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Review Article

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The Effects of Blackcurrant and Raspberry Consumption on Blood Pressure: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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ABSTRACT

A systematic review and meta-analysis were designed to summarize studies conducted on the effects of raspberry and blackcurrant consumption on blood pressure (BP). Eligible studies were detected by searching numerous five online databases including PubMed, Scopus, Web of Science, Cochrane Library, and Google Scholar, until December 17, 2022. We pooled the mean difference and its 95% confidence interval (CI) by applying a random-effects model. Overall, the impact of raspberry and blackcurrant on BP was reported in ten randomized controlled trials (RCTs) (420 subjects). Pooled analysis of six clinical trials revealed that raspberry consumption has no significant reduction in systolic blood pressure (SBP) (weighted mean differences [WMDs], −1.42; 95% CI, −3.27 to 0.87; p = 0.224) and diastolic blood pressure (DBP) (WMD, −0.53; 95% CI, −1.77 to 0.71; p = 0.401), in comparison with placebo. Moreover, pooled analysis of four clinical trials indicated that blackcurrant consumption did not reduce SBP (WMD, −1.46; 95% CI, −6.62 to 3.7; p = 0.579), and DBP (WMD, −2.09; 95% CI, -4.38 to 0.20; p = 0.07). Raspberry and blackcurrant consumption elicited no significant reductions in BP. More accurate RCTs are required to clarify the impact of raspberry and blackcurrant intake on BP.

Keywords: Raspberry; Blackcurrant; Blood pressure

INTRODUCTION

Hypertension increases the risk of cardiovascular disease (CVD) and stroke [1,2]. The linear relationship between blood pressure (BP) levels and the risk of CVD is considered in people at serious risk [2,3]. Therefore, hypertension prevention and treatment are particularly crucial for enhancing the population's quality of life. Because pharmacological treatments always have side effects, nutrition intervention in disease treatment is very noticeable [3].

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Conflict of Interest
The authors declare that they have no competing interests.

Author Contributions
Conceptualization: Amini MR; Data curation: Amini MR; Formal analysis: Amini MR; Methodology: Nikparast A; Project administration: Hekmatdoost A; Supervision: Hekmatdoost A; Writing - original draft: Nikparast A, Tavakoli S; Writing - review & editing: Sheikhhossein F, Nikparast A.

Therefore, according to the therapeutic and preventive effects of flavonols, flavanols, and anthocyanidins, ingredients for nutraceutical and functional foods, using these dietary supplements is becoming increasingly popular in communities [4]. These components are the subclasses of natural antioxidants' polyphenols, called flavonoids [5]. Flavonoids are present in berries abundantly [6]. Raspberry and blackcurrant belong to the berry family, which contains large amounts of flavonoids, and have been shown to have antioxidant, anti-inflammatory, and anti-atherosclerotic effects [7]. Several trials have shown the improvement effect of intake of raspberry and blackcurrant on BP, lipid profiles, and cardiovascular function [8]. Indeed, it is evident from this study that consuming flavonoids, whether in the form of food or extracted, dramatically enhances vascular health [9]. Also, they improved vascular endothelial function as a result of inducing nitric oxide (NO) production [10] and reduced brachial BP or central arterial stiffness [11].

A systematic review study evaluated the potential antihypertensive activity of berries in lowering BP [12]. In another study, findings show that raspberry reduces BP after 1 week [13]. In this context, the study of Jeong et al. reported that the changes in systolic blood pressure (SBP) in the raspberry consumption groups were significantly reduced, but no alleviated signs were noted in diastolic blood pressure (DBP) among them in an 8-wk follow-up [14].

Regarding a study, short-term blackcurrant intake reduces central BP in older adults [15]. In contrast, in an intervention study on overweight adults, receiving blackcurrant for 6 weeks showed no effect on BP [16].

However, evidence of the effectiveness of raspberry and blackcurrant on BP has not been conclusive. This study aimed to systematically review and perform meta-analysis on all available human intervention studies to evaluate the potential effects of consumption of raspberry and blackcurrant on BP in randomized controlled trials (RCTs).

MATERIALS AND METHODS

The current review was designed based on the protocols of the Cochrane Handbook for Systematic Reviews and Meta-Analysis (PRISMA) statement [17].

