

PHYTONUTRIENTS OF BILBERRY FRUIT AND SASKATOON BERRY IN THE PREVENTION AND TREATMENT OF DYSLIPIDEMIA

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ABSTRACT

The epidemiologic studies from the recent years indicate that high consumption of foods rich in bioactive compounds has a positive effect on human health and could diminish the risk of numerous diseases, such as cancer, heart disease, stroke, Alzheimer's disease, diabetes, cataracts, and even diseases related to age. From all species of fruit, definitely consumption of berries due to its high content of bioactive constituents prevents the risk of cardiovascular disease, oxidative stress and diabetes. The primary phenolic compounds in berries are flavonoids, particularly the anthocyanins. They have potential preventative and therapeutic effects on many diseases such as cancers, inflammation and cardiovascular diseases, obesity, neurodegenerative pathologies, and muscular degeneration. Bilberry fruits have been an important part of local diets in many countries, including Slovakia. They are valued for their pleasant taste and aroma and are often processed into jams, preserves, juices, and alcoholic beverages. In the last two decades, the Saskatoon berry has been cultivated in many parts of the world for its suitability for various food products and due to its high content of nutrients and polyphenols. Cardiovascular disease (CVD) remains the world's leading cause of morbidity and mortality. Dyslipidemia, which results from one or more abnormalities of blood lipids metabolism, remains a major key factor for progression of CVD and leads to the development of atherosclerotic plaques. The aim of this review is to compare and summarize the research evidence on the potential of bilberries and saskatoon berries with an emphasis on recent studies in humans in improving cardiovascular risk factors especially dyslipidemia.

Key words: cardiovascular disease, lipid profile, bilberry, saskatoon berry, anthocyanins

INTRODUCTION

Phytonutrients or phytochemicals are natural bioactive compounds obtained from plants that perform specific biological activities and modify different physiological functions to improve general human health [10, 77]. The mechanisms of action for the various compounds, especially as related to reduced risk of disease in individuals, are not fully understood [8, 31, 90].

Fruits are rich sources of numerous classes of biologically active compounds [49, 89]. From all species of fruit, definitely consumption of berries due to its high content of bioactive constituents prevents the risk of numerous diseases, such as cancer, cardiovascular disease, Alzheimer's, diabetes, cataracts, and even diseases related to age [4, 5, 12, 32, 58, 65, 68, 75, 78, 30, 95, 96, 100]. They are considered to be a good source of phenolic compounds, especially flavonoids and phenolic acids,

which mostly contribute to their high antioxidant activity [5, 30, 78, 96]. Many of the health benefits, associated with berry fruits, may be linked to their high content of anthocyanins [54].

Bilberry (*Vaccinium myrtillus* L.) fruits have been an important part of local diets in many countries, including Slovakia. They are valued for their pleasant taste and aroma and are often processed into jams, preserves, juices, and alcoholic beverages. They are rich in anthocyanins which make for the intense dark purple coloration of the fruit, as well as all processed foods made from the berries. Their high market value is caused by their relatively difficult availability - bilberry bushes only grow in wild, montane areas. It is not possible to cultivate them due to very specific soil demands and the fruit harvesting is a tedious, tiring work, as it is done using either hands or small harvesting rakes [71, 94, 106].

In the last two decades, the saskatoon berry (*Amelanchier alnifolia*) has been cultivated in many

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parts of the world [84] for its suitability for various food products and due to its high content of nutrients and polyphenols [59]. Up to now saskatoon berry has been used as an ornamental plant species in Slovak and Czech Republic. Recently, the cultivation of *Amelanchier* combining decorative quality and high biological value of fruit has been gaining in popularity [46].

The aim of this review is to compare and summarize the research evidence on the potential of bilberries and saskatoon berries with an emphasis on recent studies in humans in improving cardiovascular risk factors especially dyslipidemia.

BOTANICAL NOMENCLATURE AND DEFINITION

Bilberry (*Vaccinium myrtillus* L.)

