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Effects of grape antioxidant dietary fiber in cardiovascular disease risk factors

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Abstract

Objective: The objective of the study was to evaluate the effects of a grape product rich in dietary fiber and natural antioxidants on cardiovascular disease risk factors.

Methods: A randomized, controlled parallel-group trial was carried out. Thirty-four non-smoking (21 normocholesterolemic and 13 hypercholesterolemic) adults were supplemented for 16 wk with 7.5 g/d of grape antioxidant dietary fiber, a natural product containing 5.25 g of dietary fiber and 1400 mg of polyphenols. Nine non-supplemented non-smokers were followed as a control group. Fasting blood samples, blood pressure, and anthropometric readings were obtained at baseline and at week 16. Subjects were allowed to consume their regular diet, which was monitored weekly.

Results: Grape antioxidant dietary fiber (7.5 g/d) reduced significantly ($P < 0.05$) total cholesterol (9%), low-density lipoprotein cholesterol (9%), and systolic and diastolic blood pressures (6% and 5% respectively). Greater reductions in total cholesterol (14.2%) and low-density lipoprotein cholesterol (11.6%, $P < 0.05$) were observed in hypercholesterolemic subjects. No changes were observed in the control group. There was a reduction of 2.5 points in the Framingham Global Risk Score in the supplemented group. A significant reduction in triacylglycerol concentration took place in the supplemented hypercholesterolemic subjects (18.6%, $P < 0.05$).

Conclusion: Grape antioxidant dietary fiber showed significant reducing effects in lipid profile and blood pressure. The effects appear to be higher than the ones caused by other dietary fibers, such as oat fiber or psyllium, probably due to the combined effect of dietary fiber and antioxidants.

Keywords: Clinical trial; Normocholesterolemic; Hypercholesterolemic; Polyphenols; Antioxidants; Dietary fiber

Introduction

Cardiovascular disease is a leading cause of morbidity and mortality among adults in Western countries. Major risk factors are cigarette smoking, elevated blood pressure, elevated serum total cholesterol and low-density lipoprotein (LDL) cholesterol, low serum high-density lipoprotein (HDL) cholesterol, diabetes mellitus, and advanced age [1,2].

Diets rich in plant foods have been associated with a reduction in the risk of coronary heart disease [3] and associated mortality [4,5]. Dietary fiber and antioxidants are two constituents of plant foods that may contribute to these effects.

Several studies have indicated that increased dietary fiber intake is associated with lower rates of coronary artery disease morbidity and mortality [6,7]. This relation would be the result of favorable effects of dietary fiber on serum

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lipids [8], glucose and insulin metabolism [9], blood pressure [10], and inflammation [11]. In this way, the American Heart Association has recommended increasing dietary fiber intake to 25 to 30 g/d [12]. Also, the U.S. Food and Drug Administration (FDA) has approved health claims that consumption of products rich in dietary fiber, e.g., oat fiber and psyllium, reduce heart disease risk [13].

In contrast, fruits, vegetables, and some beverages such as wine, rich in antioxidants, are associated with a lower incidence of heart disease and ischemic stroke [14–18]. Because these chronic diseases are associated with increased oxidative stress and flavonoids are strong antioxidants in vitro, it has been suggested that flavonoids may exert health benefits through antioxidant mechanisms [19,20].

In summary, dietary fiber and antioxidants are two dietary factors involved in cardiovascular disease risk reduction. However, few clinical trials have evaluated the effects of the combinations of these two dietary factors in the incidence of cardiovascular risk factors in humans.

The aim of this work was to evaluate the possible effects of supplementation with grape antioxidant dietary fiber (GADF), a natural product rich in dietary fiber and flavonoids, in different cardiovascular risk factors.

Materials and methods

Subjects and study design

The study was a randomized, controlled, parallel-group trial. Forty-three non-smokers (27 women and 16 men with an average age of 33.7 ± 12.2 y) were recruited within the university community. Of these, 25 were hypercholesterolemic (serum cholesterol level >200 mg/dL) and were not taking any medication to reduce it, and 18 were normocholesterolemic.

