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Berries: emerging impact on cardiovascular health

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Abstract

Berries are a good source of polyphenols, especially anthocyanins, micronutrients, and fiber. In epidemiological and clinical studies, these constituents have been associated with improved cardiovascular risk profiles. Human intervention studies using chokeberries, cranberries, blueberries, and strawberries (either fresh, or as juice, or freeze-dried), or purified anthocyanin extracts have demonstrated significant improvements in LDL oxidation, lipid peroxidation, total plasma antioxidant capacity, dyslipidemia, and glucose metabolism. Benefits were seen in healthy subjects and in those with existing metabolic risk factors. Underlying mechanisms for these beneficial effects are believed to include upregulation of endothelial nitric oxide synthase, decreased activities of carbohydrate digestive enzymes, decreased oxidative stress, and inhibition of inflammatory gene expression and foam cell formation. Though limited, these data support the recommendation of berries as an essential fruit group in a heart-healthy diet.

Keywords

anthocyanins; berries; inflammation; lipid peroxidation; nitric oxide

INTRODUCTION

Consumption of fruits and vegetables has been correlated with decreased risks of cardiovascular disease (CVD). National health objectives reflected in *Healthy People 2010* advocate increasing fruit consumption by more than 75% or to at least two servings per day in persons 2 years of age and older.[1] Currently, only 32% of adults and 13% of adolescents meet this goal of fruit intake.[2,3] Between the years 2000 and 2020 overall fruit consumption in the United States is anticipated to grow by 24–27%. This increase is attributed in part to an increase in per capita consumption, and in part to a predicted increase in the total consumers in the US market.[4]

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The consumption of berry fruits and their contribution to improving cardiovascular health is a subject of considerable interest. The commonly consumed berries in the United States include blackberry, black raspberry, blueberry, cranberry, red raspberry, and strawberries. Less commonly consumed berries include acai, black currant, chokeberry, and mulberries. Berries are low in calories and are high in moisture and fiber. They contain natural antioxidants such as vitamins C and E, andmicronutrients such as folic acid, calcium, selenium, alpha and beta carotene, and lutein. Phytochemicals found in berries include polyphenols along with high proportions of flavonoids including anthocyanins and ellagitannins. Table 1 lists the commonly consumed berries and their selected nutrient and phytochemical composition as identified in the USDA food composition database.[5,6] Anthocyanins comprise the largest group of natural, water-soluble, plant pigments and impart the bright colors to berry fruits[7–10] and to flowers. Approximately 400 individual anthocyanins have been determined. They are generally more concentrated in the skins of fruits, especially berry fruits. However, red berry fruits, such as strawberries and cherries, also have anthocyanins in their flesh. Anthocyanin content is usually proportional to the color intensity and can range from 2 to 4 g/kg, increasing as the fruit ripens. Evidence suggests that Americans consume an average of 12.5–215 mg of anthocyanins per day.[11] Studies have shown that berry anthocyanins are poorly bioavailable, are extensively conjugated in the intestines and liver, and are excreted in urine within 2–8 hours post consumption.[12,13] Post-harvest processing, such as pressing, pasteurization, and conventional and vacuum drying, can significantly affect the polyphenol (including anthocyanin) and vitamin content of berries, and therefore their bioactivities and effects on CVD risk factors.[14–16]