Among the colorful berries, *Vaccinium corymbosum* (called American the blueberry), and the wild-growing blueberry *Vaccinium myrtillus* L. (called bilberry) are popularly used in the human diet either fresh or in processed forms [19]. Both bilberries and blueberries belongs to the family Ericaceae, subfamily Vaccinoideae, genus *Vaccinium*, which includes approximately 450 species [33, 76, 79, 84, 85]. The bilberry (*Vaccinium myrtillus* L.) is a low-growing shrub native to northern Europe, but is now also found in parts of North America and Asia. Bilberry is also known as European blueberry, whortleberry, huckleberry and blaeberry. Bilberries are sometimes also called as blueberries because both have similar appearance and are close relatives, but the true blueberry is native to the United States [28, 29, 93]. These berries are very similar, but considerably differ from each other in some qualitative parameters, market availability and price [104].

Saskatoon berry (*Amelanchier alnifolia* Nutt.)

Saskatoon berry plant (*Amelanchier alnifolia* Nutt.) also referred to as saskatoon, chuckley pear, juneberry, western juneberry, serviceberry, pacific serviceberry, western serviceberry, alder-leaf shadbush, dwarf shadbush, prairie berry, and pigeon berry, is a type of tall shrub naturally growing in western regions of North America [46, 57, 87, 101], cultivated in many regions of the world [64]. Saskatoon berry is a native species of the North American plains. In the last two decades, his cultivation has expanded from North America to various countries in Asia and Europe, including Finland, Poland, and Czech Republic [102].

Although the Saskatoon berry appears similar to the blueberry, they are more closely related to the apple family and belong to the family *Rosacea* [34,

50, 57]. Other fruits belonging to *Rosaceae* family include apples, pears, prunes, plums, cherries, apricots, strawberries, raspberries and blackberries [63]. The fruit is a berry-like pome, red to purple to nearly black at maturity, 5–15 mm in diameter, insipid to delectably sweet, maturing at the end of June/beginning of July [63, 87].

NUTRITIONAL VALUE OF BILBERRY FRUIT AND SASKATOON BERRY

The chemical composition and quality of berries are variable, qualitatively and quantitatively depending on numerous factors, e.g. cultivar, geographic origin, climatic conditions, maturity at harvest and storage conditions [23, 104].

Generally, 100 g of fresh *Vaccinium* berries contains water (84%), carbohydrates (9.7%), proteins (0.6%), fat (0.4%) and 0.3 g of ash [65, 78]. Similarly, chemical studies on saskatoon berries have shown that water is their major constituent followed by carbohydrates. They contain about 82–84% water, 15–20% sugar, small amounts of protein and fat [45, 46, 57, 59, 63, 64]. Mazza et al. [63] reported that saskatoon fruits are slightly lower in water content than blueberries (79.6% vs. 84.2%).

Dietary fibre content in blueberries and bilberries varies between 3–3.5% of fruit weight [48, 78], they contain pectin, hemicellulose, and cellulose, the hemicellulose being mostly xylan [35]. Likewise, saskatoon contains a fair amount of fiber [45, 46, 57, 59, 63, 64], fresh saskatoonberries contain more fiber than blueberries [21].

Vaccinium myrtillus contain relatively higher levels of organic acids (e.g., citric and ascorbic acids), [48, 68, 78]. Organic acids account for 0.5% of the fresh weight of ripe saskatoon berries [81]. A considerably high content of minerals (e.g., phosphorus, potassium, and magnesium) are also found in bilberries [48, 78]. Saskatoon contains relatively large amounts of potassium, iron, magnesium and phosphorous calcium, copper, manganese and potassium [45, 46, 57, 59, 61, 64]. On average, saskatoon berries have significantly higher iron, magnesium, potassium, calcium and phosphorus levels than blueberries [21].

The vitamins C, thiamin, riboflavin, pantothenic acid, nicotinamide and β -carotene have been reported in fresh bilberry fruit [69]. Vitamins found in saskatoon berries include ascorbic acid, thiamin, riboflavin, pantothenic acid, pyridoxine, folic acid, tocopherols [45, 57, 59, 63]. Although saskatoonberries are not one of the best sources of vitamins, their vitamin content is similar to that of blueberries [63]. In comparison with blueberries, saskatoon serviceberry fruits contain a higher content of thiamin, and riboflavin [63].