At baseline, participants were randomly assigned to the GADF or the control group. Thirty-four subjects consumed GADF for 16 wk (GADF group) and nine subjects were studied as controls. The number of subjects in each group was chosen based on the variation coefficients observed in a previous work [21] in the evolution of the ratio of LDL cholesterol to HDL cholesterol in the intervention and in the control group, which was higher in the former. In the GADF group, there were 22 women and 12 men, and 21 were hypercholesterolemic and 13 normocholesterolemic. In the control group, there were five women and four men, and five were hypercholesterolemic and four normocholesterolemic.

No statistical differences in anthropometrics and biochemical evaluation were found between the GADF and control groups at baseline (Table 1). The GADF group consumed 7.5 g of GADF provided daily in individual sterile packets. Subjects were allowed to consume their regular diet during the study. Blood samples for biochemical determination, blood pressure, and anthropometric information were collected at the baseline and at week 16.

Table 1
Group characteristics for age, body mass index, blood pressure, and blood lipid profile at the beginning of the study (time 0)*

	Experimental group	Control group
No. of volunteers	34	9
Age (y)	35.5 ± 11.8	34.6 ± 12.4
Sex		
Male	12	4
Female	22	5
Body mass index (kg/m^2)	26.1 ± 4.7	22.7 ± 2.4
Body fat (%)	27.0 ± 7.8	23.8 ± 6.4
Total cholesterol (mg/dL)	250.7 ± 64.3	207.2 ± 43.8
LDL cholesterol (mg/dL)	176.6 ± 54.2	149.7 ± 34.9
HDL cholesterol (mg/dL)	47.7 ± 13.1	42.5 ± 11.0
Triacylglycerols (mg/dL)	120.7 ± 76.4	75.2 ± 19.1
Systolic blood pressure (mmHg)	126.5 ± 22.1	121 ± 14
Diastolic blood pressure (mmHg)	78.2 ± 11.7	71 ± 14
Hemoglobin (g/dL)	14.4 ± 1.1	14.8 ± 1.3
Glucose (mg/dL)	89.1 ± 9.8	85.0 ± 9.1
GOT (U/L)	25.1 ± 8.5	28.1 ± 19.8
GPT (U/L)	24.6 ± 11.0	24.1 ± 7.7
ALP (U/L)	143 ± 49	137 ± 28
Bilirubin (mg/dL)	0.66 ± 0.16	0.59 ± 0.18

ALP, alkaline phosphatase; GOT, glutamic oxalacetic transaminase; GPT, glutamic pyruvic transaminase; HDL, high-density lipoprotein; LDL, low-density lipoprotein

* No statistical differences were found ($P > 0.05$) between groups after applying a paired t test within each group.

Subjects gave their informed consent to participate in the intervention, and the study protocols were approved by the ethics committee of Hospital Carlos III (Madrid, Spain).

Grape antioxidant dietary fiber

Grape antioxidant dietary fiber, a natural product produced specially for this study, was obtained from red grapes (Cencibel variety, vintage year 2005, La Mancha region, Spain). GADF combines large amounts of dietary fiber and phenolic antioxidants such as phenolic acid, anthocyanidin, proanthocyanidin, catechin, and other flavonoids [22,23].

The proximate composition of GADF and the composition per dose given to the volunteers are presented in Table 2. GADF has a high content of dietary fiber (73%) and polyphenols (18.7%), with the major fraction being proanthocyanidins (condensed tannins). Polyphenolic compounds provide GADF with a high antioxidant capacity, measured by 2,2′-azino-bis(3-ethylbenz-thiazoline-6-sulfonic acid) and oxygen radical absorbance capacity assays.

The American Organization of Analytical Chemists dietary fiber enzymatic-gravimetric method of determination was followed [24], introducing a separation of soluble and insoluble fibers through a dialysis system [25,26].