EPIDEMIOLOGICAL OBSERVATIONS: BERRIES IN CARDIOVASCULAR HEALTH

Nutritional epidemiology provides convincing evidence of the cardioprotective effects of frequent consumption of fruits and vegetables high in fiber, micronutrients, and several phytochemicals.[17–20] Data reported from the INTERHEART study, comprising dietary patterns from 52 countries, revealed a significant inverse association between the prudent dietary pattern high in fruits and vegetables, and risk of acute myocardial infarction.[21] Evaluation of selected nutrients and food group intakes among 2,757 overweight US adults diagnosed with type 2 diabetes, which is an established risk factor of CVD, showed that less than 50% of subjects consumed the minimum recommended servings of fruits and vegetables.[22] A comparative study between the US and French populations revealed significantly lower fruit and vegetable consumption among American men and women versus French adults.[23] Analyses of 24-h recall data from the National Health and Nutrition Examination Survey (NHANES), 1999–2000, revealed that only 40% of Americans consumed five or more servings of fruits and vegetables per day.[24] These data indicate a significant gap between the actual amounts of fruit and vegetable consumption and the recommended number of servings for the US population.[25] Furthermore, NHANES (2001–2002) data reported the pattern of fruit intake among US adults, who mainly consumed apples, pears, and bananas, followed by melons, citrus fruits, and grapes.[26] Thus, berries do not seem to be commonly consumed fruits by the US population in spite of their benefits, as documented in emerging nutrition and health research.

Studies have also reported specific associations between berries or berry flavonoids (anthocyanins) and cardiovascular health. Data reported from the Kuopio Ischemic Heart Disease Risk Factor Study (KIHD) showed a significantly lower risk of CVD-related deaths among 1,950 men in the highest quartile of berry intake (>408 g/day) versus men with the lowest intake (<133 g/day) during a mean follow-up of 12.8 years. These findings were based on a model adjusted for major CVD risk factors, which further showed an inverse

correlation between intakes of fruits, berries, and vegetables and serum haptoglobin, a marker of inflammation.[27] Post-menopausal women (n = 34,489) participating in the Iowa Women's Health Study, showed a significant reduction in CVD mortality associated with strawberry intake during a 16-year follow-up period. In the case of blueberries, an age- and energy-adjusted model showed a significant decrease in coronary heart disease mortality, though the significance did not persist following adjustment for other confounding variables. For both strawberries and blueberries, the significant reduction in relative risk was associated with at least once per week consumption. The data also reported that a mean anthocyanin intake of 0.2 mg/day was associated with a significantly reduced risk of CVD mortality in these postmenopausal women.[28]

Female US health professionals enrolled in the Women's Health Study (n = 38,176), a randomized controlled trial of low-dose aspirin and vitamin E, provided dietary information using a 131-item validated semi-quantitative food frequency questionnaire. Strawberry intake was described as "never" or "less than one serving per month" up to"6+ servings per day" of fresh, frozen, or canned strawberries. Analyses of baseline strawberry intake revealed that only 7.7% of subjects consumed greater than two servings of strawberries per week, whereas 42% of subjects reported an intake of 1–3 servings per month. During a follow-up period of approximately 11 years, a decreasing trend for CVD was observed for subjects consuming higher amounts of strawberries (P = 0.06). The study also showed a borderline significant risk reduction of elevated C-reactive protein (CRP) levels (≥3 mg/L) among women consuming higher amounts of strawberries (≥2 servings/week). Blueberry intake was also examined in the study and no significant association was reported with risks of CVD or CRP.[29] Elevated CRP has been significantly associated with inflammation and is a high risk factor of CVD.[30] Analyses of NHANES data (1999–2002) revealed a significant inverse association between serum CRP and anthocyanin intakes among US adults.[31] These observational data suggest a potential anti-inflammatory role of berry flavonoids, which may contribute to overall reduction of CVD risk.