Search strategy

The systematic search was conducted in major databases, including PubMed, Scopus, Web of Science, Cochrane Library, and Google Scholar, from inception to December 17, 2022, with no publication time or language restrictions. Detailed information relating to the search strategy of databases as well as the Medical Subject Heading (MeSH) and non-MeSH keywords used to search the online databases to identify relevant studies are provided in **Supplementary Table 1**. The reference lists of the relevant literature were also searched manually for any missing potentially eligible trials. We did not include data from unpublished or gray literature, such as conference abstracts, theses, and patents.

Inclusion and exclusion criteria

Relevant studies were selected based on the PICOS framework [18]. Two authors (MRA and AN) independently selected the trials if they met the following criteria: 1) studies that were conducted on adults (≥ 18 years old); 2) received blackcurrant or raspberry consumption compared to a control group 3) reported weighted or standardized mean differences along

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with 95% confidence intervals (CIs) 4) reported SBP and DBP as outcome measures. We excluded studies with insufficient data or other study design. We also excluded primary trials in the meta-analysis if they: 1) were trials without a control group; 2) blackcurrant or raspberry consumption along with other nutrients.

Data extraction

The first author's name, country, publication year, number of primary studies, and participant number were extracted and then tabulated. Furthermore, for each primary RCT from included meta-analyses, we also extracted the following required data: duration of intervention, participants' health status, participant number, mean ± standard deviation (SD) or changes in SBP and DBP, and the dose of consumption if necessary. WebPlotDigitizer software (Copyright 2010–2022, Ankit Rohatgi) was used to estimate the number of measures when they were reported in figures and charts in the original papers. The data extraction was done by two independent authors (MRA and AN), and the possible discrepancies were resolved by discussion with AH.

Quality assessment of studies

A systematic assessment of the risk of bias in the included studies was fulfilled using the Revised Cochrane Risk-of-Bias Tool (RoB 2) [19] and by using the following criteria: 1) random sequence generation, 2) allocation concealment, 3) blinding of participants and personnel, 4) blinding of outcome assessment, 5) incomplete outcome data, 6) selective reporting, and 7) other potential threats to validity. Studies were categorized into low risk of bias, high risk of bias, and some concerns, based on Cochrane Handbook recommendations (**Table 1**).

Statistical analysis

The estimated effect size was the difference in mean changes SD of SBP and DBP (change in the treatment group/period minus the change in the control group/period) in each of the included studies. If the studies didn't report mean and SD, we converted the available statistical data into mean and SD by applying the suitable formula: $SD_{difference}$ = square root $[(SD_{pre\text{-}treatment})^2+(SD_{post\text{-}treatment})^2 - (2\times R \times SD_{pre\text{-}treatment}\times SD_{post\text{-}treatment})]$, assuming a correlation coefficient (R) 0.8 as it is a conservative estimate for an expected range of 0–1 [27]. Were used to calculate the SD for mean changes. Weighted mean differences (WMDs) and 95% CIs were calculated for net changes by using the random-effects model, which takes the between-study heterogeneity into account. The between-study heterogeneity was assessed using the Cochrane Q test. Furthermore, to calculate the percentage of total variation explained by the between-study heterogeneity, the I^2 statistic (which is an estimate ranging from 0 to 100% with lower values indicating less heterogeneity) was used. The analysis was carried out using

Table 1. Risk of bias for randomized controlled trials, assessed according to the revised Cochrane risk-of-bias tool for randomized trials (RoB 2)

Publications	Random sequence generation	Allocation concealment	Blinding of participants, personnel and outcome assessors	Incomplete outcome data	Selective outcome reporting	Other bias
Montanari et al. [20] (2021)	L	S	L	L	L	L
Okamoto et al. [15] (2020)	L	S	L	L	L	H
Khan et al. [16] (2014)	L	S	L	L	L	L
Ohguro et al. [21] (2012)	L	S	H	L	L	L
Heneghan et al. [22] (2017)	L	S	H	L	L	L
Jeong et al. [14] (2016)	L	S	L	L	L	L
Cho et al. [23] (2020)	L	L	L	L	L	L
Franck et al. [24] (2020)	L	S	H	L	L	L
Jeong et al. [25] (2016)	L	S	L	L	L	L
Schell et al. [26] (2019)	L	S	H	L	L	L

L, low risk of bias; H, high risk of bias; S, some concerns.

