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Low-energy cranberry juice decreases lipid oxidation and increases plasma antioxidant capacity in women with metabolic syndrome

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Abstract

Cranberries, high in polyphenols, have been associated with several cardiovascular health benefits, although limited clinical trials have been reported to validate these findings. We tested the hypothesis that commercially available low-energy cranberry juice (Ocean Spray Cranberries, Inc, Lakeville-Middleboro, Mass) will decrease surrogate risk factors of cardiovascular disease, such as lipid oxidation, inflammation, and dyslipidemia, in subjects with metabolic syndrome. In a randomized, double-blind, placebo-controlled trial, participants identified with metabolic syndrome (n = 15-16/group) were assigned to 1 of 2 groups: cranberry juice (480 mL/day) or placebo (480 mL/day) for 8 weeks. Anthropometrics, blood pressure measurements, dietary analyses, and fasting blood draws were conducted at screen and 8 weeks of the study. Cranberry juice significantly increased plasma antioxidant capacity (1.5 ± 0.6 to 2.2 ± 0.4 μmol/L [means ± SD], $P < .05$) and decreased oxidized low-density lipoprotein and malondialdehyde (120.4 ± 31.0 to 80.4 ± 34.6 U/L and 3.4 ± 1.1 to 1.7 ± 0.7 μmol/L, respectively [means ± SD], $P < .05$) at 8 weeks vs placebo. However, cranberry juice consumption caused no significant improvements in blood pressure, glucose and lipid profiles, C-reactive protein, and interleukin-6. No changes in these parameters were noted in the placebo group. In conclusion, low-energy cranberry juice (2 cups/day) significantly reduces lipid oxidation and increases plasma antioxidant capacity in women with metabolic syndrome.

Keywords: Cranberry; Oxidized LDL; Malondialdehyde; Plasma antioxidant capacity; Metabolic syndrome; Women
Abbreviations: CAD, coronary artery disease; CRP, C-reactive protein; CV, coefficient of variation; CVD, cardiovascular disease; IL-6, interleukin-6; HNE, hydroxynonenal; LDL, low-density lipoprotein; MDA, malondialdehyde; Ox-LDL, oxidized low-density lipoprotein.

1. Introduction

Available data report a wide range of cardiovascular health benefits associated with cranberries (*Vaccinium macrocarpon* Ait.), which are rich in polyphenols such as flavonoids and ellagic acid [1,2]. Cranberries, as dried fruits and juice, have been highly ranked in antioxidant capacity among apricots, figs, prunes, and raisins, as well as polyphenol-rich beverages such as green tea and red wine [3]. Cranberry juice consumption has been associated with a reduction of surrogate biomarkers of cardiovascular disease (CVD) risks as reported in clinical studies. Postprandial studies have shown increased plasma antioxidant capacity

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after cranberry juice consumption in healthy volunteers [4]. Intervention trials, with or without placebo control, ranging from 2 to 16 weeks have reported that cranberries improve oxidative stress, postprandial glycemic response, dyslipidemia, and atherosclerotic markers in healthy volunteers [5-7] and in patients with type 2 diabetes mellitus [8,9]. Among these studies, two 12-week interventions in type 2 diabetic patients consuming cranberry juice concentrate powder or cranberry extract powder showed a significant decrease in serum insulin [8] or in total and low-density lipoprotein (LDL) cholesterol levels [9], respectively. In contrast to these significant findings, Duthie et al [10] in a 2-week study in healthy female volunteers reported no substantial changes in blood or cellular antioxidant status or surrogate biomarkers of CVD and cancer risks after cranberry juice vs placebo intervention. Few mechanistic studies support the antioxidant and antihypertensive effects of cranberries, after cranberry juice or cranberry powder treatment in animal models [11,12]. Though limited, these studies provide some evidence on the therapeutic effects of cranberries on glucose and lipid metabolism in type 2 diabetic patients, which warrants further investigation in larger trials.

