Review

Nutritional evaluation of commonly consumed berries: composition and health effects

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Summary

Introduction – **It is well known that berries have beneficial effects on health, owing to their content of phenolic molecules, such as anthocyanin, quercetin and phenolic acid, as well as their content of vitamins, minerals and fiber. There is a gradually increasing body of evidence suggesting that these bioactive molecules have antioxidant, anti-inflammatory, antimicrobial, anticarcinogenic, antimutagenic and neuroprotective effects. Owing to their antioxidant effects, berry consumption brings positive effects against cardiovascular diseases, obesity, ageing and neurodegenerative diseases.** *Specific objectives* – **This paper was aimed to highlight natural compounds and health effects of the berries; some mechanisms explored by experimental studies, and to outline human intervention trial. Thus, this review could be useful to develop consumption recommendations and following research in health outcomes.**

Keywords
blackberry (*Rubus* spp.), blackcurrant (*Ribes nigrum*), blueberry (*Vaccinium corymbosum*), chokeberry (*Aronia* spp.), cranberry (*Vaccinium macrocarpon*), lingonberry (*Vaccinium vitis-idaea*), raspberry (*Rubus* spp.), strawberry (*Fragaria* × *ananassa*), nutritional value, phenolics, antioxidant activity

Résumé

Evaluation nutritionnelle des petits fruits rouges couramment consommées: composition et valeur santé.

Introduction – **Il est reconnu que les petits fruits rouges (ou baies) ont des effets bénéfiques sur la santé en raison de leur teneur en composés phénoliques, tels que les anthocyanes, quercétine et acides phénoliques, ainsi que leurs teneurs en vitamines, minéraux et fibres. Au fil du temps, un nombre croissant de preuves suggère que ces molécules bioactives ont des effets antioxydant, anti-inflammatoire, antimicrobien, anti-cancérigène, antimutagène et neuroprotecteurs. Au regard de leur activité antioxidante, la consommation de baies confère des effets positifs contre les maladies cardio-vasculaires, l'obésité, le vieillissement et les maladies neurodégénératives.** *Objectifs spécifiques* – **Ce document vise à mettre en évidence les composés naturels et la valeur santé des petits fruits rouges, ainsi que certains mécanismes explorés dans différentes études expérimentales, et de délimiter le domaine d'intervention humaine. Ainsi, cet article de synthèse contribue à l'élaboration de recommandations en termes de consommation et de pistes de recherche en santé humaine.**

Mots-clés
mûre (*Rubus* spp.), cassis (*Ribes nigrum*), myrtille (*Vaccinium corymbosum*), aronia (*Aronia* spp.), canneberge (*Vaccinium macrocarpon*), airelle (*Vaccinium vitis-idaea*), framboise (*Rubus* spp.), fraise (*Fragaria* × *ananassa*), valeur nutritionnelle, composés phénoliques, propriétés antioxidantes

Significance of this study

What is already known on this subject?

- Berries contain high concentrations of the antioxidants which have health-promoting properties.

What are the new findings?

- This paper is aimed to explore some mechanisms and health effects of the berries by experimental studies. This review could be useful to develop consumption recommendations.

What is the expected impact on horticulture?

- It is considered that there is need to expand the production and to increase the consumption of berries through increasing awareness.

Introduction

In recent years, following the identification of the relationship between diet and health, there has been growing interest in healthy nutrition. A variety of nutritional recommendations have been developed to delay ageing and reduce the risk of certain health problems such as cardiovascular diseases (Paredes-López *et al*., 2010). The World Health Organization (WHO) reports that the daily consumption of 400 g fruit and vegetables can reduce the risk of many diseases when associated with body exercise – especially of cardiovascular diseases and cancer (World Health Organization, 2003).

Berries are defined as functional food since they contain high concentrations of polyphenols which have health-promoting properties (Szajdek and Borowska, 2008). The potential health benefits and biological activity of berries are nowadays mentioned in many sources (Yang and Kortesniemi, 2015; Pojer, 2013; Rodriguez-Mateos *et al*., 2013; Jimenez-Garcia *et al*., 2013; Afrin *et al*., 2016; Skrovankova *et al*., 2015). Berries have beneficial effects on health, owing to

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their phenolics (Kim *et al*., 2011; Plessi *et al*., 2007), vitamin (Borges, 2010), mineral (Plessi *et al*., 2007) and fiber content (Acosta-Montoya *et al*., 2010). Hence, berries contain a large variety and concentration of antioxidants and phytochemicals (Fu *et al*., 2015). The antioxidant compositions are mainly represented by polyphenols including anthocyanins and phenolic acids (Szajdek and Borowska, 2008). Owing to these components, berries have beneficial effects on issues such as viral adhesion and infectivity inhibition (Weiss *et al*., 2005), antiproliferative and antioxidant activity (Qiao *et al*., 2015), hypoglycemic activity and lipid oxidation biomarkers reduction (Basu and Lyons, 2012; Lila, 2011).

Commonly consumed berries include blackberries (*Rubus* spp.), black raspberries (*Rubus occidentalis*), blueberries (*Vaccinium corymbosum*, *V. angustifolium*), cranberries (*Vaccinium macrocarpon*), red raspberries (*Rubus ideus*) and strawberries (*Fragaria* × *ananassa*) (Côté *et al*., 2010; Saltmarch *et al*., 2003). Consumption amounts of these and bioavailability of their components must be known to understand the impact of berries (Gioxari *et al*., 2016). Moreover, owing to their delicious taste (Skrovankova *et al*., 2015) and productivity under diverse environmental conditions (Krüger and Josuttis, 2014), high consumption potential throughout the world is interesting for the nutritionist to develop global recommendation. For these reasons, berries are one of the priority issues interested in by nutritionists.

This review evaluates the most consumed berries including blueberry, lingonberry, blackberry, strawberry, blackcurrant, chokeberry, cranberry and raspberry, in terms of bioactive compounds and consumption. It is aimed to (i) outline natural compounds related health-promoting properties of the berries; (ii) report some mechanisms explored by experimental studies; (iii) highlight health effects of berries especially based on human intervention trials considering the lacking information about recommended amount of berries consumption.

Composition of berries and bioavailability of its nutrients

Bioactive molecules in berries vary as a result of such different factors that include genetics, harvesting, storage, *etc*. (Bobinaite *et al*., 2012). Berries contain large amounts and varieties of phytochemicals that mainly comprise phenolic molecules of over 60 different compounds (mainly anthocyanins, ellagitannins, procyanidins and phenolic monomers) (Dudonné *et al*., 2015). Phenolic monomers of berries include hydroxycinnamic and hydroxybenzoic acids. Flavonoids of berries include anthocyanin, catechin, epicatechin, quercetin and kaempferol (Bobinaite *et al*., 2012). In general, total phenolic and anthocyanin contents of raspberry (red raspberry 'Heritage') (Fredes *et al*., 2014), cranberry (*Vaccinium macrocarpon* 'Ben Lear') (Zheng and Wang, 2003), chokeberry (*Aronia melanocarpa*) (Zheng and Wang, 2003), blackcurrant (*Ribes* L. species) (Moyer *et al*., 2002), strawberry (strawberry 'Camarosa', 'Sabrina', 'Sabrosa' and 'Siba') (Fredes *et al*., 2014), blackberry (ten cultivated blackberries) (Koca and Karadeniz, 2009), lingonberry (*Vaccinium vitis-idaea* 'Amberland') (Zheng and Wang, 2003), and blueberry (*Vaccinium corymbosum*) (Koca and Karadeniz, 2009) are shown in Figure 1. Blackcurrant has the highest total phenolic content. However, chokeberry contains the highest total anthocyanin. Moreover, as shown in Figure 2, chokeberry has the highest antioxidant capacity. Most abundant anthocyanin content of the berries and their health effects are presented in Table 1. Most abundant anthocyanin variant of lingonberry and chokeberry is cyanidin-3-galactoside. Dominant anthocyanin content of blueberry, blackberry, strawberry, blackcurrant, cranberry and raspberry are delphinidin-3-galactoside, cyanidin-3-glucoside, pelargonidin-3-glucoside, delphinidin-3-rutinoside, peonidin-3-galactoside and cyanidin-3-sophoroside, respectively. Additionally, antioxidant capacity profiles of the berries per serving (145 g approximately) appear as shown in Figure 2.