BERRIES AND CARDIOVASCULAR HEALTH: INTERVENTION STUDIES

As summarized in Table 2, a number of intervention studies have investigated the effects of acai berries, black currants, bilberries, boysenberries, blueberries, chokeberries, cranberries, lingonberries, raspberries, strawberries, and wolfberries in healthy human subjects or in subjects with CVD risk factors.[32–51] The most significant outcomes of these clinical studies show an increase in plasma or urinary antioxidant capacity, a decrease in LDL oxidation and lipid peroxidation, a decrease in plasma glucose or total cholesterol, and an increase in HDL-cholesterol following berry intervention. Since elevated plasma glucose, lipids, and lipid oxidation have been associated with coronary artery disease (CAD),[52,53] these data suggest the potential role of edible berries in ameliorating these risk factors. Of 20 trials reviewed, nine involved measures of post-prandial status, in which berry consumption was shown to significantly decrease postprandial oxidative stress, especially lipid peroxidation.[32–35,37–39,42,48] Thus, dietary inclusion of berries may be an effective strategy to counteract postprandial metabolic and oxidative stresses that are associated with CAD.[54] In addition, specific berries, such as bilberry and black currant extracts, chokeberry juice, cranberry extracts, and freeze-dried strawberries were shown to have favorable effects on plasma glucose or lipid profiles in subjects with metabolic risk factors including type 1 or type 2 diabetes mellitus, dyslipidemia, or metabolic syndrome.[37,47,50,51] These studies ranged in duration from 4 to 12 weeks and used conventional berry products or purified anthocyanin extracts, suggesting that both these forms of delivery are effective. Berries were also shown to increase plasma antioxidant capacity[36] and to decrease lipid peroxidation[42] in smokers who are at high risk of developing CVD.[55]

Of 20 trials conducted using different varieties of fresh and processed berry products, only two showed a significant decrease in systolic blood pressure: one was conducted in healthy men following cranberry juice supplementation[46] and the other was in subjects with CVD risk factors following mixed berry supplementation.[49] These data suggest a need for future studies on berry supplementation as a potential dietary therapy for the management of pre-hypertension or hypertension. Interestingly, none of these clinical studies showed any significant effect of berry intervention on biomarkers of inflammation, with the exception of a significant decrease in adhesion molecules following cranberry juice supplementation in healthy volunteers.[46] This suggests a need to investigate the effects of cranberry intervention, per se or in combination with other berries, on adhesion molecules or inflammatory biomarkers such as C-reactive protein or interleukins in subjects with the pro-inflammatory conditions metabolic syndrome or diabetes mellitus.[56,57]

MECHANISMS: BERRIES, ENDOTHELIAL FUNCTION, AND ATHEROSCLEROSIS

Oxidative stress and inflammation play a pivotal role in the initiation and progression of atherosclerosis and CVD.[58,59] Several lines of evidence indicate a role for berry anthocyanins in significantly decreasing oxidative damage and inflammation in cellular and animal models of CVD. Youdim et al. have reported the incorporation of elderberry anthocyanins by endothelial cells, following a 4-h incubation at a concentration of 1 mg/mL. In addition to the cellular bioavailability, elderberry anthocyanins significantly decreased cytotoxicity caused by chemical inducers of oxidative stress.[60] Anthocyanins from blackberry extract were shown to protect against peroxynitrite-induced oxidative damage in human umbilical vein endothelial cells.[61] Mulberry anthocyanins have also exhibited antioxidative and antiatherogenic affects, by inhibiting oxidation of LDL and formation of foamcells, respectively, in an in vitro model of atherosclerosis.[62] Anthocyanins from berries commonly consumed in the United States, such as blueberries and cranberries, have been reported to reduce TNF-α induced upregulation of inflammatory mediators in human microvascular endothelial cells.[63] In an 8-week study, DeFuria et al. have shown the attenuation of inflammatory gene expressions in male C57Bl/6j mice fed a high-fat diet supplemented with blueberry powder versus the unsupplemented group. This study also showed the protective effects of blueberries against insulin resistance and hyperglycemia, thus reducing the risk factors for CVD.[64] In a rat model of prediabetes and hyperlipidemia, Jurgoski et al.[65] further demonstrated decreased activities of inńtestinal mucosal disaccharidases (maltase and sucrose) following dietary supplementation with chokeberry fruit extract for 4 weeks. These animal and in vitro data show the potential of berries to ameliorate inflammation, glucose, and lipid abnormalities that contribute to CVD.