Metabolic syndrome, comprising several risk factors for CVD and type 2 diabetes mellitus, is increasing worldwide at an alarming rate, and therefore, is the target of diet and pharmacologic therapies [13]. Abdominal adiposity, elevated blood pressure, impaired glucose tolerance, dyslipidemia, elevated oxidative stress, and inflammation, which are the prominent features of metabolic syndrome, can be effectively altered with dietary interventions involving polyphenol-rich foods and beverages such as berries [14], green tea [15], and soy [16]. Previous intervention studies using cranberries in the form of juice or extracts have reported significant improvements in these metabolic risk factors in apparently healthy [5-7] or type 2 diabetic subjects [8,9]. However, the absence of a placebo group in the reported studies in healthy volunteers weakens the validity of the findings associated with cranberry juice intervention [5-7]. Also, no investigation has been reported on the effects of cranberry supplementation in subjects with metabolic syndrome, which therefore constitutes the scope of our study.

In our 8-week randomized placebo-controlled trial, we tested the hypothesis that low-energy commercially available cranberry juice will decrease the surrogate biomarkers of CVD: lipid oxidation, inflammation, and dyslipidemia associated with metabolic syndrome. Thus, in support of the hypothesis, our study objective was to investigate changes in plasma antioxidant capacity, oxidized LDL (ox-LDL), malondialdehyde (MDA), inflammatory biomarkers such as C-reactive protein, interleukin-6 (IL-6), and lipid profiles in subjects with metabolic syndrome. These variables were measured before and after 8 weeks of low-energy cranberry juice or placebo supplementation.

2. Methods and materials

2.1. Study beverages

Table 1 shows the nutrient and physical and chemical characteristics of the cranberry and placebo beverages used in our study. Subjects received 2 cups (1 cup, or 240 mL) of the cranberry or placebo juice daily for 8 weeks. The cranberry and placebo juices were supplied by Ocean Spray Cranberries, Inc (Lakeville-Middleboro, Mass) in identical polyethylene bottles, each bottle containing 240 mL cranberry juice or placebo, kept under refrigeration at the study site. Both participants and laboratory staff were blinded to the treatment or placebo group.

2.2. Subjects and intervention

Adults (n = 36) with features of metabolic syndrome were recruited at the Department of Nutritional Sciences Clinical Assessment Unit at Oklahoma State University, Stillwater, and at the General Clinical Research Center at the University of Oklahoma Health Sciences Center (Table 2). Recruitment was conducted through flyers and e-mail advertisements.

Table 1
Nutrient composition, physical, and chemical characteristics of the cranberry and placebo beverages

Component	Cranberry juice	Placebo juice
	(values/240 mL) [a]	
Energy (kJ)	167.0	167.0
Sugars		
Fructose (g)	4.8	5.3
Glucose (g)	1.8	1.9
Sucrose (g)	0.1	0.1
Ascorbic acid (mg)	60.0	60.0
Total phenolics (mg)	229.0	0.0
Total anthocyanins (mg)	12.4	0.0
Cyanidin-3-galactoside (mg)	3.1	0.0
Cyanidin-3-glucoside (mg)	0.2	0.0
Cyanidin-3-arabinoside (mg)	3.0	0.0
Peonidin-3-galactoside (mg)	3.8	0.0
Peonidin-3-glucoside (mg)	0.2	0.0
Peonidin-3-arabinoside (mg)	2.1	0.0
Proanthocyanidins (mg)	119.0	0.0
pH	2.9	2.9
Brix (°B)	4.2	4.1
Haze (NTU)	27.2	5.1
Color		
Hunter L *	24.0	23.0
Hunter a *	53.0	49.0
Hunter b *	40.0	39.0
Flavor (taste and odor)	Cranberry taste, clean odor	Cranberry-like taste, clean odor

Cranberry and placebo beverages contain sucralose and acesulfame K as sweeteners; proprietary information: Ocean Spray Cranberries, Inc.
Total phenolics and anthocyanins were determined by high pressure liquid chromatography (HPLC). Placebo juice had no detectable polyphenolics but was similar in energy and absorbic acid contents to the cranberry juice.
[a] Participants received 480 mL cranberry juice or placebo juice daily for 8 weeks.
* Denotes scale in colorimetry as manufactured by the Hunter Lab.

