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Changes in plasma antioxidant capacity and oxidized low-density lipoprotein levels in men after short-term cranberry juice consumption

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Abstract

Low-density lipoprotein (LDL) oxidation is closely implicated in the development of atherosclerotic cardiovascular disease (CVD), and thus, reducing LDL susceptibility to oxidation with antoxidants could be of importance in CVD prevention. Flavonoids, polyphenolic compounds found in a large selection of fruits and vegetables, have been characterized as having a strong antioxidant potential, and intake of flavonoid-rich foods has been related to decreased morbidity and mortality from heart disease. The present study was therefore undertaken to investigate the effect of flavonoid-rich cranberry juice supplementation on plasma lipoprotein levels and LDL oxidation. For that purpose, 21 men (age ± SD, 38 ± 8 years) were enrolled in a 14-day intervention and instructed to drink cranberry juice 7 mL/kg body weight per day. Physical and metabolic measures including plasma lipid and oxidized LDL (OxLDL) concentrations as well as antioxidant capacity were performed before and after the intervention. At baseline, we found that plasma OxLDL levels were significantly associated with waist circumference ($r = 0.47$, $P = .0296$) as well as plasma triglyceride ($r = 0.68$, $P = .0007$) and apolipoprotein B ($r = 0.91$, $P < .0001$) concentrations. The intervention led to a reduction in plasma OxLDL levels (−9.9% ± 17.8%, $P = .0131$) and increase in antioxidant capacity (+6.5% ± 10.3%, $P = .0140$). However, no relationship was found between both of these changes ($r = -.01$, not significant). The intervention did not result in any improvement of plasma lipoprotein-lipid or inflammatory marker concentrations. Our results show that short-term cranberry juice supplementation is associated with significant increase in plasma antioxidant capacity and reduction in circulating OxLDL concentrations. Although the physiological relevance of our observations needs to be further examined, our study supports the potential role of antioxidant-rich foods in maintaining health and preventing CVD.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death in North America [1]. Although an elevated plasma low-density lipoprotein (LDL) cholesterol concentration is an important CVD risk factor [2], a large proportion of CVD events remain unexplained by traditional risk factors such as hypercholesterolemia [3]. This observation led to the suggestion that oxidative modifications of LDL particles should be considered in the assessment of CVD risk [4]. Indeed, through a series of events, oxidized LDL (OxLDL) particles can induce foam cell formation within the artery wall and lead to the development of atherosclerotic lesions [2,5-10].

Reactive oxygen (ROS) and nitrogen species, the so-called free radicals, are highly reactive molecules that are constantly produced through numerous cellular reactions (eg, mitochondrial respiratory chain and inflammation) which can modify other molecules such as DNA, proteins, and lipids [11-13]. Nature has provided human beings with antioxidant defenses including enzymes [14] and vitamins [15,16] which have the capacity to neutralize free radicals. Depleted antioxidant defenses can lead to oxidative stress, that is, imbalance between the rates of production and

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elimination of free radicals, increasing the likelihood of damage to other molecules. Intervention studies aimed at replenishing antioxidant reserves and their impacts on health have mostly focused on the consumption of vitamins A, C, and E, but these studies have yielded conflicting results [17], raising the questions as to whether vitamins are the most potent antioxidants available and even suggesting a pro-oxidative potential of vitamins under certain circumstances [18]. On the other hand, polyphenolic compounds such as flavonoids possess an important antioxidant capacity [19,20], and a diet rich in flavonoids has been associated with the reduction of CVD risk [15]. Flavonoids are present in a large selection of fruits and vegetables [21,22] and thus must be considered an essential component of a healthy diet. Cranberries (*Vaccinium macrocarpon*) are one of the most important sources of flavonoids, including quercetin and myricetin, which are known to be potent antioxidants [23]. Whereas consuming cranberry-related products has been shown to prevent urinary tract infections [24], not much is known of the cardioprotective potential of cranberries. The present study was therefore undertaken to explore the potential beneficial impact of short-term cranberry juice consumption on plasma antioxidant capacity and OxLDL concentrations.

