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Original Article

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Anti-hypertensive Effects of Artichoke Supplementation in Adults: A Systematic Review and Dose-response Meta-analysis of Randomized Controlled Trials

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ABSTRACT

Despite controversies, no earlier study has systematically summarized findings from earlier studies on the effect of artichoke supplementation on blood pressure. Therefore, current systematic review and meta-analysis was done on the effect of artichoke supplementation on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in adults. Five databases were searched from inception to January 2022 using relevant keywords. All randomized clinical trials investigating the impact of oral artichoke supplementation on any of the blood pressure parameters including SBP or/and DBP were included. Out of 1,507 citations, 7 trials that enrolled 472 subjects were included. Artichoke supplementation resulted in significant reduction in SBP (weighted mean difference [WMD], −2.01 mmHg; 95% confidence interval [CI], −3.78, −0.24; p = 0.026) and DBP (WMD, −1.45 mmHg; 95% CI, −2.81, −0.08; p = 0.038). Greater effects on SBP were detected in trials using ≤ 500 mg artichoke, lasted > 8 weeks, participants aged < 50 years' old and sample size ≤ 70. There was also a similar impact of artichoke on DBP. However, significant non-linear associations were found between artichoke supplementation dosage and study duration with both SBP (for dosage: $p_{non\text{-}linearity} = 0.002$, for duration: $p_{non\text{-}linearity} = 0.016$) and DBP (for dosage: $p_{non\text{-}linearity} = 0.005$, for duration: $p_{non\text{-}linearity} = 0.003$). We found a significant reduction in both SBP and DBP following artichoke supplementation in adults. It could be proposed as a hypotensive supplement in hypertension management.

Keywords: Artichoke; Hypertension; Blood pressure

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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: Sheikhhossein F; Project administration: Hekmatdoost A; Supervision: Hekmatdoost A; Writing - original draft: Alvani M, Heidarian E, Sohrabnavi S; Writing - review & editing: Sheikhhossein F, Seyyed Shoura SM.

INTRODUCTION

Hypertension (HTN) is an independent risk factor for cardiovascular disease. Constant increased pressure in blood vessels can silently damage the blood vessels, heart, brain, and kidneys [1,2]. The prevalence of HTN increased at an alarming rate between 1975 and 2015 among people aged 18 years and older [3]. HTN is also a lifestyle-related disease and lifestyle changes are effective for its management and prevention including reducing alcohol drinking; avoiding high sodium chloride intake; and consuming a diet loaded with fruits, vegetables, and low-fat dairy products with a reduced amount of saturated and total fat [1,2]. Recently adherence to the "DASH diet" which emphasizes consumption of fruit, and vegetables have emerged as an effective approach to reducing blood pressure [4]. Besides lifestyle modification, most patients will need antihypertensive drugs to confer multiple mechanisms suspected of having a role in their HTN [5]. Lowering systolic blood pressure (SBP) by 10–12 mmHg and diastolic blood pressure (DBP) by 5–6 mmHg contracts relative risk reductions of 35%–40% for stroke and 12%–16% for coronary heart disease within 5 years of initiating treatment [6]. As long-term use of medications could exert adverse effects comprising dizziness, dehydration, constipation, and drowsiness [7] adopting effective alternative therapies in particular dietary management, which could prevent future complications would be very valuable [8]. One of the therapeutic plants with a beneficial impact on HTN [9-12] is the *Cynara scolymus* L. (commonly known as artichoke). Lately, artichoke and its products have gained attention in scientific society. Artichoke is related to the traditional Mediterranean diet style, as is a well-known plant in the Mediterranean countries [13]. Artichoke's leaves contain polyphenolic compounds, prebiotics (inulin), minerals, ascorbic acids, and folate [13]. Its leaf extract is rich in dietary fibers and antioxidant components [14], proposing the extract as beneficial in the control of HTN. Based on an experimental study, artichoke leaf extract also increases endothelial nitric oxide synthase (eNOS) gene expression and nitric oxide (NO) production in cultured human vascular endothelial cells and enhances endothelium-dependent vasodilation in mice aorta [15]. The current evidence is relatively limited and non-conclusive and only a few studies have reported that the supplementation of artichoke and artichoke products have a promising effect on controlling blood pressure [9-12]. While these findings are not supported by other studies [14,16,17]. A recent meta-analysis indicated that artichoke supplementation did not affect blood pressure. However, it appears that several studies included in that meta-analysis had included artichoke supplementation in combination with other interventions (co-supplementation) that have yielded different results from the present study. For instance, in the study of Cicero et al. [18] artichoke and berberis, and in the study of Ahn et al. [19] Jerusalem artichoke and fermented soybean powder mixture supplementation have been considered combination as an intervention. Also, 2 other articles are included in the present study [16,17]. Therefore, current systematic review and meta-analysis were conducted to summarize earlier controlled clinical trials assessing the effect of artichoke intake on blood pressure.