Table 2
Baseline characteristics of female subjects

Age (y)	52.0 ± 8.0
Body mass index (kg/m^2)	40.0 ± 7.7
Hemoglobin A_{1C} (%) 5.6 ± 0.5	
Waist circumference (in)	43.3 ± 3.5
Blood urea nitrogen (mg/dL)	13.7 ± 3.3
Creatinine (mg/dL)	0.7 ± 0.1
Aspartate aminotransferase (U/L)	24.2 ± 6.5
Alanine aminotransferase (U/L)	27.8 ± 14.5
Hemoglobin (g/dL)	13.4 ± 1.2
Antihypertensive medication users (%)	20.0
Multivitamin users (%)	25.0

Data are means ± SD for n = 31; no significant differences were found (Student *t* test).

Subjects qualified if they had at least 3 of 5 features of metabolic syndrome [13]. Subjects were excluded if they were on medications for any chronic disease (cancer, CVD, diabetes mellitus), pregnant or lactating, used any form of tobacco products, consumed alcohol (>1 oz/day), used mega doses of antioxidants or fish oil supplements (> 1g/day), or had any abnormalities in hematology, liver, renal, and thyroid function tests, which were confirmed with screening laboratory reports. The 8-week study was conducted according to the guidelines laid down in the Declaration of Helsinki. All procedures involving human subjects were approved by the institutional review boards at Oklahoma State University and University of Oklahoma Health Sciences Center, and written informed consent was obtained from each subject.

Subjects who qualified were asked to refrain from other sources of berries, green tea, cocoa, and soy products while on the study. These were the commonly consumed flavonoid-rich foods by the enrolled subjects as identified by a screening food frequency questionnaire specific for flavonoids. Subjects were asked to consume 2 cups cranberry or placebo beverages daily for 8 weeks. All participants made 3 (Monday, Wednesday, and Friday) visits per week to ensure monitored compliance in cranberry juice or placebo consumption. Subjects were asked to drink the second cup at least 6 hours later in the day and were instructed to keep the juice under refrigeration, avoid exposing the drink to direct heat or light, and avoid consuming the cranberry or placebo juice with any other snack, lunch, or dinner. Subjects were asked to bring back any unconsumed juice to assess unmonitored compliance.

Anthropometric measurements were conducted by trained personnel at the screening visit and at 8 weeks of the study. Systolic and diastolic blood pressure was measured in mm Hg using Spot Vital Signs Device (Welch Allyn, Skaneateles Falls, NY). At screen and 8 weeks of the study, participants were asked to lie down and relax for approximately 8 to 10 minutes, after which 3 blood pressure measurements were recorded at an interval of 5 minutes. Blood draws were performed by certified phlebotomists. Subjects were asked to maintain their usual diet, physical activity, and lifestyle while enrolled in the study and were compensated on a biweekly basis.

2.3. Blood collection and analyses

After a 12-hour fast by the subjects, fasting blood samples (45 mL) were collected at screen (week 0) and 8 weeks of the study. Serum and plasma were separated by centrifugation at 3000 rpm for 10 minutes at 4°C using Centrifuge 5810 R (Eppendorf, Hamburg, Germany). Serum and EDTA-plasma samples were sent to Stillwater Medical Center (Stillwater, Okla) for analyses of serum glucose, lipids, liver, and renal functions tests, and hemoglobin assays were conducted using standard laboratory techniques. Plasma and serum samples were stored at −80°C for subsequent analyses of biomarkers of lipid oxidation and inflammation.

2.4. Dietary analyses

Dietary analyses were conducted at screen and 8 weeks of the study. Subjects were asked to maintain detailed 3-day food records, which were analyzed by a trained registered dietitian using Food Processor (version 8.3; ESHA Research Inc, Salem, OR, USA). Subjects were also asked to provide food labels or recipes for accurate analyses of their intakes.

2.5. Biomarkers of lipid oxidation and inflammation

Plasma concentrations of oxidized low-density lipoprotein (ox-LDL) were measured in duplicate with enzyme-linked immunosorbent assay kits (Mercodia, Uppsala, Sweden) according to the manufacturer's instructions. Lipid peroxidation was measured in serum as MDA and 4-hydroxynonenal (HNE), using a colorimetric assay according to the manufacturer's protocol (LPO-586; Oxis Health Products, Inc, Portland, Ore). The average intra-assay coefficient of variation (CV) for ox-LDL and MDA and HNE were 5.2% and 3.56%, respectively. Plasma high-sensitivity C-reactive protein (CRP) and IL-6 were measured using a quantitative sandwich enzyme immunoassay technique (R&D Systems, Minneapolis, Minn). The average intra-assay CV for high-sensitivity CRP and IL-6 were 3.5% and 4.8%, respectively. Plasma antioxidant capacity was measured using metmyoglobin assay developed by Miller et al [19]. Briefly, the assay is based on the inhibition by antioxidants of the absorbance of the radical cation of 2,2′-azinobis(3-ethylbenzothiazoline 6-sulfonate). Antioxidant capacity or percentage inhibition of the reaction was calculated as the change in absorbance readings at 660 nm. The average intra-assay CV was 4.6%.