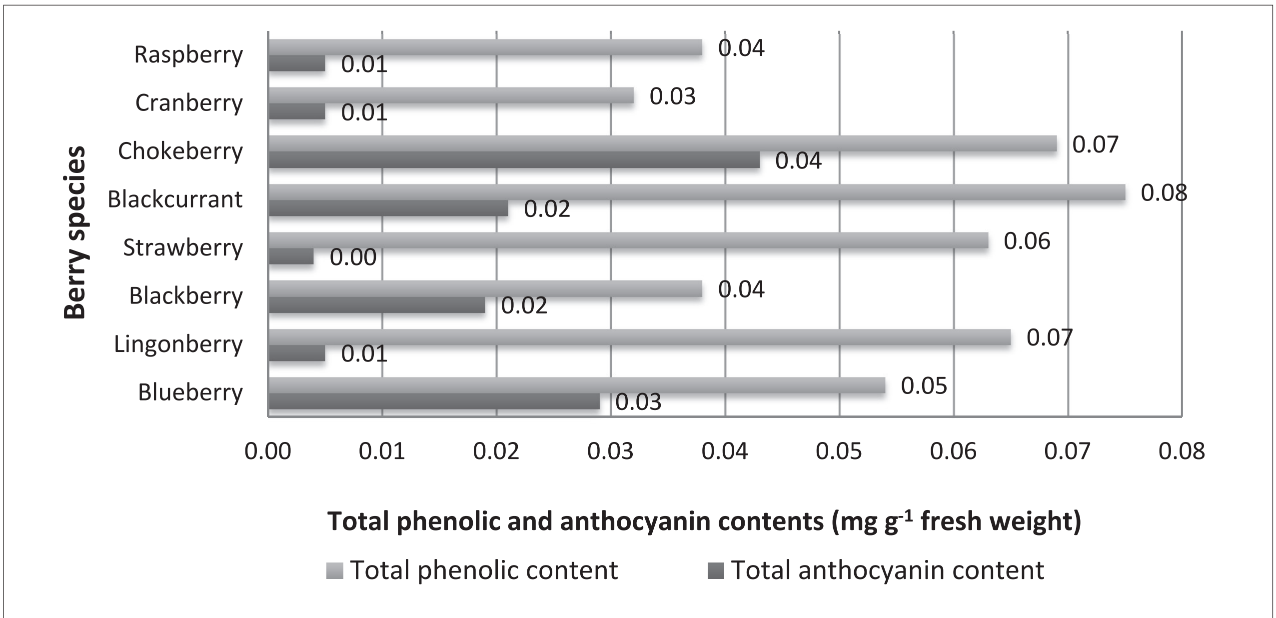

Figure 1. Total phenolic and anthocyanin contents of various berry fruits: raspberry (red raspberry 'Heritage') (Fredes *et al*., 2014), cranberry (*Vaccinium macrocarpon* 'Ben Lear') (Zheng and Wang, 2003), chokeberry (*Aronia melanocarpa*) (Zheng and Wang, 2003), blackcurrant (*Ribes* L. species) (Moyer *et al*., 2002), strawberry (strawberry 'Camarosa', 'Sabrina', 'Sabrosa' and 'Siba') (Fredes *et al*., 2014), blackberry (ten cultivated blackberries) (Koca and Karadeniz, 2009), lingonberry (*Vaccinium vitis-idaea* 'Amberland') (Zheng and Wang, 2003), and blueberry (*Vaccinium corymbosum*) (Koca and Karadeniz, 2009).

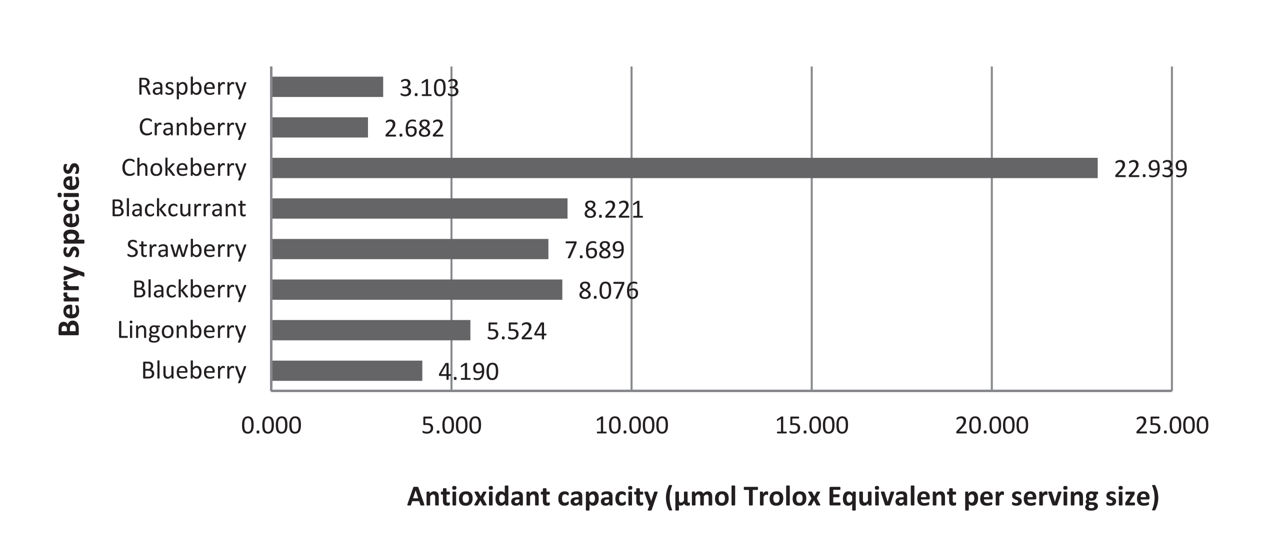

FIGURE 2. Antioxidant capacity profiles of raspberry (Kalt *et al.*, 1999), cranberry (Zheng and Wang, 2003), chokeberry (Zheng and Wang, 2003), blackcurrant (Moyer *et al.*, 2002), strawberry (Gasparrini *et al.*, 2015), blackberry (Moyer *et al.*, 2002), lingonberry (Zheng and Wang, 2003), and blueberry (Moyer *et al.*, 2002) per serving (Halvorsen *et al.*, 2006).

Berries also contain bioactive compounds known as chemoprotective agents, such as vitamins A (Agostini-Costa *et al.*, 2014) and C (Borges *et al.*, 2010). Phosphorus, sodium, magnesium, aluminum, calcium and potassium are major minerals in berries (Chandler, 1984). Also, berries contain lignans concentrated in the seeds. However, berries are consumed without crushing the seeds. Because the seeds pass through the intestine as such, the bioavailability of berry lignans is low (Smeds *et al.*, 2012).

The bioavailability and metabolism of phenolics in the berries are not determined in detail in this review because they were discussed in previous publications (Yang and Kortesniemi, 2015; Borges *et al.*, 2007; Norberto *et al.*, 2013; Del Rio *et al.*, 2013; Crozier *et al.*, 2010; Stulmach, 2014). However there is limited information regarding bioavailability and metabolism of these compounds of the berries in diet (Kait *et al.*, 2008). Assessment of absorption, metabolism and excretion is difficult because of berries containing several structurally diverse molecules (Crozier *et al.*, 2010). For example, blueberries contain approximately 12 different anthocyanins (Skrovankova *et al.*, 2015). Moreover, bioavailability and metabolism of the berries vary among individuals according to numerous factors, including genomic differences, genetic diversity and types of compounds (Huntley, 2009). Types of the compounds contribute to bioavailability depending on the glycosylation, molecular weight and methylation of the molecules (Scalbert and Williamson, 2000).

In many researches, bioavailability of the phenolic molecules was measured by evaluation of urine excretion (Borges *et al.*, 2007; Gonzalez-Barrio *et al.*, 2010; Ludwig *et al.*, 2015). Urinary recoveries of these molecules are below ten percent (Del Rio *et al.*, 2013). The bioavailability of anthocyanins have been shown to be approximately only 0.1% of the amount ingested (Crozier *et al.*, 2010; Gonzalez-Barrio *et al.*, 2010). But, phenolic molecules found in blood circulation and excreted in bile are underestimated when urinary excretion is used to estimate absorption (Norberto *et al.*, 2013).