Nitric oxide (NO), when formed through activation of inducible nitric oxide synthase (iNOS), has proinflammatory effects, leading to increased vascular permeability, induction of inflammatory cytokines, and the formation of peroxynitrite, a strong oxidizing agent.[66] Pergola et al. have reported inhibitory effects of the anthocyanin fraction of blackberry extract on NO biosynthesis in the murine monocyte/macrophage J774 cell line stimulated with lipopolysaccharide. The study also reported that blackberry anthocyanin extract inhibited inducible iNOS protein expression, thereby decreasing the inflammatory response in macrophages and inhibiting the formation of foam cells.[67] While increased iNOS expression leads to the proinflammatory effects of NO, generation of NO by endothelial nitric oxide synthase (eNOS) plays a crucial role in maintaining cardiovascular homeostasis by favorably modulating blood pressure and reducing endothelial dysfunction. Xu et al. and Lazze et al. have reported the upregulation of eNOS by cyanidin-3-glucoside in bovine artery endothelial cells, and increased protein levels of eNOS by anthocyanin treatment (cyanidin and delphinidin) in human umbilical vein endothelial cells.[68,69]

Berry anthocyanins have also been shown to affect lipid metabolism in cellular and animal models of dyslipidemia. Administration of chokeberry juice for 30 days in rats fed a standard or 4% cholesterol-containing diet, showed the anti-hyperlipidemic effects of chokeberry juice in the cholesterol-fed group.[70] Purified anthocyanins from blueberries and strawberries added to drinking water were shown to prevent the development of dyslipidemia and obesity in mice fed a high-fat diet for a period of 90 days.[71] Anthocyanin treatment of human umbilical vein endothelial cells was further demonstrated to regulate cholesterol distribution by interfering with the recruitment of tumor necrosis factor receptor-associated factors (TRAF)-2 in lipid rafts, thereby inhibiting CD40-induced proinflammatory signaling.[72]

Thus, on the basis of these data, berry anthocyanins may exert cardioprotective effects by reducing oxidative stress and inflammation through effects on iNOS activity, interfering with carbohydrate digestion and reducing glucose absorption, favorably modulating dyslipidemia, and upregulating eNOS expression so as to maintain normal vascular function and blood pressure.

CONCLUSION

Berries are emerging as a dietary source of multiple compounds and nutrients, including anthocyanins, flavonols, vitamins, and fiber, that reduce CVD risk. While limited epidemiological data inversely associate consumption of berries with inflammation and CVD, these conclusions need to be strengthened in future case-control or cohort studies investigating the long-term health benefits of berries in specific populations. Clinical studies in healthy humans, subjects with diabetes mellitus, dyslipidemia, metabolic syndrome, hypertension, or in smokers, show a significant decrease in CVD risk factors, especially glucose, lipids and lipid peroxidation, and systolic blood pressure, following berry intervention. The principal mechanisms of action underlying the potential cardio-protective effects of berries include counteracting free radical generation, attenuating inflammatory gene expression, downregulating foam cell formation, and upregulating eNOS expression; through these effects, progression of atherosclerosis is slowed and normal vascular function and blood pressure are preserved. In light of the decrease in nutritional value that occurs during processing methods, including drying and pasteurization, consumption of fresh or frozen whole berries as part of a regular diet may be better than intake of juices or extracts, which do not have the same nutritional profiles as whole berries. Since some clinical studies have also found antidiabetic and antihyperlipidemic effects of encapsulated berry supplements, these forms may be suitable for the management of specific metabolic conditions.

Further rigorous, prospective studies are needed. These need to involve large patient populations with outcomes of berry intervention that include not only CVD biomarkers, but also “hard” cardiovascular and metabolic endpoints. Also, comparative human intervention studies should address the effects of whole berries versus purified berry anthocyanins, and any potential synergistic actions with other nutrients or medications. Such studies are readily conceived but expensive and challenging to conduct.