2.6. Statistical analyses

Descriptive statistics were calculated, and data were graphed for outliers. Student *t* tests were conducted to assess the effects of cranberry juice or placebo on features of metabolic syndrome and biomarkers of oxidative stress and inflammation. The changes in parameters in each group

were assessed by calculating differences between the preintervention and postintervention measurements. A sample size of 12 in each group was calculated to be sufficient to detect a clinically significant difference of 5.5% for plasma antioxidant capacity, 20% for ox-LDL, and 8% for LDL cholesterol, with 80% power. The number per group was increased to 14, taking into consideration a dropout rate of 20%. All analyses were conducted using SPSS 16.0 for Windows (SPSS Inc, Chicago, Ill), and statistical significance was accepted at a probability value of less than .05 (2-sided test). Multiple-hypothesis testing was not accounted for, but results were reviewed for consistencies in perspective of the previously reported data. Values are presented as means ± SD.

3. Results and discussion

3.1. Low-energy cranberry juice

Our study dose of 480 mL cranberry juice has been previously administered in healthy volunteers, showing favorable effects on cardiovascular risk factors after juice intervention [5-7]. We also selected our study beverage based on the fact that the low-energy cranberry juice is commercially available in the United States, and therefore, our study findings may have relevance to public health strategies in CVD prevention. Over all, the test beverages were well tolerated for 8 weeks, and participants reported high compliance and were successfully blinded to the treatment or placebo interventions. The 27% cranberry juice used in our study, manufactured by Ocean Spray Cranberries Inc, has also been previously tested in bioavailability studies in healthy volunteers [17] and in patients with coronary artery disease (CAD) [18]. In both studies, acute consumption of the juice led to detection of phenolic antioxidants in human plasma, thus providing evidence on the bioavailability of polyphenols in commercially available cranberry juice. Milbury et al [18] administered a double-strength 480 mL cranberry juice (54% juice) to 15 patients with CAD and demonstrated low bioavailability of cranberry anthocyanins in these participants. The researchers argue that this specific dose of cranberry juice may not be adequate to alter physiological redox potential in CAD patients, hence suggesting cardiovascular health status, food matrix, dose, and related bioavailability as determinants of the metabolic effects of cranberries. However, these studies did not show the correlation of bioavailability of cranberry polyphenols with plasma or urinary biomarkers of CVD risks. From this perspective, our test dose of 480 mL cranberry juice (229 mg polyphenols) administered twice a day for 8 weeks may be optimal in lowering selected markers of lipid oxidation, as observed in our participants with metabolic syndrome. These findings need to be confirmed in further dose-response studies of cranberry juice or extracts in healthy subjects vs those with metabolic syndrome or advanced CVD.

3.2. Plasma antioxidant capacity

In our study, plasma antioxidant capacity was increased significantly in subjects consuming cranberry juice vs placebo (47% vs 7%, respectively; $P < .05$; Table 3). Similar results have been previously reported after cranberry juice intervention in healthy volunteers in an uncontrolled study [5], although herein we report similar results in subjects with metabolic syndrome in comparison with a placebo group. On the other hand, our findings are inconsistent with the 2-week placebo-controlled trial by Duthie et al [10], which showed

Table 3
Blood pressure, glucose, lipids, and biomarkers of oxidative stress and inflammation for subjects given the cranberry beverage (n = 15) and placebo beverage (n = 16)