MATERIALS AND METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines were followed in conducting this systematic review and meta-analysis [20].

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Search strategy

Online medical databases, including MEDLINE, Scopus, Cochrane Library, Embase, and Web of Science were searched from inception until January 2022. The search algorithm included all possible Medical Subject Headings (MeSH) and non-MeSH terms: (artichoke[tiab] OR artichokes[tiab] OR Cynara[tiab] OR "Cynara scolymus"[Mesh] OR Cynara[Mesh]) AND (hypertension[tiab] OR "Blood Pressure"[tiab] OR Prehypertension[tiab] OR BP[tiab] OR "Systolic blood pressure"[tiab] OR SBP[tiab] OR "Diastolic blood pressure"[tiab] OR DBP[tiab] OR cardiovascular[tiab] OR hypotensive[tiab] OR "Hypertension"[Mesh] OR "Blood Pressure"[Mesh] OR "Prehypertension"[Mesh]) AND (intervention[tiab] OR RCT[tiab] OR "controlled trial"[tiab] OR randomized[tiab] OR random[tiab] OR Randomly[tiab] OR Placebo[tiab] OR Assignment[tiab] OR "clinical trial"[tiab] OR trial[tiab] OR randomised[tiab] OR "Methods"[Mesh] OR "Randomized Controlled Trial"[Publication Type] OR "Controlled Clinical Trial"[Publication Type] OR "Placebos"[Mesh] OR "Placebo Effect"[Mesh] OR "Clinical Trial"[Publication Type] OR "Clinical Trials as Topic"[Mesh]). Moreover, to avoid missing any related studies, we manually searched the references of the included articles.

Inclusion and exclusion criteria

The search terms and strategies were constructed according to the PICOS model [21] including questions about participants (adults aged > 18 years), intervention (artichoke), comparator (placebo), outcome (SBP and DBP), and study design (parallel and cross-over clinical trial).

Studies were excluded if they were; letters, comments, conference papers, reviews, meta-analyses, and ecologic studies, if they were conducted on animals, or children, or were not placebo-controlled groups and assessed the effects of supplementation along with other interventions. Also, unpublished and grey literature, like patents, congress abstracts, and dissertations were excluded. In addition, we excluded publications examining the effects of artichoke supplementation in combination with other interventions (co-supplementation) [18,19]. We also excluded studies that did not include the placebo group [22].

Data extraction

Study selection and data extraction were performed at least twice by an independent researcher (FS). Any disagreement about eligibility was discussed with a second reviewer (MRA). The following data were collected from each study: study characteristics (first author's name, year of publication, study location, publishing year, and study design), participant characteristics (mean age and sex of participants separately by intervention and non-intervention groups, the health status of the population, number of participants in each group) and intervention (type, dose, and duration of supplementation) and mean and standard deviation (SD) of obesity indices at baseline, and end of study or changes between baseline and post-intervention.

Quality assessment of studies

The quality of studies was assessed for risk of bias by using the Revised Cochrane risk-of-bias tool (RoB 2) [23]. The following methodological domains were considered: (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. According to Cochrane Handbook recommendation, studies were stratified as low risk of bias; high risk of bias, and some concerns (**Table 1**).

