be unexpected that an intervention that increases resting diameter would not produce a further increase in diameter in response to a flow stimulus. Unfortunately, previous studies of grape-derived supplements and FMD do not report on changes in baseline diameter. Therefore, it is difficult to know whether the observed effect is unique to the muscadine supplement or not. The magnitude of the effect of the muscadine grape seed supplement on resting diameter is similar to changes in brachial dimensions documented for other cardiovascular medications including angiotensin-converting enzyme inhibitors and calcium channel blockers [31,32]. However, the absence of any data examining the association between changes in brachial diameter from a dietary intervention with subsequent risk for clinical events makes it impossible to judge the clinical implications of the observation.

The muscadine grape has a phytochemical composition unique among grape varieties [23,33,34]. Yilmaz and Toledo[23] reported that, relative to seeds from *V. vinifera* varieties, the seeds of *V. rotundifolia* contain higher concentrations of gallic acid and lower concentrations of catechin and epicatechin. Chemical analysis of the muscadine grape seed supplement used in the current study produced results similar to those reported by Yilmaz and Toledo for gallic acid and catechins; however, the concentration of epicatechin was much higher than in the Yilmaz and Toledo report (Table 1). Of these phytochemicals, catechin has the greatest antioxidant capacity and gallic acid the least. Thus, antioxidant capacity and effects on NO bioavailability and flow-mediated vasodilation derived from these phytochemicals may be less prominent features of muscadines relative to other grapes. More research on the potential effects of the muscadine polyphenolics on other pathways that modulate resting vascular tone including expression of endothelin-1, elements of the renin-angiotensin cascade, and so forth is warranted.

Several limitations must be considered when interpreting these results. Although the FMD measures were all performed in the morning <4 hours from the time of the last dose of the supplement, the exact time interval between the last dose and the FMD measurement was not recorded. Since dietary flavonoids typically have a short half-life (1–2 hours), it is possible that a real, but transient, effect of the supplement on FMD and other outcomes was missed. In addition, although a greater than 13% treatment on FMD is extremely unlikely, we cannot rule out the possibility of a more modest effect. Measures of the response to nitroglycerin were not made in this study. Therefore, it is possible that a positive effect of the muscadine supplement on NO bioavailability was obscured by a concomitant reduction in vascular smooth muscle cell responsiveness to NO. All participants in the study had established cardiovascular risk factors or a prior history of clinical cardiovascular disease, and most participants were on antihypertensive or lipid-lowering medications, which could

influence endothelial function and modify the effects of the muscadine grape seed supplement [34]. However, the stratified analysis did not suggest a differential according to use of lipid-lowering or antihypertensive medications. Despite these limitations, this is the first human study of the effects of muscadine grape seed supplementation on clinical aspects of vascular function and the largest crossover design study of endothelial function using any grape seed dietary supplement.

In summary, 4 weeks of dietary supplementation with muscadine grape seed in subjects with or at high risk for cardiovascular disease produced no measurable increase in flow-mediated vasodilation but did result in a significant increase in resting brachial diameter. The specific mechanism for the observed vasodilator effect and its clinical implications are not yet known. Additional data on the biochemical, physiologic, and clinical effects of products derived from *V. rotundifolia* are needed.

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## Table 1

Concentration of Selected Phytochemicals in the Muscadine Grape Seed Supplement

| Phytochemical | Concentration, μg/g |
|---|---|
| Ellagic acid (total) | 1020 |
| Gallic acid | 1530 |
| Resveratrol | 3.0 |
| Catechin | 75.4 |
| Epicatechin | 5406 |
| Catechin gallate | 26.0 |
| Epicatechin gallate | 268 |
| Epigallocatechin | 1.91 |
| Epigallocatechin gallate | 0.47 |
| Proanthocyanidin * | 70,860 |
| Total phenolics ** | 64,600 |
| ORAC | 895 *** |

* Expresssed as A-type proanthocyanidin dimer equivalent of microgram PAC content/gram.

** The total phenolic result is expressed as microgram gallic acid equivalent/gram.

*** ORAC = oxygen radical absorbance capacity, expressed as micromole Trolox equivalent (TE)/gram.

## Table 2

Baseline Characteristics

| | Men | Women | Total |
|---|---|---|---|
| | n = 25 | n = 25 | N = 50 |
| Age, y, mean (SD) | 52.7 (8.8) | 51.4 (7.4) | 52.1 (8.1) |
| Ethnicity, n (%) | | | |
| White | 24 (96) | 24 (96) | 48 (96) |
| African American | 1 (4) | 1 (4) | 2 (4) |
| Type 2 diabetes, n (%) | 5 (20) | 1 (4) | 6 (12) |
| Hypertension, n (%) | 17 (68) | 13 (52) | 30 (60) |
| Dyslipidemia, n (%) | 18 (72) | 11 (44) | 29 (58) |
| Current smoking, n (%) | 5 (20) | 3 (12) | 8 (16) |
| Prior myocardial infarction, n (%) | 8 (32) | 1 (4) | 9 (18) |
| Prior CABG/PCI, n(%) | 11 (44) | 1 (4) | 12 (24) |
| Blood pressure, mm Hg, mean (SD) | | | |
| Systolic | 119.8 (10.7) | 121.5 (15.4) | 120.6 (13.2) |
| Diastolic | 76.6 (6.7) | 76.9 (8.47) | 76.8 (7.6) |
| Weight, lb, mean (SD) | 197.0 (28.1) | 180.3 (47.4) | 188.6 (39.5) |

CABG = coronary artery bypass graft surgery; PCI = percutaneous coronary intervention.