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Stata software, version 14 (Stata Corp., College Station, TX, USA). The values of p less than 0.05 were regarded to be statistically significant.

RESULTS

Study selection

We screened 669 articles according to inclusion and exclusion criteria and, finally, 10 studies [14-16,20-26] were included in the present systematic review (**Figure 1**).

Study characteristics

Characteristics of the eligible studies are reported in **Table 2**. Studies were conducted in the UK [15,16], USA [26], Turkey [20], Ireland [22], Korea [14,25], and Japan [21]. Of the total ten RCTs that assessed the effect of blackcurrant and raspberry consumption on the DBP and SBP, one study [26] was crossover in design and consisted of 22 participants. Overall, 420 participants, aged 32.19 to 61.7 years, were included in these studies. The duration of the studies ranged from 1 to 24 weeks. Participants were healthy [15,16,22] with metabolic syndrome [25], type 2 diabetes [26], prehypertension [14], slight hyperinsulinemia/hypertriglyceridemia [24], healthy with endurance-trained cyclists [20], patients with open-angle glaucoma [21] and borderline-high cholesterol levels [23]. Of all ten studies, six were supplemented by raspberry [14,22-26], and the other study's intervention was blackcurrant [15,16,20,21]. Participants' BMI varied between 21.6 [15] to 35.3 kg/m^2 [26] at the study baseline.

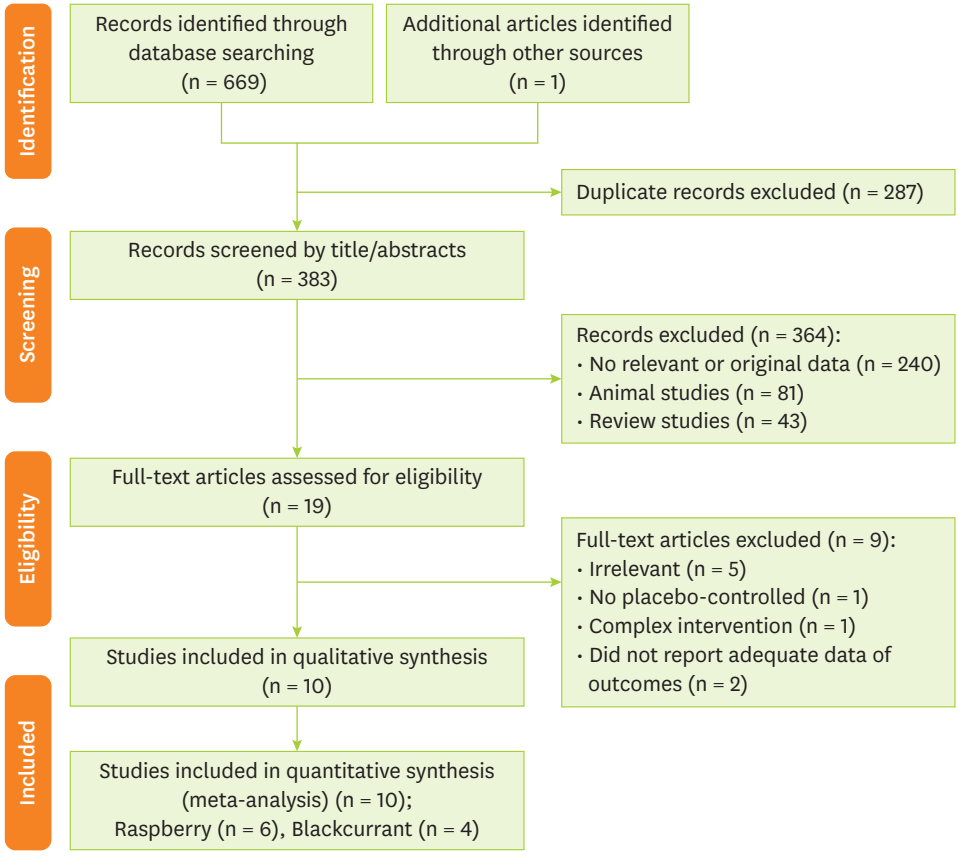

Figure 1. Flow chart of the number of studies identified and selected into the meta-analysis.