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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	Randomization process	Deviations from the intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall bias
Roghani-Dehkordi et al. (2009) [10]	L	L	L	L	L	L
Rangboo et al. (2016) [9]	L	L	S	L	L	L
Panahi et al. (2018) [14]	L	L	L	L	L	L
Ebrahimi-Mameghani et al. (2018) [11]	L	L	S	L	L	L
Rezazadeh et al. (2019) [16]	L	L	S	L	L	L
Rondanelli et al. (2020) [17]	L	L	L	L	L	L
Ardalani et al. (2020) [12]	L	L	L	L	L	L

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

Statistical analysis

We estimated the effect of artichoke on SBP and DBP by pooling mean and SD values of the baseline and the end of the studies in both intervention and control groups. If the studies did not 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 [24]. When means (± SD) of outcome measures were not directly available and a standard error of the mean (SEM) was presented in place of SD, we converted it to SD using this formula: $SD = SEM \times \sqrt{n}$, being "n" the number of subjects in each group. Ultimately, we used the GetData Graph Digitizer version 2.24 to extract data from studies that reported outcomes in the graphical form [25].

At first, a fixed-effect model was performed to determine the relationship with a forest plot. The degree of heterogeneity was defined based on I-squared statistic. The heterogeneity was substantially significant when the Cochrane's test showed I^2 greater than 50% with a p value < 0.1. Data with significant heterogeneity were analyzed using DerSimonian and Laird random-effects model, otherwise, a fixed-effect model was performed [26]. A priori subgroup analysis of intervention and duration of supplementation, sample size, dosage, and mean age was performed to detect potential sources of heterogeneity. We also performed fractional polynomial modeling to identify non-linear potential effects of artichoke dosage (mg/day) and duration of intervention (weeks) [27]. Any publication bias was investigated by visually inspecting funnel plots and quantitatively evaluated using Egger test [28]. Meta-analysis was carried out using Stata software, version 14.0 (Stata Corp LP, College Station, TX, USA). The p values less than 0.05 were regarded to be statistically significant.

RESULTS

Study selection

At first, 1,507 relevant articles were included at the initial stage, and an additional one articles were identified through hand-searching references of included papers. We identified 168 duplication records after removing duplicates, 1,340 relevant articles were screened by title and abstract, and after screening by title and abstract, unrelated studies were discarded due to the primary evaluation of inclusion criteria: unrelated title (n = 1,074), animal study (n = 135), and review (n = 114) and 17 papers were retained for full-text review. Of these articles, 10 were excluded because of the following reasons: irrelevant (n = 3), has no placebo-controlled group (n = 1), complex intervention (n = 1), without sufficient data for outcomes (n = 2), and conference abstracts (n = 3). Finally, 7 studies met all our inclusion criteria [9-12,14,16,17]. **Figure 1** demonstrates the process by which articles were selected.