Many phenolic compounds have been identified in both bilberries and saskatoon berries and differences in their phenolic profiles have been observed and linked to numerous factors. [14, 64, 88]. The primary phenolic compounds in berries are flavonoids, particularly the anthocyanins (mainly cyanidins) [59, 63, 73, 88, 102]. Bilberry has higher anthocyanin content compared to other types of berries, such as strawberry, cranberry, elderberry and raspberry [2, 13, 15, 47, 51, 56]. The total anthocyanin concentration in saskatoon berry is comparable to that of wild blueberry and higher than that in other small fruited species such as raspberry, sea buckthorn, chokeberry, and strawberry [46, 102]. The total anthocyanin content of bilberry is generally in the range of 300-700 mg per 100 g fresh fruit, although this range varies with cultivar, growing conditions and degree of ripeness of the berry [9, 92]. The European wild-type bilberry is generally known to have a higher content of anthocyanins than blueberries [28, 29]. Anthocyanin content of saskatoon berries ranges from 25 to 179 mg/100 g of berries [63]. On the other hand, the studies of *Zatylny* et al. [101] proved that the anthocyanin content in 16 cultivars of saskatoons was not to as high as in blueberries.

The anthocyanins extracted from blueberries and bilberries so far are not unique in their chemistry and are generally of the 3-O-glycoside derivatives of cyanidin, delphinidin, malvidin, and petunidin [28, 29]. Among berries, the blueberry fruit stands out due to the presence of different types of anthocyanins, including malvidin, delphinidin, petunidin, cyanidin and peonidin, with the sugar moieties of glucose, galactose and arabinose [65]. The most common encountered in blueberry are malvidin and delphinidin and might constitute almost 75% of all identified anthocyanins [28, 29, 65]. There are at least four anthocyanins in ripe saskatoon berries of which cyanidin 3-galactoside and 3-glucoside account for about 61% and 21% of the total anthocyanins, respectively. Saskatoonberries contain a distinct spectrum of anthocyanins that is different from blueberries, the major components being cyanidin-3-galactoside, cyanidin-3-glucoside, cyanidin-3-arabinoside, and cyanidin-3-xyloside [3, 73]. All major saskatoonberry anthocyanins are cyanidin glycosides [21, 102].

Other groups of phenolics identified in bilberries are flavonols, flavan-3-ols, and hydroxycinnamic acids [14, 42, 55, 66, 67, 88], considerable amounts of stilbenes (resveratrol) [80] and catechin [20, 92]. Other phenolic compounds of saskatoon characterized include phenolic acids, including 3-feruloylquinic, chlorogenic, and 5-feruloylquinic acids [45, 57, 59, 81], rutin [73, 101] and different quercetin glycosides [46, 73, 84, 101].

BILBERRY AND SASKATOON BERRY IN THE PREVENTION AND TREATMENT OF DYSLIPIDEMIA

Because of the fruit's composition, mainly concerning the content of bioactive compounds, especially polyphenols, the berries can play a very beneficial antioxidant, anti-inflammatory, antitumor, hypoglycemic, antidiabetic, antiradical [3, 24, 46, 63, 82, 101], antifungal, anti-hypertensive, anti-allergic and antiviral role [61]. They have potential preventative and therapeutic effects on many diseases such as cancers, inflammation and cardiovascular diseases, obesity, neurodegenerative pathologies, and muscular degeneration [45, 54, 73].

Cardiovascular disease (CVD) remains the world's leading cause of morbidity and mortality [7, 62]. Although multiple risk factors for progression of CVD, dyslipidemia, which results from one or more abnormalities of blood lipids metabolism, remains a major key factor for this pathology and leads to the development of atherosclerotic plaques [44, 99]. Dyslipidemia is the imbalance of lipids such as cholesterol, low-density lipoprotein cholesterol, (LDL-C), triglycerides, and high-density lipoprotein (HDL-C) [74]. High HDL-C, triglyceride (TG) and low LDL-C concentrations are risk factors for cardiovascular diseases [36, 86]. Hypercholesterolemia was reported as the highest attributable risk factor for atherosclerosis and subsequent coronary heart disease (CHD) in a given population [22, 43]. LDL-C has now largely replaced total cholesterol (T-C) as the primary lipid measurement for evaluation of risk due to atherogenic lipoproteins. LDL-C is a measure of the T-C content of LDL particles, reflecting both the number of LDL particles and their individual cholesterol content [39]. A reduction in serum cholesterol is strongly associated with a reduction in CVD risk [83]. From a public health perspective, lifestyle modification, including dietary changes, is considered a first step in controlling and treating CVD risk factors [41].