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Table 2. Demographic characteristics of the included studies

Studies	Location	Study design	Health status	Gender	Sample size	Duration (wk)	Mean age (yr)	Baseline BMI (kg/m^2)	Intervention		Outcome
									Treatment group	Control group	
Montanari et al. [20] (2021)	Turkey	Randomized, double-blind, placebo-controlled, crossover	Healthy, endurance-trained cyclists	Male	13	1	39	23.6	300 mg New Zealand blackcurrant extract	Placebo	SBP/DBP
Montanari et al. [20] (2021)	Turkey	Randomized, double-blind, placebo-controlled, crossover	Healthy, endurance-trained cyclists	Male	13	1	39	23.6	600 mg New Zealand blackcurrant extract	Placebo	SBP/DBP
Okamoto et al. [15] (2020)	UK	Randomized, double-blind, placebo-controlled, crossover	Healthy	Both	14	1	73.3	21.6	600 mg New Zealand blackcurrant extract	Placebo	SBP/DBP
Khan et al. [16] (2014)	UK	Randomized, double-blind, placebo-controlled, parallel trial	Healthy	Both	32	6	53	28.8	250 mL of low blackcurrant juice drink (6.4% juice) four times a day	Placebo	SBP/DBP
Khan et al. [16] (2014)	UK	Randomized, double-blind, placebo-controlled, parallel trial	Healthy	Both	32	6	53	28.8	250 mL of high blackcurrant juice drink (20% juice) four times a day	Placebo	SBP/DBP
Ohguro et al. [21] (2012)	Japan	Randomized, placebo-controlled, double-blind	Patients with open-angle glaucoma	Both	38	24	61.7	NA	50 mg black currant anthocyanins	Placebo	SBP/DBP
Heneghan et al. [22] (2017)	Ireland	Randomized, placebo-controlled, crossover	Healthy	Both	80	18	57.7	NA	Blackberry polyphenol enriched beverage [total polyphenol content: ~700 mg GAE/250 mL serving/d]	Low-dose polyphenol beverage [< 100 mg GAE/250 mL serving/d]	SBP/DBP
Jeong et al. [14] (2016)	Korea	Randomized, double-blind, placebo-controlled	Prehypertensive	Both	22	8	57.2	24.6	1,500 mg, moderate dose black raspberry	Placebo	SBP/DBP
Jeong et al. [14] (2016)	Korea	Randomized, double-blind, placebo-controlled	Prehypertensive	Both	23	8	57.2	24.6	2,500 mg, high-dose black raspberry	Placebo	SBP/DBP
Cho et al. [23] (2020)	Korea	Randomized, double-blind, placebo-controlled	Borderline-high cholesterol levels	Both	77	12	47.3	23.5	600 mg of freeze-dried rubus coreanus extract	Placebo	SBP/DBP
Franck et al. [24] (2020)	Canada	Randomized, placebo-controlled, parallel trial	Slight hyperinsulinemia/ hypertriglyceridemia	Both	48	8	32.19	29.9	280 g/day of frozen raspberries	Placebo	SBP/DBP
Jeong et al. [25] (2016)	Korea	Randomized, placebo-controlled, parallel trial	Metabolic syndrome	Both	51	12	58.5	25.3	750 mg, black raspberry	Placebo	SBP/DBP
Schell et al. [26] (2019)	USA	Randomized, crossover	Type 2 diabetes	Both	22	4	54	35.3	250 g frozen red raspberry	Control meal	SBP/DBP

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; GAE, gallic acid equivalents.

Effects of raspberry on SBP and DBP

Six primary trials from 10 systematic reviews and meta-analysis evaluated the impact of raspberry on SBP and DBP. We found that raspberry consumption did not reduce SBP compared to the control group (WMD, −1.42; 95% CI, −3.27 to 0.87; p = 0.224) and with no significant between-study heterogeneity (I^2= 34%, p = 0.16) (**Figure 2**). There was also no significant effect on DBP (WMD, −0.53; 95% CI, −1.77 to 0.71; p = 0.401) with significant between-study heterogeneity (I^2 = 0.0%, p = 0.897) (**Figure 3**).