Berry species and health effects

Berries, such as blueberries, blackberries, raspberries, strawberries, blackcurrants and cranberries, contain high levels of anthocyanins (Crozier *et al.*, 2006). There are numerous studies demonstrating the positive health effects of anthocyanins (McCullough *et al.*, 2012; Mursu *et al.*, 2014; Zhu *et al.*, 2011). A prospective study performed on nearly 100,000 individuals with a mean age of 70 years determined that flavonoid consumption is inversely related with the risk of cardiovascular disease-related death. It has been found that high flavanoid consumption (512 mg day^{-1}) reduces the risk of cardiovascular disease-related death by 18% (McCullough *et al.*, 2012). In a 20-year study performed on 2,000 middle-aged men, berries consumption was found to improve glucose metabolism, and to decrease the risk of type-II diabetes by 35%, independently of weight (Mursu *et al.*, 2014). In a randomized controlled clinical study, it was shown that berries and their anthocyanins had positive effects on the blood pressure of individuals with hypercholesterolemia (Zhu *et al.*, 2011).

A number of clinical investigations are available regarding the effect of various berry formulations on human health (Table 2). The most significant results obtained from the studies are that these berries have beneficial effects including cardiovascular health (Johnson *et al.*, 2015; Cao *et al.*, 1998; Paiva *et al.*, 1998; Burton-Freeman *et al.*, 2010; Qin *et al.*, 2009; Skoczyñska *et al.*, 2007; Naruszewicz *et al.*, 2007; Jeong *et al.*, 2016a, 2016b; Ruel *et al.*, 2013; Basu *et al.*, 2011), cognitive function (Whyte and Williams, 2015), anti-carcinogenesis (McAnulty *et al.*, 2014; Molan *et al.*, 2014; Wang *et al.*, 2014; Duthie *et al.*, 2006), urinary tract infections (Kontiokari *et al.*, 2001; Handeland *et al.*, 2014; Stapleton *et al.*, 2012; Efros *et al.*, 2010), glycemic and lipidemic responses (Linderborg *et al.*, 2012; Rokka *et al.*, 2013; Torronen *et al.*, 2012; Torronena *et al.*, 2012; Shidfar *et al.*, 2012), and oxidative stress (Khan *et al.*, 2014; Kardum *et al.*, 2014; Park *et al.*, 2015a). Underlying mechanisms for benefits of the berries are summarized in Table 3.

Table 1. Most abundant anthocyanin content of various berry fruits.

Berries	Most abundant health-related compounds	Potential health benefits[y]	References
Blueberry	Anthocyanin: Delphinidin 3-galactoside	AC, AD, NFB	Zheng and Wang, 2003; Joseph *et al*., 2010; Kraujalyte *et al*., 2015; Stull *et al*., 2010; Kruger *et al*., 2014
	Flavonol: Quercetin glycosides	AM, AO	Ferlemi *et al*., 2016; Spiller and Dewell, 2003
	Other compounds: Chlorogenic acid, quinic acid	AO	Ferlemi *et al*., 2016
Lingonberry	Anthocyanin: Cyanidin 3-galactoside	AC, AM, AO	Zheng and Wang, 2003; Olsson *et al*., 2004; Lee and Finn, 2012; Fan *et al*., 2011
	Flavonol: Quercetin 3-galactoside	AM	Zheng and Wang, 2003; Riihinen *et al*., 2014
	Other compounds: Caffeic acid, *p*-coumaric acid, proanthocyanidins	AOA, AM, AO	McDougall *et al*., 2009; Riihinen *et al*., 2014; Kylli *et al*., 2011; Mane *et al*., 2011
Blackberry	Anthocyanin: Cyanidin-3-glucoside	AC, AO, NFB	Koca and Karadeniz, 2009; Ding *et al*., 2006; Feng *et al*., 2004; Dugo *et al*., 2001; Felgines *et al*., 2005; Kolniak-Ostek *et al*., 2015
	Flavonol: Kaempferol glycosides	AC, AD, AO	Saw *et al*., 2014; Alkhalidy *et al*., 2015; Wang *et al*., 2008
	Other compounds: Ellagic acid	AC, AO	Wang *et al*., 2008
Strawberry	Anthocyanin: Pelargonidin-3-glucoside	AO, AC, ICH	Wu *et al*., 2007; Alvarez-Suarez *et al*., 2014; Mullen *et al*., 2008; Miao *et al*., 2016
	Flavonol: Kaempferol-3-glucoside and quercetin glycosides	AC, AD, AO	Saw *et al*., 2014; Alkhalidy *et al*., 2015; Liao *et al*., 2016
	Other compounds: Ellagic acid, ellagitannins	AC, AOA	McDougall *et al*., 2009; Wu *et al*., 2007
Blackcurrant	Anthocyanin: Delphinidin-3-rutinoside	AC, AI, AO, NFB, VH	Borges *et al*., 2010; Cyboran *et al*., 2014; Leon-Gonzalez *et al*., 2015; Matsumato *et al*., 2006; Dreiseitel *et al*., 2009; Watson *et al*., 2015
	Flavonol: Myricetin rutinoside	AO, NFB	Cyboran *et al*., 2014; Watson *et al*., 2015
	Other compounds: p-Coumaroylglucose	NFB	Watson *et al*., 2015
Chokeberry	Anthocyanin: Cyanidin-3-galactoside, cyanidin-3-glucoside	AC, AI, AO, AOA, ICH	Zheng and Wang, 2003; Naruszewicz *et al*., 2007; Olsson *et al*., 2004; Kim *et al*., 2013; Worsztynowicz *et al*., 2014; Kapci *et al*., 2014; Wiczkowski *et al*., 2010
	Flavonol: Quercetin glycosides	AC, AO	Saw *et al*., 2014
	Other compounds: Caffeic acid, quinic acid, chlorogenic acid	AO, AOA	Worsztynowicz *et al*., 2014; Grunovaite *et al*., 2016
Cranberry	Anthocyanin: Peonidin-3- galactoside, cyanidin-3-glucoside	AC, AI, AOA, AO, ICH	Borges *et al*., 2010; Basu *et al*., 2011; Kylli *et al*., 2011; Alvarez-Suarez *et al*., 2014; Kowalska *et al*., 2014; Duffey and Sutherland, 2015; Ohnishi *et al*., 2006
	Flavonol: Quercetin-3-O−galactoside	AC, AO, AOA	He and Liu, 2006; Kowalska *et al*., 2014; McKay *et al*., 2015
	Other compounds: Epicatechin, proanthocyanidins	AI, AM, AO	Kylli *et al*., 2011; La *et al*., 2010
Raspberry	Anthocyanin: Cyanidin-3-sophoroside	AC, AO	Borges *et al*., 2010; Olsson *et al*., 2004; Chen *et al*., 2013; Proteggente *et al*., 2002; Maatta-Riihinen *et al*., 2004
	Flavonol: Kaempferol-glucuronide, quercetin glycosides	AD, AO	Alkhalidy *et al*., 2015; Choi *et al*., 2015
	Other compounds: Ellagic acid, ellagitannin	AV, AC, AOA	Gonzalez-Barrio *et al*., 2010; Ludwig *et al*., 2015; McDougall *et al*., 2009; Mandal and Stoner, 1990; Aiyer *et al*., 2008

[y] AC: Anti-cancer; AD: Anti-diabetic; AI: Anti-inflammatory; AO: Antioxidant; AOA: Anti-obesity activities; ICH: Improvement of cardiovascular health; NFB: Cognitive decline; VH: Visual health.

Table 2. Human intervention trials conducted with specific berries and their outcomes.