To extract polyphenols from GADF, an extraction with acidic methanol and later with a mixture of acetone/water was performed [27]. GADF polyphenols were determined by the Folin-Ciocalteu procedure [28] and by high-

Table 2
Grape antioxidant dietary fiber composition per 100 g of dry sample and per supplemented dose

	g/100 g dry matter	g/supplemented dose*
Energy (kcal)	113.5	8.13
Dietary fiber	73.48 ± 0.79	5.25
Soluble	15.53 ± 0.11	1.10
Insoluble	57.95 ± 0.78	4.15
Polyphenols	19.74 ± 0.19	1.44
Benzoic acids	0.78	0.06
Catechins	2.31	0.17
Hydroxicinnamic acids	0.34	0.02
Other flavonoids (flavonols, isoflavones, flavanones)	0.69	0.05
Anthocyanidins	0.80	0.06
Proanthocyanidins	14.81	1.06
Fat	7.69 ± 0.49	0.55
Saturated fatty acids (%)	12.6% (16:0 0.65 g/100 g, 18:0 0.31 g/100 g)	
Monounsaturated fatty acids (%)	17.1% (*cis* 18:1Δ9 1.21 g/100 g)	
Polyunsaturated fatty acids (%)	69.8% (18:2 5.36 g/100 g)	
Protein	11.08 ± 0.46	0.79
Ash	5.25 ± 0.19	0.38
Minerals (mg/100 g)	Ca 598 ± 12, Mg 92 ± 0.9, Zn 0.88 ± 0.02, Na 24 ± 0.8, K 23 ± 0.8, Cu 0.17 ± 0.005, Fe 25 ± 0.6, Mn 1.2 ± 0.005	
Antioxidant capacity		
ABTS (μmol Trolox/g dry matter)	124.4 ± 0.3	933
ORAC (μmol Trolox/g dry matter)	214.2 ± 38	1610

ABTS, 2,2′-azinobis-(3-etilbenzotiazolin-6-sulphonic) acid; Ca, calcium; Cu, copper; Fe, iron; K, potassium; Mg, magnesium; Mn, manganese; Na, sodium; ORAC, oxygen-radical absorbance capacity; Zn, zinc
* Supplemented dose: 7.5 g of grape antioxidant dietary fiber.

performance liquid chromatographic methods [29] in these extracts. Antioxidant capacity was determined in extracts by the 2,2′-azino-bis(3-ethylbenz-thiazoline-6-sulfonic acid) [30] and oxygen radical absorbance capacity [31] assays. Proanthocyanidins were determined in HCl/butanol hydrolysate extracts [27].

Protein was determined in a LECO FP-2000 analyzer (Analytical Instruments, LCC, Golden Valley, MN, USA). Fat content was determined using a Soxtec System HT (Foss Tecator AB, Höganäs, Sweden) extractor with petroleum ether, and fatty acid composition by Gas Cromatography, after derivation to methyl esters [32]. The ash content of GADF was determined with an electric furnace for 16 h at 550°C. Minerals were determined in a Perkin Elmer 5100 PC atomic absorption spectrophotometer (Perkin Elmer, Inc., Waltham, MA, USA).

Biochemical and anthropometric measurements

Blood samples were collected from subjects after a 12-h overnight fast by venipuncture into Vacutainer tubes containing ethylene-diaminetetra-acetic acid. Total cholesterol was determined by enzymatic methods [33]. HDL and LDL were separated by ultracentrifugation (4°C) at different densities [34]. Triacylglycerols were measured enzymatically with Boehringer enzyme kits (GPO-PAP, No. 701912; Boehringer Mannheim, Mannheim, Germany). Glucose was determined by the glucose oxidase technique [35] and glycosylated hemoglobin through the procedure of Ferrell et al. [36].

Height, weight, and percentage of body fat (by bioimpedance) were recorded at baseline and 16 wk after the beginning of the intervention period. Blood pressure was measured using an electrical sphygmomanometer.

To evaluate the effect of GADF on the number of stool depositions per day, subjects filled out a daily stool record.

Dietary assessment

Twelve 24-h recalls were performed, three before the baseline period and nine during the intervention period. All weekdays were taken into account and diets were analyzed by the DIAL System (Departamento de Nutrición y Bromatología, Universidad Complutense de Madrid, Madrid, Spain).