Effects of blackcurrant on SBP and DBP

Pooling 6 effect sizes from 4 publications, including 97 participants, we found that blackcurrant did not reduce SBP (WMD, −1.46; 95% CI, −6.62 to 3.7; p = 0.579) (I^2 = 34%; p = 0.169) (**Figure 4**). For DBP, we did not find any reduction along with blackcurrant (WMD, −2.09; 95% CI, −4.38 to 0.20; p = 0.07) (I^2 = 27.2%; p = 0.232) (**Figure 5**).

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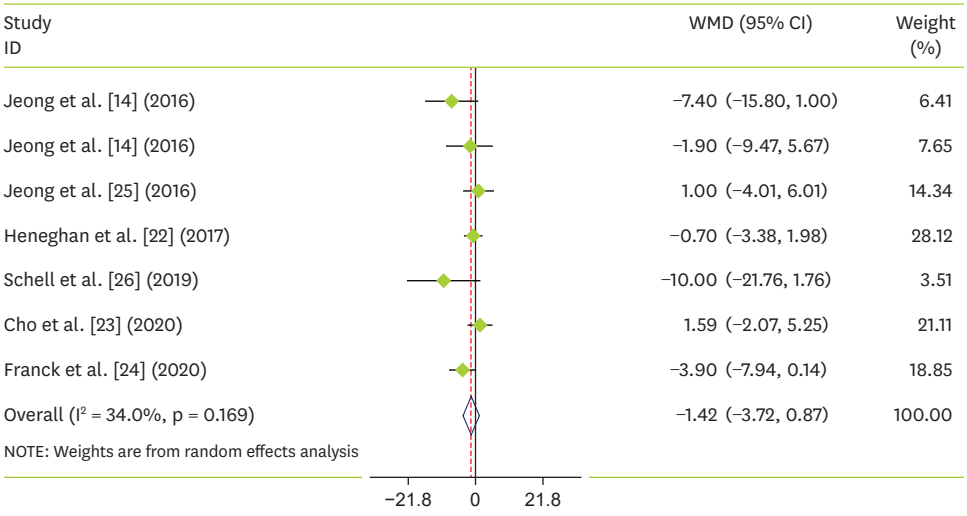

Figure 2. Forest plot detailing weighted mean difference and 95% CIs for the effect of raspberry supplementation on systolic blood pressure.
WMD, weighted mean difference; CI, confidence interval.

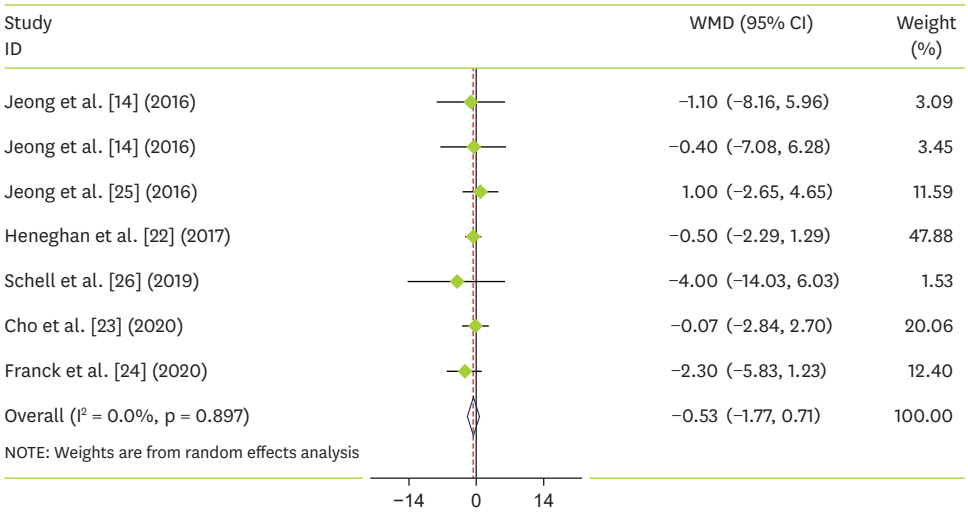

Figure 3. Forest plot detailing weighted mean difference and 95% CIs for the effect of raspberry supplementation on diastolic blood pressure.
WMD, weighted mean difference; CI, confidence interval.