Berries	Health effects	Study subjects	Study design	Dose and intervention	Outcomes of studies	References
Blueberry	Cognitive function	14 healthy children (range of age: 8–10 years)	A crossover trial	A flavonoid-rich blueberry drink contained 143 mg anthocyanins (prepared by using 200 g fresh blueberries). Two hours after consumption, subjects completed five cognitive tests.	Findings are mixed. Acute blueberry intervention provides school-aged children to encode memory items more effectively.	Whyte and Williams, 2015
	Cardiovascular health	48 healthy postmenopausal women aged 45–60 years with pre- and stage 1-hypertension	Randomized, double-blind, placebo-controlled clinical trial	Freeze-dried blueberry powder: 22 g (equates to 1 cup fresh blueberries) day^{-1} for 8 weeks.	Decrease in systolic blood pressure, diastolic blood pressure and brachial-ankle pulse wave velocity ($P<0.05$). Increase in nitric oxide levels ($P<0.01$).	Johnson *et al.*, 2015
	Anticarcinogenic	25 men and postmenopausal women aged 18–50 years	Randomized, placebo-controlled trial	Blueberry powder (equivalent to 250 g rehydrated berries) day^{-1} for 6 weeks (presupplementation). Blood samples were taken after intervention. All procedures were repeated after 6 weeks (postsupplementation).	Increase in natural killer (NK) cells; decrease in aortic augmentation index, systolic pressures, and diastolic pressures after blueberry consumption for 6 weeks.	McAnulty *et al.*, 2014
	Protection against DNA damage	10 healthy men subjects aged 20.8 ± 1.6 years.	A randomized cross-over trial	300 g blueberry day^{-1}. Peripheral arterial function was evaluated 1 h after the intake.	Decrease in H_2O_2-induced DNA damage in blood mononuclear cells 1 h after blueberry consumption ($P<0.01$).	Bo *et al.*, 2013
Lingonberry	Urinary tract infections	150 women with urinary tract infections aged 32.0 ± 9.8 years	Randomised controlled 12-month follow up trial	Daily 50 mL of cranberry-lingonberry juice concentrate for 6 months or 100 mL of lactobacillus drink five days a week for one year, or no intervention.	The cumulative rate of first recurrence of urinary tract infection during the 12-month follow up significantly lower than the other groups ($P<0.05$).	Kontiokari *et al.*, 2001
	Glycemic and lipidemic responses	10 healthy normal-weight males in the glycemia trial and 13 healthy normal-weight males aged 18–40 years in the lipemia trial	A crossover trial	200 g fat-free yoghurt with either glucose (50 g) or triacylglycerols (35 g) with or without (control) the lingonberry powder corresponds to about 270 and 400 g of fresh lingonberries. (40 g in the glycemia trial and 60 g in the lipemia trial).	No significant difference in postprandial glucose concentration between the meals (P>0.05). No lipemia-lowering effect.	Linderborg *et al.*, 2012
	Glycemic responses	9 healthy subjects	A small-scale clinical study	After consumed test foods the glycemic and insulinemic response to oat bread, oat bread with lingonberry fibre, oat-buckwheat bread and buckwheat porridge were determined.	Concluded that "buckwheat and lingonberry fibres provide new alternatives for low glycemic index foods".	Rokka *et al.*, 2013
	Glycemic and free fatty acid responses	20 healthy women aged 57 ± 10 years	A randomized, controlled, crossover study	Whole blackcurrants or lingonberries (150 g served as purees) or blackcurrant or lingonberry nectars (300 mL), each with 35 g added sucrose. In reference sucrose alone was used.	Improve in glycemic profile ($P>0.05$). Compensatory effect in free fatty acid rebound.	Torronen *et al.*, 2012

TABLE 2 continued.

Berries	Health effects	Study subjects	Study design	Dose and intervention	Outcomes of studies	References
Strawberry	Cardiovascular health	Healthy elderly females (mean age, 67 ± 0.6 years)	A randomized, controlled, crossover study	Control: coco nut drinks Intervention and dose: 240 g strawberries added to control drink for 12 weeks (Cao *et al.*, 1998) and 3 weeks (Paiva *et al.*, 1998).	Increase in plasma vitamin C, serum and urine antioxidant capacity (Cao *et al.*, 1998). Decrease in plasma carotenoids (Paiva *et al.*, 1998).	Cao *et al.*, 1998; Paiva *et al.*, 1998
		24 hyperlipidemic men and women (mean age, 50.9 ± 15 years)	Randomized, single-blind, placebo-controlled, 12-week crossover trial	Strawberry beverage containing 10 g freeze-dried fruit or placebo with high-fat challenge meal for 6 weeks.	Triglycerides and oxidized LDL-C were lower after strawberry beverage than placebo ($P<0.05$).	Burton-Freeman *et al.*, 2010
		18 subjects aged 23–91 years	A randomized, controlled, crossover study	8–9 strawberries six days a week for 4 weeks.	Increase in blood folate ($P<0.001$) Decrease in C-reactive protein ($P>0.05$).	Spiller and Dewell, 2003
Blackcurrant	Cardiovascular health	120 subjects with dyslipidemia (mean age, 55 years)	A double-blind, randomized, placebo-controlled trial	320 mg day^{-1} anthocyanin capsules (17 different natural purified anthocyanins from billberry and black currant).	Increase in HDL-cholesterol, decrease in LDL-cholesterol and activity of plasma cholesteryl ester transfer protein	Qin *et al.*, 2009
	Anticancer	30 healthy subjects (range of age: 20–60 years)	A randomized, controlled, crossover study	672 mg blackcurrant power.	Decrease in the activity of the bacterial β-glucuronidase enzyme and the fecal pH.	Molan *et al.*, 2014
	Lowering of oxidative stress	66 healthy adults (mean age, 53 years)	A double-blind, placebo-controlled, parallel group study	250 mL of placebo (flavored water) or low (27.3 mg 100 mL^{-1} total polyphenols, 4 mg 100 mL^{-1} anthocyanins) or high blackcurrant juice drink (81.5 mg 100 mL^{-1} total polyphenols, 14.3 mg 100 mL^{-1} anthocyanins) 4 times a day for 6 weeks.	Increase in plasma vitamin C concentration in the low and high blackcurrant juice drink groups ($P<0.001$) compared with the placebo group.	Khan *et al.*, 2014
	Postprandial glycemic response	10 healthy subjects (mean age, 36 ± 14 years)	A randomized, controlled, double-blind cross-over study	300 mL blackcurrant juice or a blackcurrant juice fortified with crow-berry powder (respective polyphenol contents 159 and 293 mg 100 mL^{-1}).	Fortified blackcurrant juice consumption elicited slightly attenuated and sustained plasma glucose and insulin responses.	Torronena *et al.*, 2012
Chokeberry	Cardiovascular health	58 men with diagnosed mild hypercholesterolemia without pharmacological treatment (mean age, 54.1 ± 5.6 years)	A randomized, controlled, crossover study	250 mL day^{-1} 100% chokeberry juice (426.04 mg 100 mL^{-1} total phenolics content) for 6 weeks.	Reduction of total cholesterol level, LDL cholesterol, and triglycerides ($P<0.001$). Increase in HDL cholesterol level ($P<0.001$).	Skoczyñska *et al.*, 2007
		44 patients survived myocardial infraction and have received statin therapy for at least 6 months (mean age, 66 years)	A double-blind, placebo-controlled, parallel trial	3 × 85 mg day^{-1} of chokeberry flavonoid extract (*Aronia melanocarpa* E.) or placebo for 6 weeks.	Reduction of low-density lipoprotein oxidation level, CRP level, systolic and diastolic blood pressure compared with placebo group ($P<0.05$).	Naruszewicz *et al.*, 2007
	Cellular oxidative damage	25 healthy women (mean age, 35.2 ± 7.7 years)	A crossover trial	100 mL of polyphenol-rich organic chokeberry juice daily for 3 months (386 mg 100 g^{-1} total phenolics)	Increase in superoxide dismutase and glutathione peroxidase activities ($P<0.05$). Decrease in levels of thiobarbituric acid–reactive substances ($P<0.05$).	Kardum *et al.*, 2014
	Urinary tract infections	160 females and 76 males; mean age, 85 years	A group-randomized (due to logistics), placebo-controlled, double-blind crossover trial.	156 mL day^{-1} or 89 mL day^{-1} black chokeberry juice (715 mg 100 mL^{-1} total phenolics content) or a placebo for 6-months.	In 156 mL or 89 mL black chokeberry juice groups, reduction rates of urinary tract infection incidence were 55% and 38%, respectively.	Handeland *et al.*, 2014

TABLE 2 continued.