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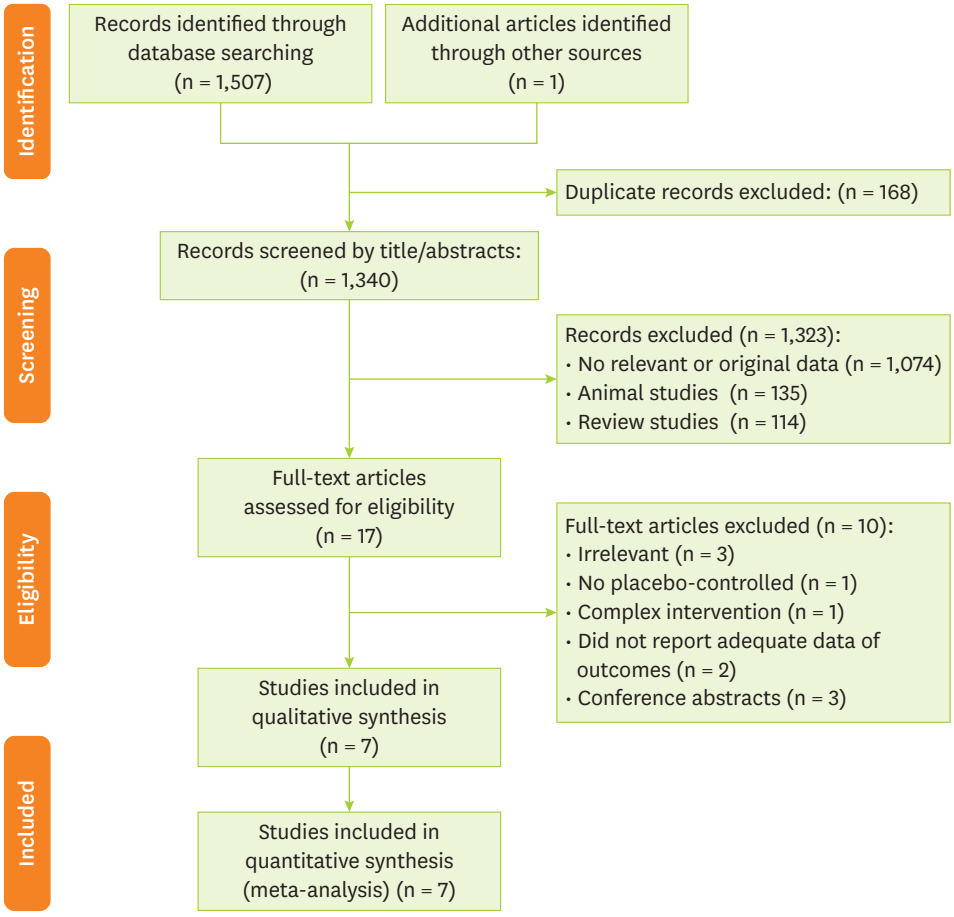

Figure 1. Flow chart of the number of studies identified and selected into the meta-analysis.

Study characteristics

The summary of the main features of the included studies is shown in **Table 2**. We identified 7 randomized clinical trials that assessed the effects of artichoke on SBP and DBP [9-12,14,16,17]. Selected eligible trials enrolled 472 participants with ages ranging from 38.4 to 51.5 years old [16,17]. These studies were carried out in various countries including Iran [9-12,14,16], and Italy [17]. Participant health status was as follows: non or mild hypercholesterolemia [9,10], hypertriglyceridemia [16], non-alcoholic fatty liver disease [14], metabolic syndrome [11], overweight and obese with newly detected impaired fasting glucose [17], and hypertensive [12]. Most of the studies recruited both sexes [9,11,12,14,16,17], however some studies were conducted in males [10]. Seven papers analyzed the effectiveness of interventions on both SBP and DBP [9-12,14,16,17]. Seven studies had parallel designs [9-12,14,16,17]. The artichoke was administrated in doses ranging from 50 mg/day [10] and 2,700 mg/day [9]. The shortest intervention period was 4 weeks [17] and the longest one was 12 weeks [10,11,16]. The sample size was different from 40 participants [12] to 89 participants [14]. Baseline body mass index was various from 24.5 kg/m^2 [10] to 34.3 kg/m^2 [11].

Effect of artichoke on SBP

Seven eligible trials including a total of 505 participants, examined the effect of artichoke supplementation on SBP. Combining their findings based on random-effects model,

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Table 2. Demographic characteristics of the included studies