Sensitivity analysis

To detect the impact of a single trial on the pooled effect sizes, we removed each study from the analysis. The effect sizes for the influence of blackcurrant and raspberry on SBP and DBP were robust in the leave-one-out sensitivity analysis.

Publication bias

Egger's weighted regression tests were conducted to find the publication bias. The results of Egger's test showed no publication bias for SBP (p = 0.161), DBP (p = 0.496), SBP (p = 0.06), DBP (p = 0.327) respectively, in the raspberry and blackcurrant groups.

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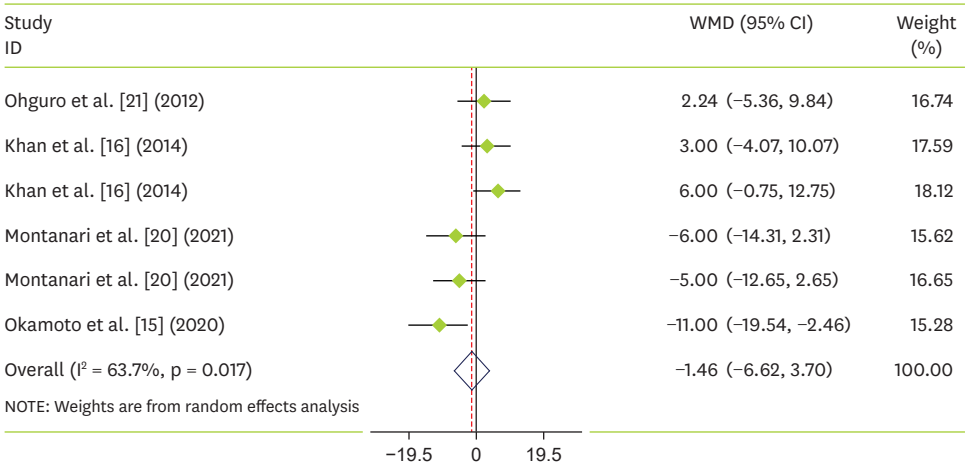

Figure 4. Forest plot detailing weighted mean difference and 95% CIs for the effect of blackcurrant supplementation on systolic blood pressure.
WMD, weighted mean difference; CI, confidence interval.

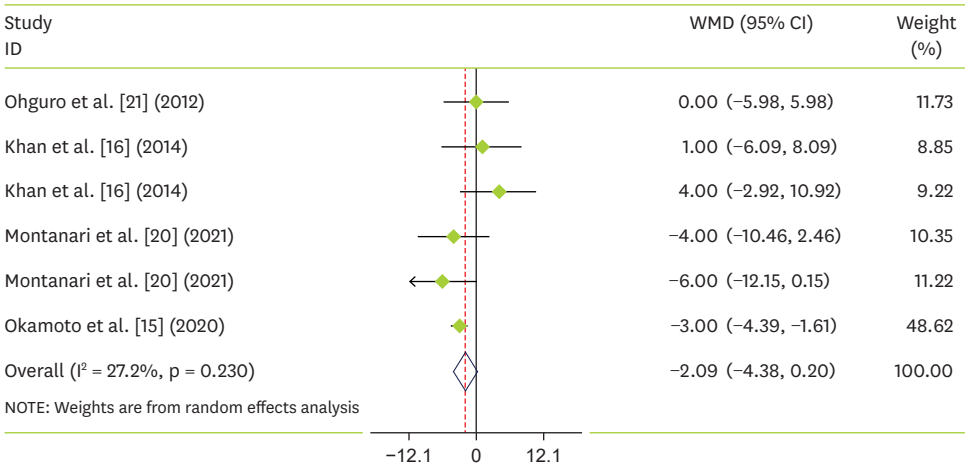

Figure 5. Forest plot detailing weighted mean difference and 95% CIs for the effect of blackcurrant supplementation on diastolic blood pressure.
WMD, weighted mean difference; CI, confidence interval.

DISCUSSION

To the best of our knowledge, the current systematic review and meta-analysis examined the efficacy of blackcurrant and raspberry on SBP and DBP for the first time. Indeed, in this meta-analysis, a comprehensive assessment of the effect of blackcurrant or blackberry on SBP and DBP was conducted.