Food rich to polyphenols are beneficial in the prevention of the cardiovascular diseases, they are connected with lower risk of stroke, ischemic heart disease, inflammatory markers and oxidation stress, type 2 diabetes even the diseases related to age and with it related memory impairment [31].

Some epidemiological studies suggest that anthocyanins attenuate the development of atherosclerotic cardiovascular diseases [16, 37, 103]. Anthocyanins are powerful antioxidants that can neutralize free radicals [11, 25, 40, 91]. In addition to their antioxidant effects, anthocyanins have been reported to suppress lipid peroxidation, stabilize DNA, modify adipocyte gene expression, improve

insulin secretion and sensitivity, and have anti-carcinogenic, anti-inflammatory, and antibacterial effects [53, 56, 84]. The most common forms of anthocyanin are cyanidin-3-glucoside, cyanidin-3-galactoside and delphinidin-3-glucoside. These three compounds interfere at multiple points in the progression of cardiovascular disease [37, 103].

From all species of fruit, definitely berries shows according to its high content of anthocyanins significant cardio-protective effect [4, 56, 65, 92]. Consumption of fresh bilberry has an important influence on the prophylaxis and progression of CVD due to its antioxidant properties and antiplatelet activity [16, 72]. Acute consumption of berries ameliorates postprandial glycemic response, improves profile of circulating inflammatory markers and increases antioxidative capacity of plasma. Long-term intake of berries and berry products may improve plasma lipid profile, reduce chronic inflammation and support cardiovascular health, especially in population with baseline metabolic profile of increased risk for metabolic syndrome [98]. The principal mechanisms of action underlying the potential cardioprotective effects of berries include counteracting free radical generation, attenuating inflammatory gene expression, down-regulating foam cell formation, and up-regulating endothelial nitric oxide synthase expression [4, 103]. Bilberry and anthocyanin supplementation have been shown to ameliorate hyperlipidemia in both animals and humans [16, 40].

A majority of the existing literature is based on in vitro and animal studies. Human intervention trials are necessary to confirm the health effects of the berries. Regular consumption of berries and/or berry products may improve plasma lipid profile and reduce the occurrence of metabolic syndrome and CVD which was confirmed by several studies. The randomized controlled clinical trial by *Karlsen et al.* [50] on subjects taking either bilberry juice or water for 4 weeks were directed to assess the effect of bilberry polyphenols supplementation on inflammation. They have shown that bilberry juice could decrease the plasma concentrations of CRP, interleukin (IL)-6 and IL-15. Another randomized controlled trial was by *Basu et al.* [4] on 48 subjects with metabolic syndrome who were taking freeze-dried blueberry beverage (50 g freeze-dried blueberries, approximately 350 g fresh blueberries) or equivalent amounts of fluids (controls, 960 ml water) daily for eight weeks. In this study, blueberry supplementation was shown to decrease systolic and diastolic blood pressures without altering the serum glucose concentration and lipid profile. The study by *Lehtonen et al.* [60] followed a randomized cross-over study design in Finland in which the