Variable	Cranberry		Placebo	
	0 wk	8 wk	0 wk	8 wk
Systolic blood pressure (mm Hg)	132.0 ± 11.6	125.4 ± 9.5	131.4 ± 10.5	128.6 ± 8.6
Diastolic blood pressure (mm Hg)	82.4 ± 9.6	81.4 ± 8.8	83.6 ± 10.5	82.4 ± 9.3
Glucose (mg/dL)	95.3 ± 7.3	101.0 ± 8.6	97.4 ± 8.5	98.5 ± 8.6
Triglycerides (mg/dL)	140.0 ± 15.4	146.0 ± 12.5	143.5 ± 10.5	139.6 ± 9.5
Total cholesterol (mg/dL)	202.0 ± 35.0	196.4 ± 30.3	198.0 ± 25.4	203.0 ± 35.0
LDL cholesterol (mg/dL)	122.0 ± 28.2	117.0 ± 23.1	120.0 ± 18.5	124.0 ± 30.0
HDL cholesterol (mg/dL)	48.0 ± 7.0	46.4 ± 8.9	45.0 ± 8.5	44.7 ± 10.4
VLDL cholesterol (mg/dL)	28.0 ± 14.2	30.0 ± 14.0	31.4 ± 8.5	29.5 ± 12.4
Ox-LDL (U/L)	120.4 ± 31.0	80.4 ± 34.6[a]	118.4 ± 24.5	98.3 ± 18.4
MDA and HNE (μmol/L)	3.4 ± 1.1	1.7 ± 0.7[a]	3.0 ± 0.8	3.2 ± 0.8
CRP (mg/L)	4.5 ± 2.0	4.8 ± 3.2	5.1 ± 3.6	4.9 ± 2.2
IL-6 (μg/L)	26.4 ± 7.5	22.6 ± 10.4	19.5 ± 8.8	24.7 ± 10.5
Plasma antioxidant capacity (μmol/L)	1.5 ± 0.6	2.2 ± 0.4[a]	1.4 ± 0.7	1.5 ± 0.5

Subjects with metabolic syndrome were supplemented with low-energy cranberry juice (2 cups/day) or placebo (2 cups/day) for 8 weeks. Blood pressure, glucose and lipid profiles, biomarkers of oxidative stress, and inflammation were analyzed at 0 and 8 weeks of the study. Data are means ± SD values; analyses were performed using Student *t* test. HDL, high-density lipoprotein; VLDL, very LDL.

[a] Significantly different between cranberry and placebo groups at 8 weeks ($P < .05$).

no significant differences in plasma antioxidant potential due to cranberry juice intervention in healthy volunteers. These differences in findings may be attributed to shorter study duration and selection of healthy volunteers in the previous study [10] in comparison with our longer study duration involving participants with metabolic syndrome. The method used by our study in assessing plasma antioxidant capacity, using the stable hydrophilic compound 2,2′-azinobis(3-ethylbenzothiazoline 6-sulfonate, has been widely used to assess the radical scavenging ability of plasma [19]. However, based on the very low bioavailable concentrations of berry anthocyanins, it remains unclear whether the increase in antioxidant capacity is due to the direct radical scavenging effects of cranberry anthocyanins or their up-regulation of endogenous antioxidants as reported previously [20]. In our study, the increased plasma antioxidant capacity may be attributed to the cranberry polyphenols, especially in a setting of inadequate dietary intakes of antioxidants, including fruits and vegetables by our participants (Table 4). However, the underlying etiology needs further confirmation in pharmacokinetic studies, simultaneously measuring circulating cranberry anthocyanins, as well as endogenous antioxidant enzymes and vitamins.