Statistics

Statistical analysis was conducted using SPSS 13.0 for Windows (SPSS, Inc., Chicago, IL, USA). Student's *t* test for related samples was performed within each group for the different parameters determined. Differences with a *P* value <0.05 were considered statistically significant. Data are presented as mean ± SD for the number of subjects in each group.

Results

No subject reported any adverse effect derived from the intake of GADF and all participants concluded the trial. Only two subjects reported slight episodes of constipation.

Effects of GADF supplementation on plasma lipids

Table 3 presents the results on plasma lipid concentrations in the GADF-supplemented and control groups at baseline and after the intervention period. Variations in dietary patterns that may affect plasma lipids concentration during the intervention period are also included.

A decrease in the intake of saturated fat took place in the GADF and control groups; although it became significant only in the GADF group, it was of a similar order in both groups (−19% in the GADF group versus −13% in the control group). Nevertheless, no statistically significant differences were observed in blood lipids in the control group during the entire intervention period, whereas a statistically significant decrease in plasma total cholesterol was ob-

Table 3
Plasma lipids in GADF-supplemented and control groups*

	0 wk	16 wk
GADF-supplemented group (n = 34)		
Plasma measurements		
Total cholesterol (mg/dL)	250.7 ± 64.3[a]	229.0 ± 53.9[b]
LDL (mg/dL)	176.6 ± 54.2	162.1 ± 50.1
HDL (mg/dL)	47.7 ± 13.1	46.4 ± 12.6
Triacylglycerols (mg/dL)	120.7 ± 76.4	101.9 ± 56.8
Diet measurements		
Total fat (g/d)	90.2 ± 23.3	82.2 ± 21.7
Saturated fat (g/d)	31.6 ± 9.8[a]	27.2 ± 9.0[b]
Polyunsaturated fat (g/d)	12.7 ± 4.5	11.6 ± 3.7
Monounsaturated fat (g/d)	38.2 ± 11.5	35.9 ± 10.6
Cholesterol (mg/(day)	320.9 ± 124.4	303.3 ± 109.4
Control group (n = 9)		
Plasma measurements		
Total cholesterol (mg/dL)	207.2 ± 43.8	204.6 ± 40.8
LDL (mg/dL)	149.7 ± 34.9	145.6 ± 33.2
HDL (mg/dL)	42.5 ± 11.0	43.7 ± 7.6
Triacylglycerols (mg/dL)	75.2 ± 19.2	76.3 ± 21.4
Diet measurements		
Total fat (g/d)	108.1 ± 44.0	95.3 ± 24.0
Saturated fat (g/d)	41.8 ± 20.0	33.5 ± 8.8
Polyunsaturated fat (g/d)	15.3 ± 10.2	12.5 ± 3.8
Monounsaturated fat (g/d)	43.6 ± 15.0	41.6 ± 13.7
Cholesterol (mg/(day)	277.1 ± 98.4	324.8 ± 82.9

GADF, grape antioxidant dietary fiber; HDL, high-density lipoprotein; LDL, low-density lipoprotein

* Different letters between columns indicate statistical differences between values ($P < 0.05$, paired t test) within each group.

served in the GADF group. Furthermore, LDL and plasma triacylglycerol concentration reductions, although not significant, were observed in the GADF group, whereas no reduction in LDL and triacylglycerol concentrations was observed in the control group.

The lipid profile of the GADF group divided into normo- and hypercholesterolemic subjects is shown in Figure 1. Total cholesterol, LDL cholesterol, and triacylglycerol decreases were significant in the hypercholesterolemic subjects, but not in the normocholesterolemic ones. The average decreases were 14.2% for total cholesterol, 11.6% for LDL cholesterol, and 18.6% for triacylglycerols. No significant change in HDL cholesterol was observed. It should be noted that there was no significant change in the intake of saturated fats in the hypercholesterolemic group.