Berries	Health effects	Study subjects	Study design	Dose and intervention	Outcomes of studies	References
Raspberry	Anticarcinogenic	14 subjects with familial adenomatous polyposis	A randomized, double-blinded, placebo-controlled trial	60 g black raspberry and suppositories (contain 720 mg black raspberry) day^{-1} for 9 months.	Decrease in cellular proliferation and DNMT1 protein expression.	Wang *et al*., 2014
	Cardiovascular health	45 patients with prehypertension aged 18–60 years	A randomized, double-blinded, placebo-controlled clinical trial	Moderate dose black raspberry extract (equivalent to 1,500 mg day^{-1}), a high-dose black raspberry extract (equivalent to 2,500 mg day^{-1}), or placebo for 8-week follow-up period.	Reduction of 24-hour and nighttime systolic blood pressure compared with placebo group ($P<0.05$).	Jeong *et al*., 2016a
		51 patients with metabolic syndrome	A randomized controlled trial	750 mg day^{-1} black raspberry for patients prospectively randomized into the black raspberry group during the 12-week follow-up period.	Decrease in radial augmentation indexes, interleukin-6, and increased in tumor necrosis factor-alpha, adiponectin levels ($P<0.05$) compared to placebo group.	Jeong *et al*., 2016b
	Lowering of oxidative stress	39 healthy male smokers aged 20–30 years	A randomized, placebo-controlled clinical trial	30 g of freeze-dried black raspberry (5.31 ± 2.65 g 100 g^{-1} total phenolic content) or placebo for 4 weeks.	Increase in the activity of glutathione peroxidase, and catalase. Reduced plasma lipid peroxidation. Black raspberry had no effect on plasma lipid profiles, LDL oxidation, and DNA damage.	Park *et al*., 2015a
Cranberry	Cardiovascular health	35 sedentary and healthy overweight men aged 45 ± 10 years	A double-blind, placebo-controlled crossover trial	500 mL cranberry juice contained 400 mg total polyphenols and 20.8 mg anthocyanins for 4 weeks.	No significant difference in augmentation index and other cardio metabolic variables such as index of arterial stiffness and cardio metabolic profile between placebo and trial groups.	Ruel *et al*., 2013
		31 adults with metabolic syndrome aged 52.0 ± 8.0 years	A randomized, double-blind, placebo-controlled trial	480 mL day^{-1} cranberry juice for 8 weeks.	Increase in plasma antioxidant capacity ($P<0.05$). Decrease in oxidized low-density lipoprotein and malondialdehyde ($P<0.05$). No significant improvements in blood pressure, glucose and lipid profiles, C-reactive protein, and interleukin-6.	Basu *et al*., 2011
	Urinary tract infections	176 premenopausal women with a history of urinary tract infections	A placebo-controlled trial	4 oz and 8 oz of cranberry juice or placebo daily for 6 months.	No significant difference in urinary tract infections risk compared with placebo.	Stapleton *et al*., 2012
		28 women with two or more episodes of urinary tract infections history in the last 6 months	Dose-escalation, single-blind trial	Oral administration of cranberry liquid blend agent at 15, 30, 45, 60 and 75 mL daily for 12 weeks.	After taking 60 mL day^{-1} cranberry liquid blend agent, 91% of the subjects remained free of recurrent urinary tract infections for 3 months.	Efros *et al*., 2010
	Anticarcinogenic	20 healthy female subjects aged 18–40 years	A randomized, placebo-controlled trial	Subjects consumed 750 mL day^{-1} of either cranberry juice or a placebo drink for 2 weeks.	No significant difference in activities of glutathione peroxidase, catalase and superoxide dismutase. 8-oxo-deoxyguanosine in urine or endogenous or H_2O_2-induced DNA damage in lymphocytes were not different from placebo group.	Duthie *et al*., 2006
	Reduction of CRP level	10,334 adults	A case study	404 mL cranberry juice day^{-1} for two days.	Decrease in level of CRP, fasting glucose, insulin, total cholesterol, and triacylglycerols.	Duffey and Sutherland, 2015
	Antidiabetic	58 type-2 diabetic males	A double-blind randomized clinical trial	240 mL cranberry juice day^{-1} for 12 weeks.	Decrease in serum glucose and apoB. Increase in serum apoA-1 and PON-1 activity.	Shidfar *et al*., 2012

Table 3. Potential mechanisms of berry fruits on health.

Health effects and references	Potential mechanisms
Prevention of obesity (Yang and Kortesniemi, 2015; McDougall *et al*., 2009; Worsztynowicz *et al*., 2014; Kowalska *et al*., 2014; Yang *et al*., 2008; Häkkinen *et al*., 1999)	Inhibit the cyclooxygenase-1 and cyclooxygenase-2 enzymes. Induction of apoptosis in adipose cells. Interfere with the course of adipogenesis by acting on PPARγ receptor. Inhibit pancreatic lipase activity. Inhibit pancreatic α-amylase activity.
Prevention of type 2 diabetes (Lehtonen *et al*., 2010; Linderborg *et al*., 2012)	Increase the levels of adiponectin and leptin. Regulate hormone-sensitive lipase and lipolysis activities.
Delays of ageing (Linderborg *et al*., 2012)	Suppress free radicals that cause DNA damage.
Reduces the risk of cardiovascular diseases (Cao *et al*., 1998; Seeram, 2008; Alvarez-Suarez *et al*., 2014; Tulipani *et al*., 2011; Henning *et al*., 2010)	Inhibit inflammation. Scavenge free radicals. Modulate eicosanoid metabolism. Develop endothelial function. Reduce blood pressure. Inhibit platelet aggregation/activation. Increase HDL-C circulation. Increases LDL-C resistance to oxidation.
Prevention of cancer (Giampieri *et al*., 2012; Akter *et al*., 2011; Wang *et al*., 2009; Boivin *et al*., 2007)	Induce metabolic enzymes (detoxification phase II enzymes). Modulate gene expression, cell proliferation, apoptosis, and intracellular signaling pathways.
Antimicrobial effects (Baliga *et al*., 2011; Rauha *et al*., 2000)	Destabilize microbial cytoplasmic membranes. Affect plasma membrane permeability. Inhibit extracellular microbial enzymes. Directly affect microbial metabolism.
Prevention of neurodegenerative diseases (Shadrina *et al*., 2010; Dreiseitel *et al*., 2009; Watson *et al*., 2015)	Reduce oxidative stress. Inhibit MAO activity.

In vitro studies have shown that anthocyanins reduced the risk of obesity, type 2 diabetes and cardiovascular disease, by inhibiting the cyclooxygenase-1 and -2 (COX-1 and -2) enzymes, increasing the secretion of the adiponectin and leptin, and regulating hormone-sensitive lipase and lipolysis activities (Yang and Kortesniemi, 2015; Olsson *et al*., 2004; McDougall *et al*., 2009). Torronen *et al.* (2013) determined that in healthy women the consumption of berries, together with white or rye bread reduced the glycemic load, with strawberries, cranberries, bilberries and blackcurrants, also reducing the insulin response. Another study determined that the consumption of 150 g berries for 20 weeks reduced the levels of alanine aminotransferase, and increased the levels of fasting plasma adiponectin (Lehtonen *et al*., 2011).

Owing to their antioxidant effects, phytochemicals in berries prevent free radicals from causing cellular damage. Increasing the consumption of berries also lowers the risk of cardiovascular diseases by inhibiting inflammation, eliminating free radicals, modulating the eicosanoid metabolism, developing endothelial function, lowering blood pressure, inhibiting platelet aggregation/activation, increasing high-density lipoprotein cholesterol (HDL-C) circulation, and increasing the oxidation resistance of low-density lipoprotein cholesterol (LDL-C) (Seeram, 2008).

Owing to their bioactive phenolic content, berries can induce metabolic enzymes (detoxification phase II enzymes). They also exhibit anticancer effects through the modulation of gene expression, cell proliferation, apoptosis and intracellular signaling pathways (Giampieri *et al*., 2012).

Anthocyanins exhibit anti-inflammatory and vasculoprotective effects. Owing to their antioxidant effects, phenolic compounds can suppress the activation of nuclear transcription factors, such as the nuclear factor-κb (NF-κb) and the activator protein-1 (AP-1) (Lee *et al*., 2014).

Nutrients classified as antioxidants also exhibit anti-neurodegenerative effects. In recent times, it is becoming increasingly clear that oxidative stress plays an important role in neurodegenerative disease pathogenesis. Oxidative stress causes reactive oxygen species to concentrate in cells, leading to the development of many neurodegenerative diseases such as Parkinson's, Huntington's, and Alzheimer's diseases (Shadrina *et al*., 2010). However, animal studies have not been able to clearly assess the passage of these compounds through the blood-brain barrier, as well as the level of accumulation resulting from long-term consumption. It is believed that the direct passage of polyphenols through the blood-brain barrier and their accumulation in brain tissues might have a role and effect on cognitive processes (Borges *et al*., 2007; Shukitt-Hale *et al*., 2008).