2. Subjects and methods

2.1. Subjects

Twenty-one healthy men (mean age ± SD, 38 ± 8 years) were recruited and selected to cover a wide range of body fatness values. To be part of the study, subjects had to be weight-stable for at least 6 months before the study and free of CVD, diabetes, as well as renal, hepatic, or endocrine disorders. Exclusion criteria also included alcohol consumption (≥2 drinks per day), smoking, unusual dietary habits, and use of medication known to affect insulin or lipoprotein-lipid metabolism. Subjects using vitamin, mineral, antioxidant, or flavonoid supplements were also excluded from the study. Individuals gave their written consent to participate in the study which was approved by the Medical Ethics Committee of the Laval University Medical Research Center.

2.2. Intervention

Subjects enrolled in the study were instructed to consume cranberry juice (Ocean Spray's Light Cranberry Juice Cocktail, Ocean Spray Cranberries, Inc, Lakeville-Middleborough, Mass) at a daily dose of 7 ml/kg of body weight for a period of 14 consecutive days. A personally calibrated glass and cranberry juice supply for the entire intervention were provided to the participants on their first visit to the investigation unit. We used the light version of the juice, artificially sweetened with sucralose (Splenda, McNeil Nutritionals LLC, Fort Washington, Pa) to avoid the potential detrimental metabolic impact of the added sugar consumption during the course of the intervention. Subjects visited the laboratory at the beginning and at the end of the study at which time anthropometric measures were made and blood sampling was performed.

2.3. Anthropometric measurements

Body weight, height, as well as waist and hip circumferences were measured following standardized procedures [25]. Body mass index (BMI) and the waist/hip ratio (WHR) were calculated.

2.4. Plasma lipid and lipoprotein concentrations

Blood samples were obtained from an antecubital vein in the morning after a 12-hour overnight fast. Cholesterol and triglyceride (TG) levels were determined in plasma by enzymatic methods using RA-1000 analyzer (Bayer Corporation Inc, Tarrytown, NY), as previously described [26]. High-density lipoprotein (HDL) levels were obtained after precipitation of apolipoprotein (apo) B containing lipoproteins in plasma with heparin and $MnCl_2$ [27]. The cholesterol and TG contents of the HDL fraction were measured as previously presented. LDL cholesterol levels were calculated using the Friedewald equation [28]. Apo B concentrations were measured in plasma by nephelometry (Dade Behring, Mississauga, Ontario, Canada). The lyophilized serum standards for apo B measurements were prepared in our laboratory and calibrated with reference standards obtained from the Centers for Disease Control (Atlanta, Ga). Distinct subpopulations of LDL particles were separated in whole plasma using nondenaturing 2% to 16% gradient gel electrophoresis as described previously [29]. LDL peak particle diameter was identified as the most prevalent subclass of LDL in each individual and was calculated from calibration curves using plasma standards of known diameter. Coefficient of variation of the technique is <2%.

2.5. Plasma antioxidant capacity, OxLDL, and inflammatory marker levels

Plasma antioxidant capacity was measured with the metmyoglobin assay developed by Miller et al [30]. 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) (ABTS). Plasma samples were mixed with ABTS, metmyoglobin, and hydrogen peroxide. Antioxidant capacity or percentage inhibition of the reaction is calculated as the change in coloration of the solution that is recorded by spectrophotometry (660 nm) at 0 and 3 minutes after mixing of the compounds. Plasma OxLDL levels were measured by enzyme-linked immunosorbent assay using a commercial kit (ALPCO Diagnostics, Windham, NH). The technique used for the measurement of OxLDL that was used in the study was developed by Holvoet et al [31]. The assay is a capture enzyme-linked immunosorbent assay in which the wells of the microtiter

Table 1
Baseline physical and metabolic characteristics of the subjects

Variables	Mean ± SD	Range
No. of subjects	21	
BMI (kg/m^2)	26.9 ± 3.8	22.3-35.9
Body weight (kg)	84.9 ± 11.9	66.7-109.1
Waist circumference (cm)	92.7 ± 12.4	73.5-117.5
Hip circumference (cm)	98 ± 8	84-115
WHR	0.95 ± 0.08	0.84-1.15
Systolic pressure (mm Hg)	110 ± 10	91-127
Diastolic pressure (mm Hg)	72 ± 7	58-82
Total cholesterol (mmol/L)	5.11 ± 0.86	3.57-7.04
TGs (mmol/L)	1.24 ± 0.42	0.61-2.12
HDL cholesterol (mmol/L)	1.24 ± 0.28	0.70-1.83
LDL cholesterol (mmol/L)	3.29 ± 0.75	2.14-4.98
Apolipoprotein B (g/L)	0.97 ± 0.20	0.59-1.32
Total/HDL cholesterol	4.27 ± 1.01	2.49-6.49
LDL particle size (nm)	25.47 ± 0.14	25.16-25.73

plates are coated with the monoclonal antibody 4E6 (mAb-4E6) that is directed against a conformational epitope in the apo B-100 moiety of LDL that is generated as a consequence of substitution of lysine residues of apo B-100 with aldehydes. All measurements were done on the same day, and the variation coefficients of both techniques is <3%.