Effects of GADF supplementation on body fat and anthropometric parameters

Table 4 presents the results on anthropometric parameters in the GADF and control group at baseline and after the intervention period. No statistically significant differences were observed in the control group, whereas a statistically significant decrease in body fat in females from the GADF group was observed. Regarding dietary parameters that could interfere in anthropometric parameters, a significant increase in food consumption was observed in the GADF group, whereas liquid intake increased in both groups. The increase in food consumption (observed also in the control group, but this was not significant) may be seasonal. However, there were no differences in fruit and vegetable intakes. The increase in food intake may be due in part to the increase in liquid consumption. The caloric intake remained the same in both groups.

Effects of GADF supplementation on blood pressure

Table 5 presents the results on blood pressure in the GADF and control groups at baseline and after the intervention period. A significant decrease in systolic and diastolic blood pressures was observed in the GADF group, but not in the control group. Sodium consumption in both groups remained unchanged during the intervention period.

Effects of GADF supplementation on fasting glucose levels and glycosylated hemoglobin

Table 6 presents the results on fasting glucose levels and glycosylated hemoglobin in the GADF and control groups at baseline and after the intervention period. A significant decrease in fasting glucose levels was observed in both groups; however, no effect on glycosylated hemoglobin was observed. Regarding total carbohydrate and sugar intakes, a significant increase was observed in the GADF group, whereas no differences were observed in the control group. These differences were associated with randomized factors.

No difference in dietary fiber intake was observed between groups at the beginning of the study, but the intake of GADF, as expected, caused a significant increase in the intake of dietary fiber in the experimental group.

Effects of GADF supplementation on number of stool depositions per day

Figure 2 shows the effect of GADF on the number of stool depositions per day. There was a significant increase ($P < 0.05$) in those subjects with an initial average of seven or fewer stools per week, whereas there was no effect in the subjects initially with at least seven stools per week.

Discussion

Grape antioxidant dietary fiber is a natural product obtained from red grapes. It exhibits the effects of dietary fiber and antioxidants, present as natural endogenous constituents that have not been subjected to extraction procedures. Extraction of antioxidants may imply an incomplete recovery of antioxidants and a loss of synergistic action present in the original vegetal matter [37].

Previous experiments with GADF in rats showed hypocholesterolemic effects [38,39] and a greater cecal antioxi-