Accordingly, we identified a total of 10 RCTs that evaluated the effect of blackcurrant or raspberry on SBP and DBP, and found that neither blackcurrant nor raspberry has beneficial effects on SBP and DBP. This is supported by the observation that high BP increases the risk of CVD as well as all-cause mortality [28-30]. Berry fruits are a rich source of nutrients and polyphenols, and there is evidence to support that increased consumption of berries may contribute to the prevention of CVD through effects on BP, blood lipid profiles, and

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vascular endothelial function [8]. In human-based studies, it has been reported that 600 mg/day of blackcurrant extract for 7 days may improve SBP and DBP in elderly people [15]. Another study showed that 24 months of blackcurrant supplementation with a dose of 50 mg/day improved glaucoma but did not have any significant effect on DBP and SBP in patients with glaucoma [21]. Heneghan et al. found that a 6-week supplementation with 700 mg/day blackberry-derived polyphenol had no significant effect on SBP and DBP [22]. On the other hand, it has been revealed that blackcurrant juice supplementation with a dose of 250 mg/day for 6 weeks has no significant effect on SBP and DBP [16]. Also, the results of another study showed that 600 mg of blackberry extraction consumed for 12 weeks did not significantly reduce SBP and DBP [23]. As well the findings from a study by Jeong et al. [25] revealed that a 12-week supplementation with 750 mg/day black raspberry did not have any significant effect on SBP and DBP. For the inconsistent results observed among studies, differing doses, differences in sample sizes, and periods of intervention need to be addressed. Blackcurrants and raspberries are rich in antioxidants, including anthocyanin and vitamin C. Blackcurrants contain a considerable amount of anthocyanins, which include cyanidin-3-O-glucoside, cyanidin-3-O-rutinoside, delphinidin-3-O-glucoside, and delphinidin-3-O-rutinoside [31]. Various biological functions are attributed to blackcurrants, including antihyperlipidemic [32], anti-inflammatory [33,34], and antiatherosclerotic [35] effects.

Blackcurrants and berries improve vascular function via two mechanisms. In one of the mechanisms that are related to the modulation of vascular tone and reactivity, researchers in an in vitro study found polyphenol extract increased NO synthesis by increasing an endothelial nitric oxide synthase (eNOS)-dependent pathway [36]. Enhanced eNOS expression and NO production are found in endothelial cells treated with resveratrol [37]. In another study in vitro, polyphenols also phosphorylated eNOS and activated endothelial-dependent vasodilatation [38]. Another mechanism involved is endothelin-1 inhibition. Polyphenols were found to inhibit the production of endothelin-1, which is derived from the endothelium and is a potent vasoconstrictor [39]. Apart from the anthocyanins present in blackcurrant and berries, vitamin C alone significantly increased the phosphorylation of Akt and eNOS. In a randomized human trial, flavonoids suppressed production of endothelin-1 [40]. Polyphenols enhance endothelial cell plasminogen activator levels, which are relevant to fibrinolysis and thrombosis [41]. Black raspberry regulates BP through the renin-angiotensin system. According to previous in vitro and in vivo studies, black raspberry decreases ACE and renin levels [42]. Isolated anthocyanins, such as delphinidin-3-O-sambubiosides and cyanidin-3-O-sambubiosides, inhibited ACE activity [43]. This evidence demonstrates the importance of blackcurrants and raspberries in preventing hypertension.

Our systematic review in conjunction with meta-analysis has several strengths. We used very precise search terms and a wide range of database searches. Statistical examinations showed no evidence of publication bias in our analyses. Our findings also had several limitations: First, due to the small number of studies, we were not able to better evaluate the effect of blackcurrant and raspberry on SBP and DBP. Second, most of the studies considered showed bias, and thus it is hard to reach a definitive conclusion. Third, the existence of uncontrollable factors in the two comparison groups, such as eating habits and lifestyle, can influence the overall results. Given these limitations, the findings of the present review should be interpreted with caution. Moreover, future intervention studies on SBP and DBP are needed to find the beneficial effect of blackcurrants and raspberries in the prevention of hypertension.

Existing evidence from RCTs in this meta-analysis suggests that treatment with neither

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blackcurrant nor raspberry is associated with significant changes in SBP and DBP. More studies are necessary to validate the effect of blackcurrant and raspberry supplementation on SBP and DBP.

SUPPLEMENTARY MATERIAL

Supplementary Table 1

Search syntax

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