2.6. Nutritional habits assessment

A 91-item validated food frequency questionnaire [32] was administered by a nutritionist during the first visit of the subjects to the hospital. The food frequency questionnaire was structured to reflect food habits of the Québec population. Food items were listed in food groups: (1) vegetables, (2) fruits, (3) legumes, nuts, and seeds, (4) cereals and grain products, (5) milk and dairy products, (6) meat/processed meat, (7) poultry, (8) fish, (9) eggs, (10) sweets, (11) oils and fats, as well as (12) fast foods and drinks. During the interview, the nutritionist used food models for a better estimation of the real portion consumed by the subjects. Data were analyzed with the Nutrition Data System for Research software (version 4.03), developed by the Nutrition Coordination Center Food and Nutrient Database 31 (University of Minnesota, Minneapolis, Minn). This database includes more than 16 000 food items for which the complete nutritional value of 112 nutrients is included.

2.7. Statistical analyses

Unless mentioned otherwise, data are presented as mean ± SD. Paired student t tests were used to determine the significance of metabolic changes induced by the intervention. In all analyses, a P value of ≤.05 was considered significant. When required, variables were $\log_{10}$-transformed for statistical comparisons, but for practical reasons, raw data are presented in tables and figures. All analyses were conducted using the SAS statistical package (version 8.2, SAS Institute, Cary, NC).

3. Results

Table 1 shows baseline physical and metabolic characteristics of the subjects. We found that waist circumference (r = 0.47, P < 0.05) was significantly associated with plasma OxLDL levels (Table 2). A dyslipidemic profile including high plasma total and LDL cholesterol, TG, and apo B concentrations and the presence of small dense particles was also associated to increased plasma OxLDL levels (Table 2). Association between plasma OxLDL and lipoprotein-lipid profile variables (total cholesterol, LDL cholesterol, TGs, and LDL particle size) were all maintained after adjustment for waist circumference (data not shown). No association was found between circulating OxLDL concentration and plasma HDL cholesterol.

Although no association was found between the intake of saturated (r = −0.33, not significant [ns]), monounsaturated

Table 2
Associations between baseline physical and metabolic characteristics and plasma OxLDL concentrations

Variables	OxLDL	
	r	P value
Weight	0.21	.3722
BMI	0.33	.1493
Waist circumference	0.47	.0296
Hip circumference	0.28	.2163
WHR	0.52	.0152
Total cholesterol	0.85	.0001
TGs	0.68	.0007
LDL cholesterol	0.86	.0001
HDL cholesterol	−0.01	.9599
Total/HDL cholesterol	0.71	.0003
Apolipoprotein B	0.91	.0001
LDL particle size	−0.61	.0031
Antioxidant capacity	−0.05	.8447

Table 3
Changes in physical and metabolic characteristics after the intervention

Variables	Change ± SD	P value
BMI (kg/m^2)	−0.14 ± 0.34	.0114
Body weight (kg)	−0.46 ± 1.02	.0516
Waist circumference (cm)	−0.12 ± 0.93	.7925
Hip circumference (cm)	−0.07 ± 1.23	.5657
WHR	0.00 ± 0.02	.7886
Systolic pressure (mm Hg)	−1.86 ± 4.50	.0730
Diastolic pressure (mm Hg)	−1.23 ± 4.00	.1713
Total cholesterol (mmol/L)	0.09 ± 0.37	.2712
TGs (mmol/L)	0.02 ± 0.26	.7728
HDL cholesterol (mmol/L)	0.01 ± 0.12	.5696
LDL cholesterol (mmol/L)	0.07 ± 0.29	.2939
Apolipoprotein B (g/L)	0.03 ± 0.09	.2255
Total/HDL cholesterol	0.05 ± 0.39	.5914
LDL particle size (nm)	0.00 ± 0.17	.9682

($r = -0.15$, ns), or polyunsaturated ($r = -0.23$, ns) fats and plasma OxLDL concentrations, we found significant negative associations between circulating OxLDL levels at baseline and dietary glucose ($r = -0.51$, $P = .0267$), fructose ($r = -0.50$, $P = .0306$), and galactose ($r = -0.49$, $P = .0324$) intake.