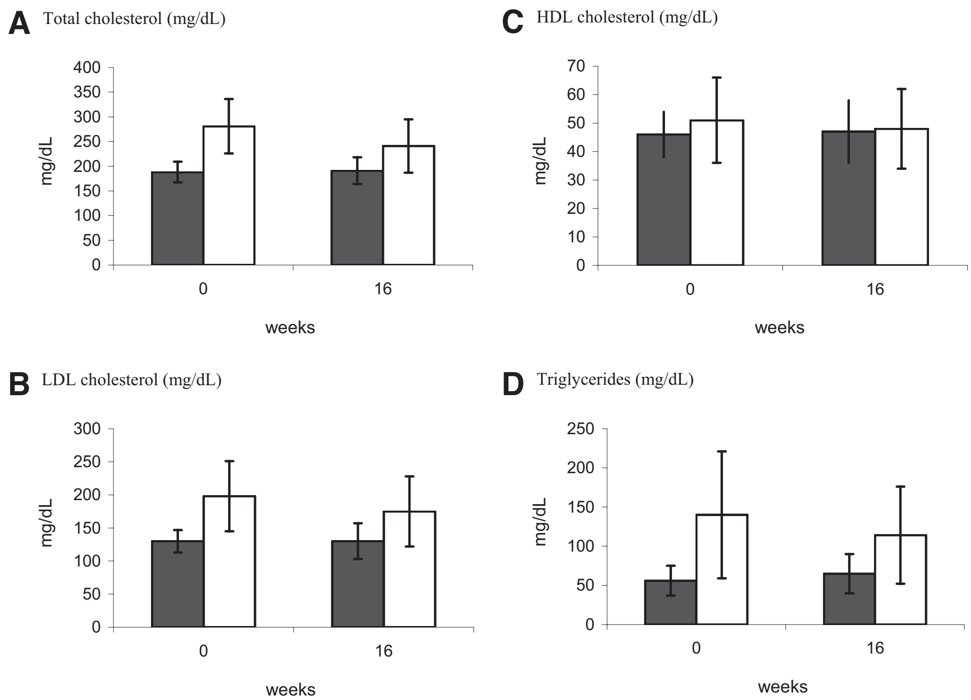

Fig. 1. (A–D) Effects of 16-wk supplementation with grape antioxidant dietary fiber on plasma lipids on normocholesterolemic (black bars) and hypercholesterolemic (white bars) subjects. HDL, high-density lipoprotein; LDL, low-density lipoprotein.

dant capacity and an increase in fat excretion [40,41]. In addition, an increase in plasma antioxidant capacity in humans after an acute intake of GADF has recently been observed [42], indicating that polyphenols present in GADF are, at least partially, bioavailable. Moreover, GADF contains relatively large amounts of proanthocyanidins (condensed tannins), which are partially bioavailable in the small intestine, but a major part reach the colon, where they may provide a high antioxidant status [27].

The daily intake of dietary fiber in Western countries is estimated at about 20 g [43]. The incorporation of 7.5 g/d of GADF in a usual diet would provide a dietary fiber intake closer to the current recommendations (25–30 g/d), along with an appreciable amount of polyphenols. This amount of polyphenols in a dose of 7.5 of GADF (1.44 g) would increase the daily intake of polyphenols by 50% in the Mediterranean Spanish diet [27].

In this trial, GADF supplementation showed effects on the serum lipid profile compared with a non-supplemented group. Dietary fiber and antioxidants may have contributed to this effect.

A reduction in the absorption of triacylglycerols in the large intestine, an increase in the synthesis and excretion of bile acids, an inhibition of the synthesis of cholesterol by short-chain fatty acids generated during fermentation, and modifications in the metabolism of lipoproteins through an increase in the amount of hepatic receptors of LDLs have been suggested as the main hypocholesterolemic mechanisms of dietary fiber [44–48]. In previous experiments in hypercholesterolemic rats supplemented with GADF, plasma total and LDL cholesterol levels were significantly lower than in the non-supplemented group [38]. Also, this supplementation led to an increased fat excretion compared with a control group [39]. The possible decrease in fat absorption after the intake of GADF may have contributed to the reduction in body fat that took place in the female subjects in the GADF group in this trial.

The hypocholesterolemic effect of GADF observed in this study (reductions of 2.53 mg/dL per gram of ingested GADF for total cholesterol and 1.46 mg/dL per gram of ingested GADF for LDL cholesterol) was more pronounced than that observed in a recent meta-analysis of 55 studies on the cholesterol-lowering effects of dietary fibers in oat fiber and psyllium, two dietary fibers with approved health claims by the FDA for their ability to reduce cardiovascular risk [49].

A possible modifying effect of lipoprotein metabolism by polyphenols, through hepatic removal of cholesterol after intake of polyphenols from red grape and wine, and an increase in fecal excretion of cholesterol, bile acids, and other dietary lipids after the intake of dietary polyphenols, particularly of proanthocyanidins, have been described as the main mechanisms of action of polyphenols in relation to lipid profile [21,40,50]. GADF presents a polyphenol composition quite similar to that of red grape or red wine, being rich in proanthocyanidins.

With regard to studies of polyphenolic antioxidants with structures similar to those of GADF, the intake by pre- and postmenopausal women of 1 freeze-dried grape led to a significant decrease of total cholesterol and triacylglycerols