It is known that the health effects and bioactive components of berries are influenced by genetic and environmental factors. The antioxidant effects of berries are directly associated with their phytochemical content (Chen *et al*., 2013).

Blueberry

Most abundant bioactive molecules

Blueberries have been shown to contain almost fifteen anthocyanins, many of which exhibited substantial antioxidant activity (Borges *et al*., 2010). Also blueberries were found to contain quercetin, proanthocyanidin and phenolic acids (Dudonné *et al*., 2015). Delphinidin-3-galactoside, included in the list of most dominant anthocyanins (Table 1), is known to work as antioxidant (Zheng and Wang, 2003; Joseph *et al*., 2010; Kraujalyte *et al*., 2015). The anthocyanin compounds of blueberries contribute to its anti-diabetic effects and cognitive function benefit of blueberries (Joseph *et al*., 2010; Kraujalyte *et al*., 2015; Stull *et al*., 2010; Kruger *et al.*, 2014). Blueberries also show antimicrobial and antioxidant activity owing to its phenolic compounds including quercetin glycosides (Ferlemi *et al.*, 2016; Deng *et al.*, 2014). Moreover, chlorogenic acid and quinic acid content of blueberries increase the antioxidant activity (Ferlemi *et al.*, 2016).

Health effects

Their antioxidant and anti-inflammatory activities have been shown to be responsible for reduced metabolic diseases (Norberto *et al.*, 2013; Esposito *et al.*, 2014). A study on individuals with metabolic syndrome demonstrated that the consumption of 400 g day^{-1} blueberries for 8 weeks effectively reduces CRP levels (Mykkanen *et al.*, 2014). It was also determined that consuming 100 g blueberries or 100 g sea buckthorn (*Hippophae rhamnoides* L.) oil every day for 33 to 35 days has the effect of reducing vascular cell adhesion molecule (VCAM) levels and atherosclerosis risk in overweight and obese women (Lehtonen *et al.*, 2010). Johnson *et al.* (2015) reported a decrease in systolic blood pressure, diastolic blood pressure and brachial-ankle pulse wave velocity after administrating freeze-dried blueberry powder to 48 healthy postmenopausal women aged 45–60 years for 8 weeks. In a 16–year follow-up study with post-menopausal women (n = 34,489), age and energy adjusted relative risks of coronary heart disease were significantly decreased in women consuming blueberries (Mink *et al.*, 2007). Similarly, in human studies assessing blueberry intake according to acute (McAnulty *et al.*, 2014) and long-term (Bo *et al.*, 2013) effects, some significant improvements were reported. One of them found a decrease in aortic augmentation index, systolic pressures, and diastolic pressures after blueberry consumption (250 g rehydrated berries) for 6 weeks (McAnulty *et al.*, 2014). In the other study, 300 g blueberry intake elicited significant decrease of H_2O_2-induced DNA damage in blood mononuclear cells (Bo *et al.*, 2013). In a randomized, double-blind, placebo-controlled clinical trial, participants received 22 g freeze-dried blueberry powder for 8 weeks. It was concluded that daily blueberry consumption might reduce blood pressure and arterial stiffness (Johnson *et al.*, 2015). Also, blueberries have hypoglycemic activities that are largely anthocyanin-specific (Yousef *et al.*, 2013). In a study aimed to identify the effect of berry anthocyanin on lipid peroxidation, blueberries have been shown to inhibit lipoperoxidation in human erythrocytes (Ramirez *et al.*, 2015). At the end of a crossover trial, acute blueberry intervention (two hours after consumption of drink containing 200 g blueberries) was found to improve memory functions. However, the results of this study are complicated (Whyte and Williams, 2015).

Lingonberry

Most abundant bioactive molecules

Anthocyanins (mainly cyanidin-3-*O*-galactoside, delphinidin-3-*O*-galactoside and peonidin-3-*O*-galactoside) (Zheng and Wang, 2003; Ogawa *et al.*, 2014; Brown *et al.*, 2014), quercetin 3-galactoside (Zheng and Wang, 2003) and proanthocyanidins are the most abundant bioactive molecules in lingonberries (Lee and Finn, 2012). *P*-coumaric acid, cafeic acid and benzoic acid were shown in lingonberries as the major phenolic acids (Dudonné *et al.*, 2015). Lingonberry flavonoids (Table 1) have been found to exhibit antioxidant, antiproliferative and antimicrobial activity (Olsson *et al.*, 2004; Riihinen *et al.*, 2014; Fan *et al.*, 2011). Anthocyanin fraction of lingonberries also has been reported to have inhibitory effects on cancer cell proliferation (Riihinen *et al.*, 2014). Proanthocyanidins from lingonberries enhance the antioxidant (Kylli *et al.*, 2011; Mane *et al.*, 2011) and antimicrobial activity (Kylli *et al.*, 2011). Proanthocyanidins from lingonberries have a high ability to reduce the pancreatic lipase activity. Owing to this function, lingonberries contribute to anti-obesity activities (McDougall *et al.*, 2009).

Health effects

When 40 g lingonberry is added to a high glucose content diet, a decrease was observed in the fasting plasma insulin response (Linderborg *et al.*, 2012). In contrast, 200 g fat-free yoghurt with lingonberry powder corresponding to about 270 and 400 g of fresh lingonberries did not appear to give significant difference in postprandial glucose concentration between the meals (Linderborg *et al.*, 2012). The study aimed to investigate whether 8 weeks treatment with Finnish berry juices, cranberry (*Vaccinium oxycoccos*), lingonberry (*Vaccinium vitis-idaea*) and blackcurrant (*Ribes nigrum*) affects blood pressure and vascular function of spontaneously hypertensive rats. At the end of the study, it was reported that long-term lingonberry juice treatment improved endothelium-dependent vasodilatation of spontaneously hypertensive rats (Kivimaki *et al.*, 2011). In another 8-week intervention study conducted with spontaneously hypertensive rats, lingonberry juice has been shown to have anti-inflammatory and anti-thrombotic effects (Kivimaki *et al.*, 2012). Intervention was conducted by Kontiokari *et al.* (2001) in which 150 women with urinary tract infections were randomized to either the placebo or active treatment providing 50 mL of cranberry-lingonberry juice concentrate day^{-1} for 6 months or 100 mL of lactobacillus drink five days a week for one year. In cranberry-lingonberry juice treatment group, cumulative rate of first recurrence of urinary tract infection during the 12-month follow-up was reported to be significantly lower than the other groups (Kontiokari *et al.*, 2001). Finally, lingonberry extracts were reported to have an antiproliferative effect against human colon cancer CaCo-2 cells (McDougall *et al.*, 2008).

Blackberry

Most abundant bioactive molecules

Blackberries contain high levels of anthocyanins (mainly cyanidin derivatives), kaempferol glycosides and ellagic acid associated with health effects (Koca and Karadeniz, 2009; Kaume *et al.*, 2012a). Cyanidin-3-glucoside (Ding *et al.*, 2006; Feng *et al.*, 2004), kaempferol glycosides and quercetin (Saw *et al.*, 2014) isolated from blackberries have been shown to inhibit proliferation of a human carcinoma cell and contribute to the antioxidant activity in blackberries. Kaempferols also improve hyperglycemia, glucose tolerance, and blood insulin levels by improving peripheral insulin sensitivity and protecting against pancreatic β-cell dysfunction (Alkhalidy *et al.*, 2015).

Health effects

Blackberry is a berry with high antioxidant activity like strawberry and black raspberry based on the oxygen radical absorbance capacity (Wada and Ou, 2002). In a study aimed to investigate whether blackberry extract reduced inflammation and photocarcinogenesis biomarkers induced by solar ultraviolet-B radiation in mice, blueberry extract was shown to protect from ultraviolet-B radiation oxidative damage and inflammation by modulating mitogen activated protein kinase and NF-κb signaling pathways (Divya *et al.*, 2015). In addition to antioxidant properties, blackberry extracts also prevent the detrimental effects of neuroinflammation in the brain (Meireles *et al*., 2015). The blackberry was demonstrated to have a protective effect on weight gain and inflammation in a rat model, owing to its anthocyanin compounds (Kaume *et al*., 2012b).