As shown in Table 3, the 14-day intervention led to a small but significant ($P = .0114$) decrease in BMI as well as a 2% reduction in systolic blood pressure in response to the intervention, although the latter failed to reach statistical significance ($P = .0730$). No change was noted in the lipoprotein-lipid profile of the subjects including LDL peak particle sizing after 14-day cranberry juice supplementation. However, as shown in Fig. 1, we noted a significant increase in plasma total antioxidant capacity (+0.11 ± 0.19 μmol/L, $P < .05$) and reduction in plasma OxLDL concentration (−6.0 ± 10.0 U/L, $P < .05$) after the intervention but noted that these changes were not related to each other ($r = -0.01$, ns; Fig. 2).

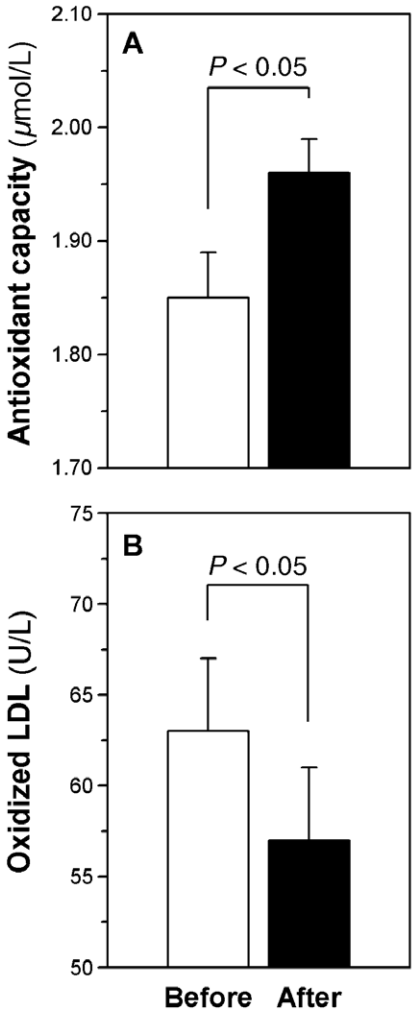

Fig. 1. Plasma (A) antioxidant capacity and (B) OxLDL levels before (white bars) and after (black bars) 14-day cranberry juice supplementation in men. Change in plasma antioxidant capacity +0.11 ± 0.04 μmol/L or +6.5% ± 2.2%. Change in plasma OxLDL −6.0 ± 2.19 U/L or −9.9% ± 3.9%. Data are presented as mean ± SEM.

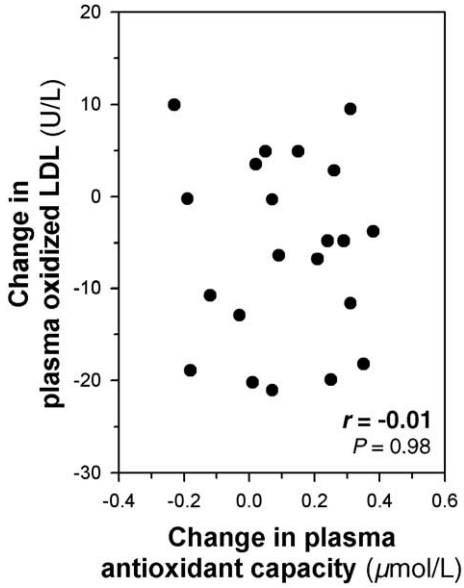

Fig. 2. Lack of association between changes in plasma antioxidant capacity and OxLDL concentrations after 14-day cranberry juice supplementation in men.

4. Discussion

Results of the present study show that short-term daily cranberry juice consumption reduces plasma OxLDL levels and increases plasma antioxidant capacity in men. Considering that cranberries are an important source of polyphenolic molecules with a potent antioxidant activity [33], our results are supportive of the health benefits that can be achieved through the consumption of antioxidant-rich foods [15]. To the best of our knowledge, this is the first study on the relationship between cranberry flavonoid supplementation and plasma OxLDL concentrations. In human beings, free radicals are produced continuously through a number of cellular events including energy production, detoxification of the body, or exhaustive exercise [34], and these free radicals have the capacity to alter the integrity of numerous molecules such as lipids, proteins, and DNA [16]. In this regard, adopting healthier dietary habits to improve body antioxidant defenses must be considered important in the global maintenance of health. Our intervention yielded a 6% increase in total plasma antioxidant capacity, a measure that has been suggested to reflect the capacity of an individual to neutralize free radicals [35,36].