Table 4
Anthropometrics in GADF-supplemented and control groups*

	0 wk	16 wk
GADF-supplemented group (n = 34)		
Anthropometrics		
Body mass index (kg/m^2)	26.1 ± 4.7	25.8 ± 4.4
Body fat (%)		
Male	21.7 ± 6.6	21.0 ± 6.1
Female	32.3 ± 5.6^{a}	31.8 ± 5.5^{b}
Diet measurements		
Energy (kcal/d)	1999 ± 427	1983 ± 352
Food ingested (g/d)	2195 ± 526^{a}	2647 ± 490^{b}
Liquids (mL/d)	945 ± 401^{a}	1287 ± 576^{b}
Fruits (portions/d)[1]	1.86 ± 1.55	1.86 ± 1.14
Vegetables (portion/d)[1]	3.26 ± 2.01	3.32 ± 1.48
Control group (n = 9)		
Anthropometrics		
Body mass index (kg/m^2)	22.7 ± 2.4	22.9 ± 2.3
Body fat (%)		
Male	16.5 ± 4.4	17.4 ± 4.4
Female	27.5 ± 2.5	27.3 ± 2.7
Diet measurements		
Energy (kcal/d)	2530 ± 1066	2441 ± 664
Food ingested (g/d)	2899 ± 722	3112 ± 1197
Liquids (mL/d)	1401 ± 830^{a}	1828 ± 973^{b}
Fruits (portions/d)†	2.29 ± 2.12	2.67 ± 1.66
Vegetables (portion/d)‡	2.66 ± 1.50	2.56 ± 1.72

GADF, grape antioxidant dietary fiber
* Different letters between columns indicate statistical differences between values ($P < 0.05$, paired t test) within each group.
† Fruit portion 120 g.
‡ Vegetable portion 150 g.

[51]. Similarly, the intake of concentrated grape juice for 2 wk caused significant decreases in total cholesterol and LDL cholesterol [52]. Reductions of the same order of total cholesterol, LDL cholesterol, and triacylglycerols were observed in the hypercholesterolemic group in this trial.

Moreover, the intake of GADF showed a positive effect in blood pressure. This effect observed in mostly normotensive subjects should be confirmed in other studies with hypertensive subjects. Actually, most of the published works on the hypotensive effects of polyphenols from grape and/or wine have been performed on hypertensive rats [52,53].

Table 5
Blood pressure in GADF-supplemented and control groups*

	0 wk	16 wk
GADF-supplemented group (n = 34)		
Systolic pressure (mmHg)	126.5 ± 22.1^{a}	118.0 ± 19.6^{b}
Diastolic pressure (mmHg)	78.2 ± 11.7^{a}	74.4 ± 12.1^{b}
Diet measurements		
Sodium (mg/d)	2309 ± 786	2253 ± 760
Control group (n = 9)		
Systolic pressure (mmHg)	121.5 ± 14.0	113.7 ± 9.4
Diastolic pressure (mmHg)	71.4 ± 14.4	71.3 ± 8.7
Diet measurements		
Sodium (mg/d)	2771 ± 1545	2164 ± 897

GADF, grape antioxidant dietary fiber
* Different letters between columns indicate statistical differences between values ($P < 0.05$, paired t test) within each group.

Table 6
Plasma glucose in GADF-supplemented and control groups*

	0 wk	16 wk
GADF-supplemented group (n = 34)		
Serum measurements		
Fasting glucose (mg/dL)	89.1 ± 9.8^{a}	83.2 ± 8.7^{b}
Glycosylated hemoglobin (%)	4.92 ± 0.33	5.01 ± 0.41
Diet measurements		
Total carbohydrate (g/d)	185.3 ± 49.8^{a}	199.6 ± 36.7^{b}
Sugars (g/d)	94.0 ± 29.3^{a}	107.8 ± 24.4^{b}
Dietary fiber (g/d)†	11.4 ± 6.8^{a}	15.6 ± 3.4^{b}
Control group (n = 9)		
Serum measurements		
Fasting glucose (mg/dL)	85.0 ± 9.1^{a}	77.9 ± 5.5^{b}
Glycosylated hemoglobin (%)	5.10 ± 0.60	4.72 ± 0.54
Diet measurements		
Total carbohydrate (g/d)	286.9 ± 121.3	275.2 ± 117.0
Sugars (g/d)	163.9 ± 70.6	160.0 ± 63.5
Dietary fiber (g/d)	9.0 ± 4.7	9.9 ± 3.3

GADF, grape antioxidant dietary fiber
* Different letters between columns indicate statistical differences between values ($P < 0.05$, paired t test) within each group.
† Dietary fiber intake includes the dietary fiber supplemented by GADF (5.25 g/d).