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Table 1

Berries with select nutrient and phytochemical profiles expressed in values per 100 g of edible portion.[5,6]

Fruit	Total anthocyanidin content (mg)*	Total flavan-3-ols (mg)†	Total flavonols (mg)‡	Calories (kcal)	Fiber (g)	Vitamin C (mg)	Vitamin E (mg)
Blackberry	90.46	42.5	2.49	43	5.3	21	1.17
Blueberry	163.52	51.71	9.72	57	2.4	9.7	0.57
Bilberry	430.91	4.13	NF	NF	NF	NF	NF
Chokeberry, raw	437.22	NF	8.90	NF	NF	NF	NF
Cranberry juice (unsweetened)	NF	0.92	20.82	46	0.1	9.3	1.20
Cranberry juice cocktail	0.46	0.19	1.79	54	NF	42.3	0.22
Cranberry (dried, sweetened)	0.72	NF	6.91	NF	NF	NF	NF
Cranberry sauce (canned, sweetened)	0.14	NF	5.11	151	1.0	2.0	0.83
Currant, black, raw	272.44	1.17	12.69	63	NF	181	1.0
Mulberries, raw	NF	NF	2.47	43	1.7	36.4	0.87
Black raspberry	324.02	NF	NF	NF	NF	NF	NF
Red raspberry (raw)	38.68	6.63	1.32	52	6.5	26.2	0.87
Strawberry	33.63	4.51	1.6	32	2.0	58.5	0.29

*Total anthocyanidins (cyanidin, delphinidin, peonidin, petunidin).

†Total flavan-3-ols [(−)-epicatechin, (−)-epicatechin 3-gallate, (−)-epigallocatechin, (−)-epigallocatechin 3 gallate, (+)-catechin, (+)-gallocatechin].

‡Total flavonols (kaempferol, myricetin, quercetin).

Abbreviation: NF, not found in the USDA food composition database.

Table 2

Summary of berry intervention trials.

Reference	Duration	Study design	Study subjects	Control	Berry intervention	Significant findings
Cao et al. (1998)[32]	Postprandial	Controlled trial	Eight healthy female subjects (mean age, 67 ± 0.6 years)	Coconut drink	240 g strawberries added to the control drink	Increase in plasma vitamin C, serum and urine antioxidant capacity ($P < 0.05$)
Paiva et al. (1998)[33]	Postprandial	Controlled trial	Seven healthy elderly women (mean age, 67 ± 0.6 years)	378 mL coconut drink	240 g fresh, whole, and homogenized strawberries added to the control drink	Decreased plasma carotenoids versus baseline ($P < 0.02$)
Marniemi et al. (2000)[34]	Eight weeks and postprandial	Randomized controlled trial	Sixty healthy adults (mean age, 60 years)	500 mg calcium gluconate	100 g deep-frozen berries (bilberries, lingonberries, or black currants); 240 g berries in postprandial study	Increase in serum ascorbate ($P < 0.05$); slight decrease in LDL oxidation ($P = 0.07$), and slight increase in serum antioxidant capacity ($P = 0.08$) in berry group; decrease in LDL oxidation in postprandial study ($P < 0.05$)
Pedersen et al. (2000)[35]	Postprandial	Randomized controlled trial	Nine healthy female volunteers (mean age, 31 ± 2 years)	9% (w/v) sucrose in water (500 mL)	500 mL blueberry juice (Beutelsbacher, Germany) or cranberry juice (Ocean Spray, UK)	Increase in plasma antioxidant capacity, vitamin C and phenols with cranberry juice ($P < 0.05$); no effects with blueberry juice
Van den Berg et al. (2001)[36]	Three weeks with a two-week washout period	Randomized controlled crossover trial	Twenty-two male smokers (mean age, 33 ± 11 years)	Control drink (330 mL)	Fruit drink (330 mL); 30% clarified blueberry juice concentrate (SVZ International, the Netherlands)	Increase in vitamin C, carotenoids, and plasma antioxidant capacity with fruit drink ($P < 0.05$)
Simeonov et al. (2002)[37]	Three months and postprandial	Baseline and post intervention effects	Sixty-two patients with type 1 or 2 diabetes mellitus (median age, 46.2 ± 4.04 years)	None	200 mL chokeberry juice (*Aronia melanocarpa*)	Decrease in fasting glucose, HbA_{1C}, and lipids ($P < 0.001$) in the three-month intervention
Kay and Holub (2002)[38]	Postprandial phases, one week apart	Single-blind crossover study	Eight middle-aged male subjects (mean age, 47 ± 2 years)	High-fat meal (McDonald's Corp.)	High-fat meal supplemented with 100 g freeze-dried wild blueberry powder	Increase in serum antioxidant status ($P < 0.05$)
Mazza et al. (2002)[39]	Postprandial phases, one week apart	Single-blind crossover study	Five male subjects (mean age, 47 ± 2 years)	High-fat meal (McDonald's Corp.)	High-fat meal supplemented with 100 g freeze-dried wild blueberry powder	Increase in serum antioxidant status ($P < 0.05$)
Bub et al. (2003)[40]	Ten weeks	Randomized crossover study	Twenty-seven non-smoking men (mean age, 35 ± 4 years)	None	Anthocyanin-rich juice containing aronia, blueberries, and boysenberries in a mixture of apple, mango, and orange juice (76% w/w water); 330 ml/day	Decrease in plasma TBARS; decrease in oxidative DNA damage in lymphocytes ($P < 0.05$)