This increase in plasma antioxidant capacity is concordant with a recent study showing an increase in plasma flavonoid as well as phenolic and benzoic acid concentrations after cranberry juice consumption [37]. Surprisingly, the increase in plasma antioxidant capacity noted in the present study was not associated with the decrease in circulating OxLDL concentrations. It is known [37] that

after cranberry juice consumption, there is a rapid degradation of dietary and possibly active flavonoids in plasma. Because antioxidant capacity is a fasting measurement, it may not represent the active antioxidant molecule and thus could explain the lack of association between change in plasma antioxidant capacity and OxLDL levels.

Obesity and especially a preferential accumulation of fat in the abdominal region have been suggested to be associated with a state of oxidative stress, depletion of antioxidant reserves, and oxidative modifications of plasma lipoproteins and lipids [38]. We found a positive association between waist circumference and plasma OxLDL concentrations. A reduction of abdominal fat accumulation cannot, however, be considered as an explanation for the lower OxLDL levels at the end of the intervention, as no change in waist circumference nor WHR was noted. Although subjects were instructed to maintain their usual dietary habits during the course of the intervention, spontaneous changes in the diet of the subjects could also explain our observations. Unfortunately, this issue could not be addressed in our study because nutritional information was only collected at baseline. Thus, our understanding of the present observations is that antioxidants present in cranberry juice are most likely responsible for the reduction in plasma OxLDL levels in men of our study. However, the exact physiological mechanisms by which such an effect takes place remain to be determined.

Although previous reports had suggested that cranberries could have LDL cholesterol lowering and HDL cholesterol raising effects [39], our intervention is not supportive of such an effect as no change in either plasma LDL cholesterol or HDL cholesterol concentrations was noted. The discrepancies between results from these previous studies and the present one could be explained by the short duration of the intervention. Indeed, the favorable impact of cranberry juice on LDL cholesterol and HDL cholesterol concentrations was noted after 4- and 12-week interventions. The lack of effect noted in our study is, however, concordant with a previous 2-week study investigating the effect of flavonoid-rich purple grape juice on plasma lipids [40].

The cross-sectional analysis of the baseline data also allowed us to investigate the metabolic alterations that could be associated with the presence of high plasma OxLDL levels. We found that abdominally obese–dyslipidemic individuals are most likely to show high circulating concentrations of OxLDL. As OxLDL plays an important role in atherogenesis [5,41-43] and has been associated with CVD risk [44], our observations could provide further insights into the increased CVD risk noted in the abdominally obese population [45]. Furthermore, monounsaturated fatty acids have been shown to reduce LDL oxidation compared with saturated and polyunsaturated fatty acids [46]. In the present study, we found no association between either the absolute or relative consumption of saturated fatty acids, monounsaturated fatty acids, or polyunsaturated fatty acids and plasma OxLDL concentrations at baseline. However, we found that a greater consumption of glucose, fructose, and galactose was associated with low plasma OxLDL levels. Because these carbohydrates mostly come from fruits and dairy products, our observations are concordant with the health benefits than can be retrieved from consuming these foods [47].

In summary, the present study shows that regular cranberry juice consumption is associated with a reduction in plasma OxLDL concentrations and increase in plasma antioxidant reserves. Further studies are needed to confirm the physiological relevance of these observations. It must be pointed out that the absence of a placebo group is an important limitation of our study. However, the information obtained through our intervention warrants the conduction of further studies on the importance of consuming antioxidant-rich foods in maintaining health and preventing chronic diseases.