**Table 3**

Effect of Muscadine Grape Seed Supplementation on Brachial Artery Measurements

| | Placebo | | | MGS Supplement | | | MGS vs Placebo |
|---|---|---|---|---|---|---|---|
| | Baseline | Follow-up | | Baseline | Follow-up | | |
| Brachial Measurements | Mean (SEM) | Mean (SEM) | *p* Value* | Mean (SEM) | Mean (SEM) | *p* Value* | *p* Value** |
| Baseline diameter, mm | 4.12 (0.11) | 4.12 (0.10) | 0.93 | 4.05 (0.09) | 4.23 (0.10) | 0.002 | 0.027 |
| Maximum diameter, mm | 4.33 (0.12) | 4.33 (0.10) | 0.98 | 4.25 (0.10) | 4.43 (0.10) | 0.004 | 0.054 |
| Change in diameter, mm | 0.21 (0.01) | 0.21 (0.01) | 0.83 | 0.21 (0.01) | 0.19 (0.01) | 0.12 | 0.35 |
| FMD, % | 5.27 (0.42) | 5.18 (0.38) | 0.82 | 5.22 (0.32) | 4.57 (0.32) | 0.06 | 0.25 |

MGS = muscadine grape seed; FMD = flow-mediated dilation.

* Least squares means contrast from the mixed linear model.

** Test of treatment effect in the mixed linear model.

**Table 4**

Effect of Muscadine Grape Seed Supplementation on Selected Cardiovascular Risk Markers

| | Placebo | | | MGS Supplementation | | | MGS vs Placebo |
|---|---|---|---|---|---|---|---|
| | Baseline | Follow-up | | Baseline | Follow-up | | |
| Risk Marker | Mean (SEM) | Mean (SEM) | *p* Value* | Mean (SEM) | Mean (SEM) | *p* Value* | *p* Value** |
| SBP, mm Hg | 124.6 (1.8) | 123.2 (2.0) | 0.48 | 122.4 (1.6) | 125.2 (2.0) | 0.10 | 0.09 |
| DBP, mm Hg | 75.3 (1.2) | 72.8 (1.1) | 0.02 | 72.8 (1.2) | 73.2 (1.3) | 0.79 | 0.07 |
| Total cholesterol, mg/dL | 190.4 (5.7) | 189.5 (5.6) | 0.82 | 191.6 (6.3) | 191.54 (6.2) | 0.98 | 0.86 |
| LDL cholesterol, mg/dL | 111.0 (4.6) | 104.7 (4.1) | 0.02 | 111.0 (4.9) | 109.4 (4.4) | 0.53 | 0.13 |
| HDL cholesterol, mg/dL | 46.3 (1.4) | 47.0 (1.5) | 0.43 | 45.9 (1.3) | 45.6 (1.3) | 0.67 | 0.36 |
| Log triglycerides, mg/dL | 5.02 (0.07) | 5.07 (0.08) | 0.13 | 5.03 (0.08) | 5.04 (0.08) | 0.97 | 0.29 |
| Glucose, mg/dL | 102.5 (2.0) | 101.7 (2.3) | 0.56 | 102.8 (2.3) | 101.9 (3.1) | 0.58 | 0.97 |
| Log CRP, mg/dL | −1.49 (0.13) | −1.28 (0.12) | 0.02 | −1.54 (0.12) | −1.38 (0.12) | 0.03 | 0.69 |
| Log IL-6, pg/mL | −2.22 (0.15) | −2.00 (0.17) | 0.23 | −2.25 (0.15) | −2.03 (0.15) | 0.82 | 0.99 |

SBP = systolic blood pressure; DBP = diastolic blood pressure; LDL = low-density lipoprotein; HDL = high-density lipoprotein; CRP = C-reactive protein; IL = interleukin.

* Least squares means contrast from the mixed linear model.

** Test of treatment effect in the mixed linear model.

**Table 5**

Effect of Muscadine Grape Seed Supplementation on Markers of Lipid Peroxidation and Antioxidant Capacity

| | Placebo | | | MGS Supplement | | | MGS vs Placebo** |
|---|---|---|---|---|---|---|---|
| | Baseline | Follow-up | | Baseline | Follow-up | | |
| Marker | Mean (SEM) | Mean (SEM) | *p* Value* | Mean (SEM) | Mean (SEM) | *p* Value* | *p* Value |
| MDA, μM | 0.50 (0.04) | 0.43 (0.03) | 0.05 | 0.54 (0.03) | 0.44 (0.03) | 0.01 | 0.61 |
| 8-isoprostane, pg/mL | 152.7 (11.0) | 179.7 (12.0) | 0.002 | 157.0 (11.4) | 161.9 (11.8) | 0.64 | 0.08 |
| Total antioxidant capacity, mM† | 0.65 (0.01) | 0.66 (0.01) | 0.86 | 0.65 (0.01) | 0.65 (0.01) | 0.85 | 0.80 |

MGS = muscadine grape seed; MDA = malondialdehyde.

*Least squares means contrast from the mixed linear model.

**Test of treatment effect in the mixed linear model.

†mM uric acid equivalents.