Reference	Duration	Study design	Study subjects	Control	Berry intervention	Significant findings
Chambers and Camire (2003)[41]	Twelve weeks	Randomized controlled trial	Twenty-seven adults with type 2 diabetes (mean age, 56 ± 13 years)	Colored powder as placebo capsules (6 capsules/day)	Cranberry juice concentrate powder (6 capsules/day)	No effect on fasting glucose, lipids, or HbA_{1C} ($P > 0.05$)
McAnulty et al. (2005)[42]	Three weeks or postprandial	Randomized controlled trial	Twenty smokers (mean age: blueberry group, 26 ± 3.3; control group, 29 ± 4.2 years)	Usual diet and lifestyle with restriction of large amounts of fruits and vegetables and all vitamin supplements	Acute or daily consumption of 250 g blueberries	Decrease in lipid hydroperoxides in blueberry group versus control at 3 weeks ($P < 0.001$)
Ruel et al. (2005)[43]	Fourteen days	Baseline and post-intervention effects	Twenty-one healthy men (mean age, 38 ± 8 years)	None	7 mL/kg body weight cranberry juice per day (Ocean Spray's Light Cranberry Juice, Ocean Spray Cranberries, Inc., USA)	Decrease in plasma ox-LDL ($P < 0.05$); increase in plasma antioxidant capacity ($P < 0.05$) at 14 days
Ruel et al. (2006)[44]	Four successive 4-week phase (including 4-week run-in phase)	Placebo-controlled trial	Thirty healthy men (mean age, 51 ± 10 years)	Placebo juice (Ocean Spray Cranberries, Inc., USA); 500 mL/day	Increasing doses of cranberry juice cocktail (125, 250, 500 mL/day, Ocean Spray Cranberries, Inc., USA) during three successive 4-week periods	Increase in plasma HDL-cholesterol at the end of 4 weeks of 250 mL/day cranberry juice intake ($P < 0.01$); decreases in body weight, BMI, and waist circumference at the end of the study ($P < 0.05$)
Duthie et al. (2006)[45]	Two weeks	Randomized controlled trial	Twenty healthy female volunteers (mean age, 28 ± 7 years)	Natural mineral water with strawberry flavor + sucrose (9 g/ 100 mL); 750 mL/day	Cranberry juice (Ocean Spray Cranberry Select, UK); 750 mL/day (3 × 250 mL)	No effects on blood or cellular antioxidant status, lipid status, or oxidative DNA damage in cranberry group versus placebo ($P > 0.05$)
Ruel et al. (2008)[46]	Sixteen weeks	Successive 4-week phases of increasing dose of cranberry juice	Thirty healthy men (mean age, 51 ± 10 years)	Placebo juice; cranberry flavored and low calorie (500 ml/day for 4 weeks)	125, 250, and 500 mL/day cranberry juice cocktail (Ocean Spray Cranberries, Inc., USA); each dose for 4 weeks	Decrease in plasma ox-LDL, adhesion molecules (ICAM, VCAM), and systolic blood pressure following cranberry intervention at 12 or 16 weeks ($P < 0.05$)
Lee et al. (2008)[47]	Twelve weeks	Randomized, placebo-controlled, double-blind study	Thirty type 2 diabetic subjects (mean age, 65 ± 1 years)	Placebo capsules (3/day)	Cranberry extract powder; 500 mg/ capsule; 3 capsules/ day (Triarco Industries Inc., USA)	Decrease in total and LDL-cholesterol and total:HDL-cholesterol ratio in cranberry versus placebo groups ($P < 0.05$); no effects on glucose or glycated hemoglobin
Jensen et al. (2008)[48]	Postprandial	Randomized, double-blind, placebo-controlled, crossover trial	Twelve healthy subjects (mean age, 19–52 years)	Placebo capsules (0.5 g each) prepared by mixing white potato flakes with a purplish food-coloring blend, redrying, grinding, and providing in vegetable-based capsules	120 mL juice blend containing acai berry, cranberry, blueberry, wolfberry, and bilberry in addition to other fruit juices	Increase in serum antioxidant status and inhibition of lipid peroxidation versus placebo ($P < 0.03$)