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References

[1] American Heart Association. Heart disease and stroke statistics—2005 update. Dallas (Tex): American Heart Association; 2005.
[2] Ross R. Atherosclerosis—an inflammatory disease. N Engl J Med 1999;340:115-26.
[3] Genest JJ, McNamara JR, Salem DN, Schaefer EJ. Prevalence of risk factors in men with premature coronary artery disease. Am J Cardiol 1991;67:1185-9.
[4] Sniderman AD, Bergeron J, Frohlich J. Apolipoprotein B versus lipoprotein lipids: vital lessons from the AFCAPS/TexCAPS trial. CMAJ 2001;164:44-7.
[5] Tsimikas S, Witztum JL. Measuring circulating oxidized low-density lipoprotein to evaluate coronary risk. Circulation 2001;103:1930-2.
[6] Tsimikas S, Palinski W, Witztum JL. Circulating autoantibodies to oxidized LDL correlate with arterial accumulation and depletion of oxidized LDL in LDL receptor-deficient mice. Arterioscler Thromb Vasc Biol 2001;21:95-100.
[7] Tsimikas S. Noninvasive imaging of oxidized low-density lipoprotein in atherosclerotic plaques with tagged oxidation-specific antibodies. Am J Cardiol 2002;90:22L-7L.
[8] Tsimikas S, Shaw PX. Non-invasive imaging of vulnerable plaques by molecular targeting of oxidized LDL with tagged oxidation-specific antibodies. J Cell Biochem Suppl 2002;39:138-46.
[9] Gaziano JM, Manson JE, Buring JE, Hennekens CH. Dietary antioxidants and cardiovascular disease. Ann N Y Acad Sci 1992; 669:249-58 [discussion 258-249].