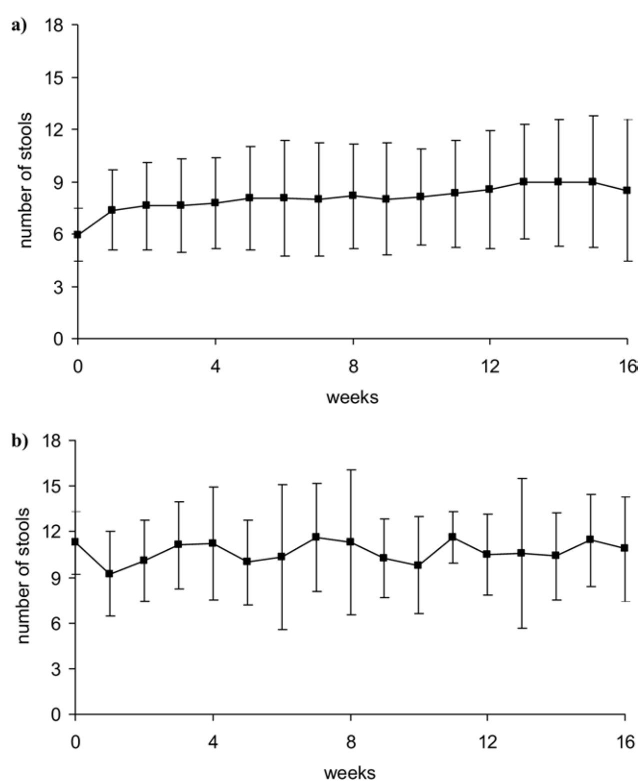

Fig. 2. Evolution in the number of weekly stools in subjects who received grape antioxidant dietary fiber with an average of (a) seven or fewer stools per week (n = 25) or (b) more than seven stools per week (n = 9) at the beginning of the trial.

The stimulation of the release of nitric oxide, with vasorelaxing and anti-aggregating properties, by the vascular endothelium observed after the intake of grape juice by humans [54] and the inhibition of the absorption of sodium ions in the large intestine after the supplementation of rats with psyllium [48] have been suggested as the mechanisms by which polyphenols and dietary fiber, respectively, would exert their hypotensive effect.

In a meta-analysis of 24 assays on the relation between fiber and blood pressure, it was established that daily supplementation with an average dose of 11.5 g/d reduced systolic pressure in a non-significant way and diastolic pressure significantly [55]. In this trial, GADF has shown a significant effect in systolic and diastolic pressures, even though the amount provided was quite smaller than the average amount used in these studies.

Grape antioxidant dietary fiber also seemed to have a protective effect on plasma glucose, because in the GADF group, even with greater total carbohydrate and sugar intakes during the intervention period, no increases were observed in glycosylated hemoglobin; moreover, fasting glucose levels were significantly decreased. In this way, several studies have suggested that dietary fiber may have a positive effect on glucose levels and/or the prevention of diabetes [53].

The effect of dietary fiber in the treatment of constipation is widely known [56]. GADF increased the number of stool depositions per day in those subjects with an average of seven depositions or less per week at baseline, but not in those with seven or more. Similarly, an improvement in constipation and a prevention of diarrhea episodes were reported after the intake of psyllium [57].

At the beginning of the study, the Framingham Global Risk Score was 2.5 for the entire GADF group, and after 16 wk of GADF supplementation the score was reduced to 0 (principally by lowering total cholesterol and systolic blood pressure). In the case of hypercholesterolemic subjects, the reduction in the Framingham Global Risk Score was 1.5.

Conclusions

Grape antioxidant dietary fiber showed significant reducing effects in lipid profile and blood pressure. The effects appeared to be greater than those caused by other dietary fibers, such as oat fiber or psyllium, probably due to the combined effect of dietary fiber and antioxidants. Further research on the relative contributions of fibers and flavonoids to prevent cardiovascular disease is needed.

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