Strawberry

Most abundant bioactive molecules

Anthocyanins are the most common polyphenolic compounds of strawberries although the anthocyanin content is lower than in blueberry, blackberry and raspberry (Fredes *et al*., 2014). Strawberries are the berries with the highest ellagic acid content. In addition to its high vitamin C content, strawberries are also rich in folate. A daily strawberry consumption of 250 g can supply nearly 30% of the European and U.S. folate recommended daily allowances (approximatively 20–25 µg folate 100 g^{-1} fresh fruit) (Giampieri *et al*., 2012). Anthocyanins in strawberries are most effective in antioxidant activity, inhibiting cancer cell proliferation (Wu *et al*., 2007) and improvement of cardiovascular health (Alvarez-Suarez *et al*., 2014). But, in addition to anthocyanin, also other phenolics including kaempferol, quercetin and ellagitannins (Saw *et al*., 2014; Wu *et al*., 2007; Liao *et al*., 2016) are responsible for cancer prevention activity of strawberries. Strawberries have also been shown to have anti-obesity activities due to its ellagitannins (Table 1) (McDougall *et al*., 2009).

Health effects

Ellagic acid was reported to have antiviral and antioxidant properties, and to display protective effects against colon, lung and esophageal cancers (Kalt *et al*., 1999). In a prospective study, performed with 34,489 postmenopausal and overweight women, strawberry consumption was found to be inversely related with cardiovascular disease mortality after a 16-year follow-up period (Mink *et al*., 2007). In contrast, a cross-sectional study, performed on 26,966 postmenopausal overweight women, showed that the consumption of strawberries was not associated with cardiovascular disease incidence, lipid levels and CRP protein levels. However, it has also been reported that the risk of cardiovascular disease is lower among women who consume large amounts of strawberries (at least two portions a week) than among women who do not consume strawberries (Sesso *et al*., 2007). A previous study demonstrated that consuming 500 g fresh strawberries for 30 days improves the plasma lipid profile and the total antioxidant capacity (Alvarez-Suarez *et al*., 2014). Similar results were reported by Burton-Freeman *et al*. (2010), who administrated strawberry beverage containing 10 g freeze-dried fruit or placebo with high-fat challenge meal for 6 weeks to 24 hyperlipidemic men and women and found significant decrease in triglycerides and oxidized LDL-C. An important finding from another study on strawberries is that both acute (Cao *et al*., 1998) and long-term (Tulipani *et al*., 2011) consumption has the effect of significantly increasing the total antioxidant capacity. These results were associated with an increase in plasma vitamin C levels. Following the long-term consumption of strawberries for two to three weeks, it was observed that the LDL-C peroxidation lag became longer, and that the erythrocytes' resistance to oxidative damage increased (Henning *et al*., 2010).

Blackcurrant

Most abundant bioactive molecules

Blackcurrants are berries with a rich source of anthocyanin (mainly 3-*O*-glucoside and 3-*O*-rutinoside) (Maatta *et al*., 2003) and vitamin C (Nour *et al*., 2011). Antioxidant effects of blackcurrant depend not only on the anthocyanins but also on its all polyphenol content (Cyboran *et al*., 2014). Blackcurrant with its major anthocyanins is responsible for antiproliferative effect on cancer cells (Leon-Gonzalez *et al*., 2015). Moreover, anthocyanins in blackcurrant have been shown to improve visual function by distributing in ocular tissue (Matsumato *et al*., 2006). Delphinidin-3-rutinoside has been shown to reverse neurodegenerative disease by inhibition in MAO activity (Dreiseitel *et al*., 2009). Interestingly, in addition to anthocyanin, it was thought that other compounds could be responsible for the MAO inhibition (Table 3) (Watson *et al*., 2015).

Health effects

It was observed that the consumption of 250 g blackcurrant-based (15%) beverage by healthy males together with a high-energy meal increased their plasma ascorbic acid levels as well as their free-radical scavenging capacity (Huebbe *et al*., 2012). In another study, at the end of the 6 weeks [blackcurrant juice (81.5 mg 100 mL^{-1} total polyphenols, 14.3 mg 100 mL^{-1} anthocyanins) 4 times a day for 6 weeks], significant increases were found in the levels of plasma vitamin C concentration with consumption of the blackcurrant juice compared to placebo (Khan *et al*., 2014). In a randomized, double-blind, placebo-controlled crossover study conducted with healthy young adults, cognitive benefit of acute blackcurrant supplementation was demonstrated in participants (Watson *et al*., 2015). Blackcurrant supplementation was found to reduce obesity-induced inflammation in adipose tissue as a result of *in vivo* study (Benn *et al*., 2014). Torronena *et al.* (2012) tested postprandial effects of 300 mL blackcurrant juice or blackcurrant juice fortified with crowberry powder (respective polyphenol contents 159 and 293 mg 100 mL^{-1}) in 10 healthy subjects. At the end of the study, slightly attenuated and sustained plasma glucose and insulin responses were reported (Torronena *et al.*, 2012). Moreover, another health effects of blackcurrant, including improved endothelial function (Khan *et al*., 2014), inhibition of pathogenic bacterial proliferation (Parkar *et al*., 2014), reduced cardiovascular disease biomarkers (Qin *et al*., 2009; Fa-lin *et al*., 2010) and chemoprevention against cancer (Molan *et al*., 2014; Bishayee *et al*., 2011) have been determined.

Chokeberry

Most abundant bioactive molecules

Chokeberry is a rich source of anthocyanins (mainly cyanidin 3-*O*-glucoside, cyanidin 3-*O*-galactoside, cyanidin 3-*O*-arabinoside, and cyanidin 3-*O*-xyloside) (Oszmianski and Wojdylo, 2005). Also it contains phenolic acids and quercetins (Kulling and Rawel, 2008). Anthocyanin and quercetin contents of chokeberries contribute to the inhibition of proliferation in cancer cell (Olsson *et al*., 2004) and improvement of antioxidant activity (Saw *et al*., 2014; Kim *et al*., 2013). Anthocyanins of chokeberries, especially cyanidin 3-*O*-glucoside, also have an important role on weight gain and adipogenesis. Not only cyanidin 3-*O*-glucoside is responsible for these effects but chlorogenic acid in chokeberries is responsible, too. It has been reported that these compounds exhibit strong anti-obesity activities by inhibition of the reaction catalyzed by α-amylase and lipase (Table 3) (Worsztynowicz *et al*., 2014).

Health effects

Studies have suggested that chokeberry and its products have beneficial effects on antioxidant activity (Hwang *et al*., 2014), non-alcoholic fatty liver disease (Park *et al*., 2015b) and cellular oxidative damage (Kardum *et al*., 2014). The study used a crossover design in which 25 healthy women consumed daily 100 mL of polyphenol-rich organic chokeberry juice for 3 months. Subjects showed significant increases in superoxide dismutase and glutathione peroxidase activities ($P<0.05$), whereas thiobarbituric acid-reactive substances were found to decrease ($P<0.05$) (Kardum *et al*., 2014). Handeland *et al*. (2014) studied long-term effects of black chokeberry juice (156 mL day^{-1} or 89 mL day^{-1} black chokeberry juice for 6 months) on 160 females and 76 males. Significant decrease in urinary tract infection incidence was found in both study groups (decrease ratio in subjects consumed high and low amount of black chokeberry juice; 55% and 38%, respectively) (Handeland *et al*., 2014). In another study, chokeberry juice was found to inhibit CaCo-2 cell proliferation by causing G2/M cell cycle arrest (Bermúdez-Soto *et al*., 2007). A randomized controlled crossover intervention was conducted by Skoczyñska *et al.* (2007), in which 58 men were found with diagnosed mild hypercholesterolemia providing 250 mL day^{-1} 100% chokeberry juice for a period of 6 weeks. Significant reduction in total cholesterol, LDL cholesterol, triglycerides ($P<0.001$) and increase in HDL cholesterol level ($P<0.001$). Similar beneficial effects of chokeberry on cardiovascular health were demonstrated in another trial (Naruszewicz *et al*., 2007). Finally, chokeberry extracts were reported to inhibit the proliferative activity in HT-29 cells (Jing *et al*., 2008).