[10] Steinberg D, Parthasarathy S, Carew TE, Khoo JC, Witztum JL. Beyond cholesterol. Modifications of low-density lipoprotein that increase its atherogenicity. N Engl J Med 1989;320:915-24.
[11] Urso ML, Clarkson PM. Oxidative stress, exercise, and antioxidant supplementation. Toxicology 2003;189:41-54.
[12] Parthasarathy S, Santanam N, Ramachandran S, Meilhac O. Oxidants and antioxidants in atherogenesis. An appraisal. J Lipid Res 1999; 40:2143-57.
[13] Aviram M. Review of human studies on oxidative damage and antioxidant protection related to cardiovascular diseases. Free Radic Res 2000;33(Suppl):S85-S97.
[14] Libby P. Inflammation in atherosclerosis. Nature 2002;420:868-74.
[15] Duthie GG, Bellizzi MC. Effects of antioxidants on vascular health. Br Med Bull 1999;55:568-77.
[16] Catapano AL, Maggi FM, Tragni E. Low density lipoprotein oxidation, antioxidants, and atherosclerosis. Curr Opin Cardiol 2000;15:355-63.
[17] Bassuk SS, Albert CM, Cook NR, Zaharris E, MacFadyen JG, Danielson E, et al. The women's antioxidant cardiovascular study: design and baseline characteristics of participants. J Womens Health (Larchmt) 2004;13:99-117.
[18] Eder K, Flader D, Hirche F, Brandsch C. Excess dietary vitamin E lowers the activities of antioxidative enzymes in erythrocytes of rats fed salmon oil. J Nutr 2002;132:3400-4.
[19] Pietta PG. Flavonoids as antioxidants. J Nat Prod 2000;63:1035-42.
[20] Aviram M, Fuhrman B. Polyphenolic flavonoids inhibit macrophage-mediated oxidation of LDL and attenuate atherogenesis. Atherosclerosis 1998;137(Suppl):S45-S50.
[21] Hakkinen SH, Karenlampi SO, Heinonen IM, Mykkanen HM, Torronen AR. Content of the flavonols quercetin, myricetin, and kaempferol in 25 edible berries. J Agric Food Chem 1999;47:2274-9.
[22] Zheng W, Wang SY. Oxygen radical absorbing capacity of phenolics in blueberries, cranberries, chokeberries, and lingonberries. J Agric Food Chem 2003;51:502-9.
[23] Fuhrman B, Aviram M. Flavonoids protect LDL from oxidation and attenuate atherosclerosis. Curr Opin Lipidol 2001;12:41-8.
[24] Kontiokari T, Sundqvist K, Nuutinen M, Pokka T, Koskela M, Uhari M. Randomised trial of cranberry-lingonberry juice and Lactobacillus GG drink for the prevention of urinary tract infections in women. BMJ 2001;322:1571.
[25] van der Kooy K, Seidell JC. Techniques for the measurement of visceral fat: a practical guide. Int J Obes Relat Metab Disord 1993;17:187-96.
[26] Moorjani S, Dupont A, Labrie F, Lupien PJ, Brun D, Gagne C, et al. Increase in plasma high-density lipoprotein concentration following complete androgen blockage in men with prostatic carcinoma. Metabolism 1987;36:244-50.
[27] Burstein M. Determination of cholesterol in the alpha- and beta-lipoproteins of the serum by a method based on selective precipitation of beta-lipoproteins. Pathol Biol (Paris) 1960;8:1247-9.
[28] Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972; 18:499-502.
[29] St-Pierre AC, Ruel IL, Cantin B, Dagenais GR, Bernard PM, Despres JP, et al. Comparison of various electrophoretic characteristics of LDL particles and their relationship to the risk of ischemic heart disease. Circulation 2001;104:2295-9.
[30] Miller NJ, Rice-Evans C, Davies MJ, Gopinathan V, Milner A. A novel method for measuring antioxidant capacity and its application to monitoring the antioxidant status in premature neonates. Clin Sci (Lond) 1993;84:407-12.
[31] Holvoet P, Vanhaecke J, Janssens S, Van de Werf F, Collen D. Oxidized LDL and malondialdehyde-modified LDL in patients with acute coronary syndromes and stable coronary artery disease. Circulation 1998;98:1487-94.
[32] Goulet J, Nadeau G, Lapointe A, Lamarche B, Lemieux S. Validity and reproducibility of an interviewer-administered food frequency questionnaire for healthy French-Canadian men and women. Nutr J 2004;3:13.
[33] Sun J, Chu YF, Wu X, Liu RH. Antioxidant and antiproliferative activities of common fruits. J Agric Food Chem 2002;50: 7449-54.
[34] Moller P, Wallin H, Knudsen LE. Oxidative stress associated with exercise, psychological stress and life-style factors. Chem Biol Interact 1996;102:17-36.
[35] Miller NJ, Rice-Evans C, Davies MJ. A new method for measuring antioxidant activity. Biochem Soc Trans 1993;21:95S.
[36] Pedersen CB, Kyle J, Jenkinson AM, Gardner PT, McPhail DB, Duthie GG. Effects of blueberry and cranberry juice consumption on the plasma antioxidant capacity of healthy female volunteers. Eur J Clin Nutr 2000;54:405-8.
[37] Zhang K, Zuo Y. GC-MS determination of flavonoids and phenolic and benzoic acids in human plasma after consumption of cranberry juice. J Agric Food Chem 2004;52:222-7.
[38] Vasankari T, Fogelholm M, Kukkonen-Harjula K, Nenonen A, Kujala U, Oja P, et al. Reduced oxidized low-density lipoprotein after weight reduction in obese premenopausal women. Int J Obes Relat Metab Disord 2001;25:205-11.
[39] Reed J. Cranberry flavonoids, atherosclerosis and cardiovascular health. Crit Rev Food Sci Nutr 2002;42:301-16.
[40] Freedman JE, Parker III C, Li L, Perlman JA, Frei B, Ivanov V, et al. Select flavonoids and whole juice from purple grapes inhibit platelet function and enhance nitric oxide release. Circulation 2001; 103:2792-8.
[41] Kita T, Kume N, Minami M, Hayashida K, Murayama T, Sano H, et al. Role of oxidized LDL in atherosclerosis. Ann N Y Acad Sci 2001;947:199-205 [discussion 205-916].
[42] Holvoet P, Harris TB, Tracy RP, Verhamme P, Newman AB, Rubin SM, et al. Association of high coronary heart disease risk status with circulating oxidized LDL in the well-functioning elderly: findings from the Health, Aging, and Body Composition study. Arterioscler Thromb Vasc Biol 2003;23:1444-8.
[43] Ehara S, Ueda M, Naruko T, Haze K, Itoh A, Otsuka M, et al. Elevated levels of oxidized low density lipoprotein show a positive relationship with the severity of acute coronary syndromes. Circulation 2001;103:1955-60.
[44] Holvoet P, Kritchevsky SB, Tracy RP, Mertens A, Rubin SM, Butler J, et al. The metabolic syndrome, circulating oxidized LDL, and risk of myocardial infarction in well-functioning elderly people in the health, aging, and body composition cohort. Diabetes 2004; 53:1068-73.
[45] Despres JP. Health consequences of visceral obesity. Ann Med 2001;33:534-41.
[46] Kratz M, Cullen P, Kannenberg F, Kassner A, Fobker M, Abuja PM, et al. Effects of dietary fatty acids on the composition and oxidizability of low-density lipoprotein. Eur J Clin Nutr 2002; 56:72-81.
[47] Ness AR, Powles JW. Fruit and vegetables, and cardiovascular disease: a review. Int J Epidemiol 1997;26:1-13.