only difference between the intervention (33–35 days) and wash-out (30–39 days) periods was the bilberry products consumed. There was statistically significant decrease in waist circumference and body weight after bilberry diet. A further randomized, controlled dietary intervention trial study in Finland was by *Kolehmainen et al.* [52] in which participants consumed either a diet rich in bilberries or a control diet. The bilberry group consumed daily an equivalent dose of 400 g fresh bilberries, while the control group maintained their habitual diet. After eight weeks of dietary intervention and four weeks recovery period, no differences were found between the groups in body weight, glucose, or lipid metabolism, but bilberry supplementation tended to decrease serum high-sensitivity CRP, IL-6 and IL-12 concentrations. In a subsequent study involving 122 hypercholesterolemic subjects, supplementation for 24 weeks with anthocyanins (320 mg/day) purified from bilberry and blackcurrant enhanced the HDL-associated protein paraoxonase 1 (PON1) activity, increased the antioxidant effects and enhanced the cholesterol efflux capacity of HDL, and resulted in an increase in HDL cholesterol and decrease in LDL cholesterol concentrations [105]. The study by *Habanova et al.* [27] on women and men taking 150 g of frozen stored bilberries three times a week for six weeks showed that regular intake of bilberries in women was associated with a decrease TG, LDL-C, glucose, and a positive increase in HDL-C. In men, favorable changes were observed in T-C, glucose and HDL-C. *Huang et al.* [38] conducted a meta-analysis with a sequential trial analysis in order to estimate the effect of berry consumption on CVD risk factors and observed that LDL-C was significantly lower for subjects who consumed the berries than for the placebo-treated subjects. The study by *de Mello et al.* [18] was based on eight weeks intervention study on 47 metabolic syndrome patients who were randomized to receive either of bilberry or placebo diet or a control diet. They have shown that fasting serum hippuric acid is increased after consumption of anthocyanin-rich bilberries, and may contribute to the beneficial effect of bilberry consumption. *Arevström et al.* [1] hypothesized that standard medical therapy supplemented with freeze-dried bilberry after acute myocardial infarction (AMI) would have a more beneficial effect on cardiovascular risk markers and exercise capacity than medical therapy alone. The study conducted by *Curtis et al.* [17] showed no favorable effects of the intervention on glucose, insulin resistance index (HOMA-IR), and glycated hemoglobin (HbA1c). In this study, which lasted 24 weeks, a trend towards a dose-related increase in HDL-C was obtained. However, the intervention had no effect on T-C and LDL-C

after the consumption of freeze-dried blueberry (150 g/day or 75 g/day). In addition, TG levels differed significantly in the group treated with 75 g/day of blueberries, compared with the placebo. The study of *Habanova et al.* [26] investigating the effect of berries/apple juice consumption on human lipid profile of healthy volunteers (36 women and 14 men). The consumption of 300 mL juice/day resulted in a significant decrease of T-C and LDL-C levels (only for men group), and significantly increased HDL-C and total antioxidant status. Finally the study of *Chan et al.* [40] showed that bilberry supplementation (1.4 g/day of anthocyanins extract) for 4 weeks had tendency to reduce HbA1c; however, no significant improvement in glycemic control, cardiovascular risk, antioxidant-oxidative stress, or inflammatory status was observed.

To date, there are very few human studies examining the effect of phytonutrients from saskatoon berry on the risk factors of cardiovascular diseases. Saskatoon berry has potential preventative and therapeutic effects on diseases such as diabetes, cancers, inflammatory and cardiovascular diseases, obesity, neurodegenerative pathologies, and muscular degeneration [45, 57, 73, 102]. *Wang et al.* [97] found that a concentrated crude extract of *Amelanchier alnifolia* berries inhibited nitric oxide production in activated macrophages, indicating a potential protective role against chronic inflammation. Results from animal study demonstrated hypoglycemic and hypolipidemic effects of saskatoon berry [102].

CONCLUSION

In the past years, a growing demand for healthy food has been noted in the market. Consumers are primarily interested in food, which is appealing and helps in preventing various diseases and contains high levels of promoted bioactive compounds. Bilberries and saskatoon berry have achieved a superfood status with implications of beneficial health outcomes under a variety of pathological conditions. The polyphenolic composition dominated by anthocyanins are the primary active components for these health claims. Berries have recently received much attention for their health benefits, including antimutagenesis and anticarcinogenic activity for the prevention of various cancers and age-related diseases. This review to demonstrate the beneficial effects of bilberry and saskatoon berry supplementation on risk factors of cardiovascular diseases. Based on these results, regular consumption of fresh berries and/or berry products may improve plasma lipid profile and reduce the occurrence of metabolic syndrome and cardiovascular diseases.

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Conflict of interest

The authors declare no conflict of interest.

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