Reference	Duration	Study design	Study subjects	Control	Berry intervention	Significant findings
Erlund et al. (2008)[49]	8 weeks	Randomized, single-blind, placebo-controlled, trial	72 subjects with cardiovascular risk factors (mean age: control group, 58.4 ± 5.6 years; berry group, 57.5 ± 6.3 years)	One of four control products each day to match the energy intake in the berry group; 2 dL sugar-water, 100 g sweet semolina porridge, 100 g sweet rice porridge, or 40 g marmalade sweets	Two portions of berries daily; whole bilberries (100 g) and a nectar of 50 g crushed lingonberries every other day; black currant or strawberry puree (100 g, 80% black currants) and cold-pressed chokeberry and raspberry juice (0.7 dL, 80% chokeberry) on alternating days	Inhibition of platelet function; increase in HDL-cholesterol; decrease in systolic blood pressure in berry versus control group ($P < 0.05$)
Qin et al. (2009)[50]	12 weeks	Randomized, double-blind, placebo-controlled, trial	120 subjects with dyslipidemia (mean age: placebo group, 55.1 ± 5.4 years; anthocyanin group, 55.3 ± 5.0 years)	Placebo capsules pullulan and maltodextrin (2 capsules twice daily)	Anthocyanin capsules 320 mg/day (2 capsules twice daily); 17 different natural purified anthocyanins from bilberry and black currant	Increased HDL-cholesterol, decreased LDL-cholesterol, decreased mass and activity of plasma cholesteryl ester transfer protein in anthocyanin group versus placebo ($P < 0.05$)
Basu et al. (2009)[51]	Four weeks	Baseline and post-intervention effects	Sixteen women with metabolic syndrome (mean age, 51 ± 9.1 years)	None	50 g of freeze-dried strawberry powder as beverage (California Strawberry Commission, USA)	Decrease in total and LDL-cholesterol and lipid peroxidation at 4 weeks versus baseline ($P < 0.05$)

Abbreviations: ICAM, intracellular adhesion molecule; VCAM, vascular cell adhesion molecule; ox-LDL, oxidized LDL.