3.3. Oxidized LDL and MDA

In our short-term study, cranberry juice intervention caused a significant decrease in both ox-LDL and MDA vs placebo treatment (−33% vs −17% and −50% vs +7%, respectively; $P < .05$; Table 3). Interestingly, we also observed a nonsignificant decrease in ox-LDL in the placebo group at 8 weeks, although both cranberry and placebo groups had no significant differences in ox-LDL and MDA at baseline. These findings remained significant when data were analyzed without subjects on stable multivitamin supplements. Our study findings of decreased ox-LDL and MDA are in accordance with previous interventions on cranberry juice supplementation in healthy volunteers [5,7], but inconsistent with the findings reported by Lee et al [9], which detected no difference in ox-LDL in type 2 diabetic patients, or Duthie et al [10], which showed no change in urinary MDA in healthy volunteers after cranberry intervention. However, the results from the previous studies by Ruel et al [5,7] must be interpreted with caution, because significance was reported vs baseline and not in comparison with a parallel placebo arm. Thus, our placebo-controlled study substantiates the in vivo antioxidant effects of cranberry juice polyphenols in subjects with metabolic syndrome. Oxidized LDL and MDA are stable biomarkers of oxidative stress, especially indicating lipid oxidation, and have been strongly correlated with metabolic syndrome and CAD [21,22]. Interestingly, baseline ox-LDL in our subjects with metabolic syndrome were higher than the previously reported uncontrolled trials in healthy volunteers [5,7], which confirms the reported observations of elevated oxidative stress in metabolic syndrome [23]. Also, because dietary intakes of antioxidant vitamins, fruits, and vegetables were not significantly altered in our study participants at 8 weeks, it may be reasonable to conclude that the cranberry juice polyphenols most likely produced the observed effects. To the best of our knowledge, the effects of cranberry juice polyphenols in lowering MDA, as a marker of lipid peroxidation, have not been reported previously. However, serum MDA has been shown to be decreased by green tea and strawberry supplementation in subjects with metabolic syndrome [15,24]. Thus, in comparison with reported studies, we provide more comprehensive data on the antioxidant effects of cranberry juice polyphenols in significantly increasing plasma antioxidant capacity and concomitantly decreasing ox-LDL and MDA vs placebo group.

Table 4
Dietary intakes at 0 and 8 weeks for the subjects given the cranberry beverage (n = 15) and placebo beverage (n = 16)

Variables	Cranberry		Placebo	
	0 weeks	8 weeks	0 weeks	8 weeks
Energy (kJ)	9674.35 ± 232.0	9532.49 ± 252.5	10032.00 ± 285.5	9896.56 ± 393.3
Carbohydrates (g)	260.7 ± 40.0	248.3 ± 28.9	270.2 ± 32.6	264.0 ± 25.0
Proteins (g)	70.8 ± 18.5	68.7 ± 42.6	73.7 ± 15.4	68.0 ± 22.2
Total fats (g)	98.4 ± 20.5	89.5 ± 33.5	105.5 ± 24.0	75.4 ± 28.4
Saturated fats (g)	31.5 ± 14.2	28.5 ± 16.3	28.4 ± 12.4	32.6 ± 12.5
Monounsaturated fats (g)	22.6 ± 13.5	23.1 ± 8.4	26.3 ± 14.4	27.0 ± 9.5
Polyunsaturated fats (g)	35.6 ± 3.2	33.2 ± 4.2	34.5 ± 12.7	30.5 ± 12.5
Dietary fiber (g)	10.6 ± 5.7	12.5 ± 3.2	12.2 ± 4.7	11.0 ± 6.0
Vitamin A (IU)	2211.7 ± 375.0	2421.5 ± 412.0	2185.7 ± 618.0	2051.4 ± 583.7
Vitamin E (mg)	5.2 ± 2.7	4.8 ± 3.9	6.5 ± 2.5	7.2 ± 3.2
Vitamin C (mg)	42.6 ± 10.6	42.0 ± 12.8	41.6 ± 13.7	44.6 ± 7.6
Fruit intake (servings/d)	1.2 ± 0.4	1.1 ± 0.3	1.0 ± 0.5	1.1 ± 0.4
Vegetable intake (servings/d)	1.5 ± 0.5[a]	1.3 ± 0.6	1.0 ± 0.4	1.0 ± 0.5

Dietary intakes included fruits and vegetables at 0 and 8 weeks of the study. Data were analyzed using Student t test and expressed as means ± SD values.
[a] Significantly different between cranberry and placebo groups at baseline (0 week; $P < .05$).

3.4. C-reactive protein and IL-6

Our data showed no significant effects of cranberry juice intervention on selected biomarkers of inflammation, such as CRP and IL-6 in subjects with metabolic syndrome (Table 3). C-reactive protein, mainly synthesized by the liver, has been demonstrated to be an independent predictor of cardiac risk, whereas adipocytokine IL-6 has been correlated with insulin resistance, adiposity, and metabolic syndrome [25,26]. Clinical trials have reported conflicting results on the effects of polyphenol supplementation on biomarkers of inflammation. In a short-term, 4-week trial in subjects with at least 1 CVD risk factor, bilberry juice supplementation was shown to decrease plasma CRP and IL-6 [27], whereas green tea supplementation for 8 weeks showed no effects on these inflammatory parameters in subjects with metabolic syndrome [28]. Thus, a higher dose of cranberry polyphenols or additional lifestyle changes, such as increasing physical activity to affect adiposity, may be better anti-inflammatory strategies and need investigation in future trials.