Cranberries

Most abundant bioactive molecules

One of the major significant flavonoids is quercetin. Anthocyanins (mainly peonidin-3-O-galactoside, cyanidin-3-O-galactoside, cyanidin-3-O-arabinoside) and proanthocyanidins are also present in cranberries (Brown and Shipley, 2011; Carpenter *et al*., 2014). In addition to antioxidant activities of the anthocyanin compounds in cranberries (Basu *et al*., 2011; He and Liu, 2006), they also contribute to anti-inflammatory property by inhibitory effects on production of cytokines IL-1β, IL-6 and TNF-R (Kylli *et al*., 2011). Anthocyanins from cranberries also have been demonstrated to have antiproliferative activity on cancer cells (Vu *et al*., 2012). Cranberries, owing to its quercetin and anthocyanin contents, have been reported to be effective in adipose tissue mass modulation by down-regulation of the expression of major transcription factors of adipogenesis pathway (Table 3) (Kowalska *et al*., 2014). Moreover, proanthocyanidins in cranberries have been found to improve anti-inflammatory effects by reducing in activation of the nuclear factor-κB (NF-κB) p65 pathway (La *et al*., 2010).

Health effects

Cranberries have various health effects including decreased cardiovascular disease risk (Novotny *et al*., 2015), anticancer activity (Vu *et al*., 2012), dyslipidemia and hypertension (Juturu *et al*., 2011). In a randomized double-blind placebo-controlled trial on 31 participants identified with metabolic syndrome, after consuming 480 mL day^{-1} cranberry juice for 8 weeks, it was concluded that cranberry juice significantly increased plasma antioxidant capacity in women with metabolic syndrome (Basu *et al*., 2011). In contrast, Ruel *et al.* (2013) reported no significant change in cardiometabolic variables after 500 mL day^{-1} cranberry juice for 4 weeks. It has been reported that the consumption of cranberries, together with whole grain and oily fish, increased cholesterol transport in individuals with metabolic diseases and contributed to the improvement of cardiovascular diseases (Lankinen *et al*., 2014). In another study, 42 men with lower urinary tract symptoms who supplemented cranberry fruit powder (1,500 mg) for 6 months were found to have no significant change in fasting plasma CRP (Vidlar *et al*., 2010). Similarly, Stapleton *et al.* (2012) conducted a placebo-controlled trial on 176 premenopausal women with a history of urinary tract infections. Compared to a placebo group, no significant change in the risk of urinary tract infections was observed in the treatment group after consumption of 4 oz and 8 oz of cranberry juice or placebo daily for 6 months. In contrast, recurrent urinary tract infections did not appear in 91% of the subjects for 3 months after oral administration of 60 mL day^{-1} cranberry liquid blend agent for 12 weeks (Efros *et al*., 2010). In another study, fifty-eight ($n=58$) type 2 diabetic males consumed 240 mL cranberry juice day^{-1} for 12 weeks (Shidfar *et al*., 2012). Consumption of the juice led to a significant decrease in serum glucose and apoB and increase in serum apoA-1 and PON-1 activity.

Raspberry

Most abundant bioactive molecules

Anthocyanins (mainly cyanidin-3-glucoside, cyanidin-3-sophoroside and cyanidin-3-rutinoside) (Borges *et al*., 2010; Chen *et al*., 2013) and ellagic acid (Bobinaite *et al*., 2012) are the most common compounds of raspberry. Anthocyanins in raspberries owing to their antioxidant activity (Olsson *et al*., 2004; Proteggente *et al*., 2002) have been reported to contribute to the anticarcinogenic effects of raspberries (Olsson *et al*., 2004). Also, quercetin and kaempferol are well-known other compounds in raspberries for their antioxidant effects (Choi *et al*., 2015). Kaempferols treatment has been found to promote insulin sensitivity by improving islet β-cell mass (Alkhalidy *et al*., 2015); however, this study was conducted with kaempferol supplementation. Raspberry has been found one of the most effective berry types in inhibition of pancreatic lipase activity due to its ellagitannin compound (Table 1) (McDougall *et al*., 2009).

Health effects

Various health effects of raspberries were summarized to include anti-inflammatory, antiviral, antidiabetic, anti-obesity, antidepressant, anticancer and neuroprotective functions (Kim *et al*., 2015).

Raspberries are the berries with the highest quercetin content. *In vitro* studies have indicated that quercetin is an antioxidant molecule that inhibits platelet aggregation. Quercetin also exhibits anticancer properties by affecting cell differentiation and inhibiting protein tyrosine kinase (Ramadan *et al*., 2008). In a study conducted on postmenopausal women who smoke, based on the hypothesis that consuming 45 g day^{-1} raspberries for a 9-month period would help prevent bone loss, it was demonstrated that raspberries have a protective effect against the bone loss caused by smoking (Kaume *et al*., 2014). Similar to cranberries, strawberries and blueberries; raspberries also contain large amounts of vitamin C that assist in the development of connective tissues and provides protection against pathogenic microorganisms. In addition, the phytochemicals in berries also protect the liver, gall bladder and kidney against microbial infections (Kellogg *et al*., 2010). Raspberries, as well as compounds isolated from raspberries (such as lutein, vectin, quercetin and rutin), have positive effects on normal human visual functions. Furthermore, berries and their leaves also have various effects on sore throat, stomatitis, diabetes, diarrhea, cancer and inflammation (Victoria *et al*., 2012). The antioxidant, anti-inflammatory and chemoprotective anthocyanins in raspberries and blackberries are known to have protective effects against esophageal, colon and oral cancers (Akter *et al*., 2011). Similar effects were reported by Park *et al.* (2015a), who administered 30 g of freeze-dried black raspberry or placebo for 4 weeks to 39 healthy male smokers and found an increase in the activity of glutathione peroxidase, catalase, and decrease in plasma lipid peroxidation. In a previous study, evaluating the consumption of frozen Korean raspberries (*Rubus coreanus* Miquel) at 15 g day^{-1} by 15 healthy males, no changes were observed in lipid peroxidation levels, while an increase was observed in the glutathione peroxidase activity (Lee *et al*., 2011). Studies on black raspberries and resveratrol in particular, have shown that they inhibit the proliferation of cancer cells (Wang *et al*., 2009; Stoner *et al*., 2007). A study investigating the antioxidant and antiproliferative effects of berries determined that red raspberries showed the highest effectiveness in blocking the cell proliferation of different types of cancer (Boivin *et al*., 2007). Berries are reported to have various antibacterial, antifungal and antiviral effects (Baliga *et al*., 2011). In two other investigations, the studies reported a beneficial impact of black raspberry on selected cardiovascular health biomarkers such as systolic blood pressure, tumor necrosis factor-alpha and interleukin-6 (Jeong *et al*., 2016a, 2016b).

Red raspberry polyphenols and ellagitannin fractions exhibit strong antimicrobial effects again intestinal pathogens, such as *Klebsiella oxytoca* and *Proteus mirabilis* (Rauha *et al*., 2000). These compounds show antimicrobial effects through mechanisms such as cytoplasmic membrane destabilization, increased plasma membrane permeability, extracellular microbial enzyme inhibition, direct effects on microbial metabolism, and the elimination of compounds necessary for microbial growth (Bautista-Ortín *et al*., 2012).

Overall, the efficacy of the certain whole berries in diet shows to be comparable to the effects elicited with the intake of berry extracts. Daily consumption of 300 g raspberries (Maatta-Riihinen *et al*., 2004), 150 g various berries (Erlund *et al*., 2008), 500 g strawberry (Alvarez-Suarez *et al*., 2014), 60 g black raspberry (Mentor-Marcel *et al*., 2012), 200 g blueberry (Whyte and Williams, 2015), varying amounts of cranberry juice (Ruel *et al*., 2013; Basu *et al*., 2011; Efros *et al*., 2010; Duffey and Sutherland, 2015) and chokeberry juice (Skoczyñska *et al*., 2007; Handeland *et al*., 2014; Kardum *et al*., 2014) were demonstrated to provide health benefits in human intervention trials.

Conclusion

Owing to their contents of anthocyanins, procyanidins, vitamins, minerals, ellagic acid and other polyphenolic compounds, berries exhibit various antioxidant, antimicrobial, anticarcinogenic, antimutagenic and neuroprotective effects. Consuming 400 g of fruit and vegetables every day is known to have a positive effect on health, particularly when associated to body exercise. Including berries in the diet, and consuming a wide variety of such fruits, is believed to provide protection against many different types of health problems. By investigating the bioactive compounds in each type of berry, as well as the bioavailability and effects of these compounds consumed in diet, it will be possible to develop recommendations for consumption. Through *in vivo*, *in vitro*, animal and human studies, it will be possible to clearly demonstrate health effects of the berries and to develop consumption recommendations accordingly.

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