3.5. Features of metabolic syndrome

According to the definition of metabolic syndrome, the 3 most prominent features in our study subjects were enlarged waist circumference (>35 in for women) (Table 2), elevated systolic blood pressure (≥130 mm Hg), and low high-density lipoprotein (<50 mg/dL) (Table 3) at baseline. Cranberry juice consumption for 8 weeks showed no significant effects on these features, namely, waist circumference, blood pressure, fasting glucose, and lipid profiles. However, systolic blood pressure showed a nonsignificant decrease at 8 weeks compared with baseline in the cranberry group (−5.3%; $P = .07$), whereas no changes in these parameters were noted in the placebo group (Table 3). Previous clinical trials have reported significant improvements in insulin resistance, lipid profiles, and blood pressure, after cranberry intervention as encapsulated concentrates or extracts for 12 weeks [8,9] or successively increasing doses of cranberry juice for 16 weeks vs baseline [7]. On the other hand, no change in plasma lipids was observed in a 2-week cranberry juice treatment period in healthy volunteers [10]. Thus, in comparison with our study intervention (~480 mL cranberry juice/day for 8 weeks) and corresponding findings, a higher dose of cranberry polyphenols, especially as extracts or unsweetened dried whole fruit, administered for a longer period of time may be more effective in metabolic syndrome. However, it should also be noted that low-energy cranberry juice intervention for 8 weeks did not adversely affect adiposity, glucose, and lipid profiles in our subjects. In perspective of the reported adverse health effects of low polyphenol sugar-sweetened fruit juices and diet beverages in metabolic syndrome [29], the choice of select juices, such as low-energy cranberry juice, may favorably reverse lipid oxidation while remaining neutral on adiposity, glucose, and lipid profiles.

3.6. Dietary intakes and compliance

As noted in Table 4, our study subjects had low daily intakes of fruits and vegetables when compared with the dietary guidelines for US adults [30]. All participants reported no intake of berries, other than the test cranberry or placebo beverage, throughout the study period. Though baseline vegetable intake was significantly higher in the cranberry vs placebo group, the average servings were much below the national recommendations [30]. Thus, the observed antioxidant effects of cranberry juice supplementation may have been made more pronounced in our subjects with inadequate dietary antioxidant intakes vs those on a balanced diet. Compliance to juice and placebo intakes were 100% for the enrolled subjects. Four subjects dropped on account of time constraints, and 1 withdrew due to the development of nausea upon juice consumption in the first week of the study. The daily intervention was administered as a midmorning and early-evening snack, and all subjects adhered to refraining from berries, green tea, soy, cocoa, and related supplements throughout the study period.

In conclusion, our study findings support the hypothesis that low-energy cranberry juice will reduce the surrogate biomarkers of cardiovascular risk factors associated with metabolic syndrome. We observed significant improvements in lipid oxidation via decreases in plasma ox-LDL and MDA and an increase in plasma antioxidant capacity, although biomarkers of inflammation, glucose, and lipids were not significantly affected after cranberry juice intervention. Certain limitations of our study include a small sample size, a result of which our study findings cannot be generalized to other populations; short study duration; and mechanisms of action not addressed in the study design. Furthermore, our biochemical assays did not measure serum variables such as fasting insulin, lipoprotein subclass fractions, protein oxidation products, or antioxidant enzymes to gain a detailed understanding of the effects of cranberry juice on metabolic and oxidative stress parameters in subjects with metabolic syndrome. This remains the scope of future studies. However, the findings of our study indicate that commercially available low-energy cranberry juice has beneficial effects on lipid oxidation in subjects with metabolic syndrome. Though fresh fruits and vegetables remain the cornerstone of a healthy diet [31], readily available low-energy cranberry juice may provide additional health benefits. These findings need further investigation in larger trials that are carefully designed to include the optimal dose and form of cranberry intervention, study duration, and subject characteristics.

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