First author (yr)	Location	Study design	Health status	Sex	Sample size	Duration (wk)	Mean age (yr)	Baseline BMI (kg/m^2)	Intervention		Outcome
									Treatment group	Control group	
Roghani-Dehkordi et al. (2009) [10]	Iran	Randomized, double-blind, placebo-controlled, parallel trial	Non or mild hypercholesterolemic	Male	56	12	42.5	24.5	50 mg artichoke leaf extract	Placebo	SBP/DBP
Roghani-Dehkordi et al. (2009) [10]	Iran	Randomized, double-blind, placebo-controlled, parallel trial	Non or mild hypercholesterolemic	Male	51	12	42.5	24.5	100 mg artichoke leaf extract	Placebo	SBP/DBP
Rangboo et al. (2016) [9]	Iran	Randomized, double-blind, placebo-controlled, parallel trial	Non or mild hypercholesterolemic NASH patients	Both	66	8	48.9	NA	2,700 mg artichoke leaf extract	Placebo	SBP/DBP
Panahi et al. (2018) [14]	Iran	Randomized, double-blind, placebo-controlled, parallel trial	Patients with NAFLD	Both	89	8	46.2	29.1	600 mg artichoke leaf extract	Placebo	SBP/DBP
Ebrahimi-Mameghani et al. (2018) [11]	Iran	Randomized, double-blind, placebo-controlled, parallel trial	Metabolic syndrome	Both	68	12	38.9	34.3	1,800 mg artichoke leaf extract	Placebo	SBP/DBP
Rezazadeh et al. (2019) [16]	Iran	Randomized, double-blind, placebo-controlled, parallel trial	Hypertriglyceridemia	Both	48	12	38.4	33.8	1,800 mg artichoke leaf extract	Placebo	SBP/DBP
Rondanelli et al. (2020) [17]	Italy	Randomized, double-blind, placebo-controlled, parallel trial	Overweight and obese with newly detected IFG	Both	54	4	51.5	30.0	500 mg artichoke leaf extract	Placebo	SBP/DBP
Ardalani et al. (2020) [12]	Iran	Randomized, double-blind, placebo-controlled, parallel trial	Hypertensive	Both	40	8	45.0	29.5	1,000 mg artichoke leaf extract	Placebo	SBP/DBP

BMI, body mass index; NASH, nonalcoholic steatohepatitis; NAFLD, non-alcoholic fatty liver disease; IFG, impaired fasting glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure; NA, not reported.

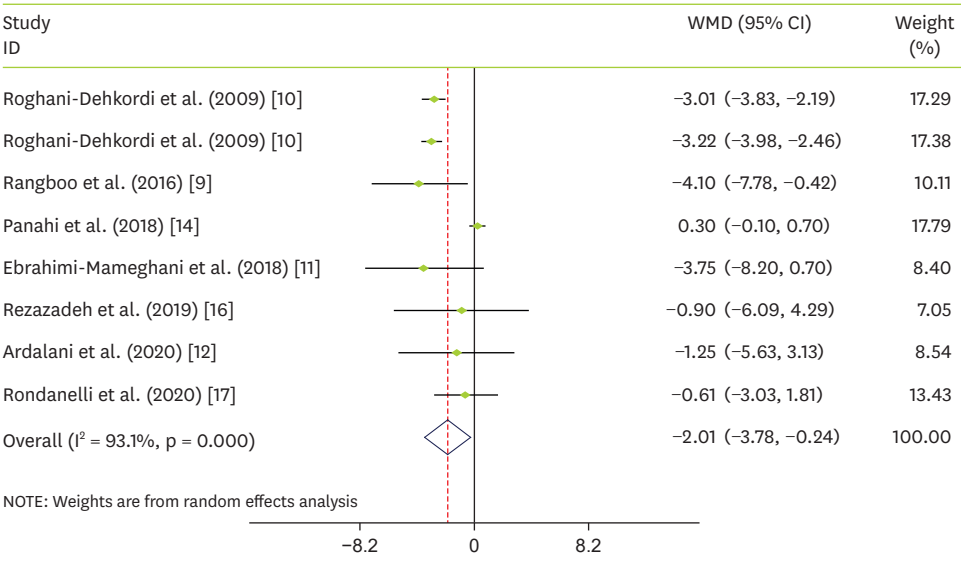

Figure 2. Forest plot detailing WMDs and 95% CIs for the effect of artichoke supplementation on systolic blood pressure.
WMD, weighted mean difference; CI, confidence interval.

we found that SBP was significantly reduced in artichoke group compared to the control (weighted mean difference [WMD], −2.01 mmHg; 95% confidence interval [CI], −3.78, −0.24; p = 0.026), including a significant heterogeneity between studies (I^2= 93.1%; P < 0.001) (**Figure 2**).

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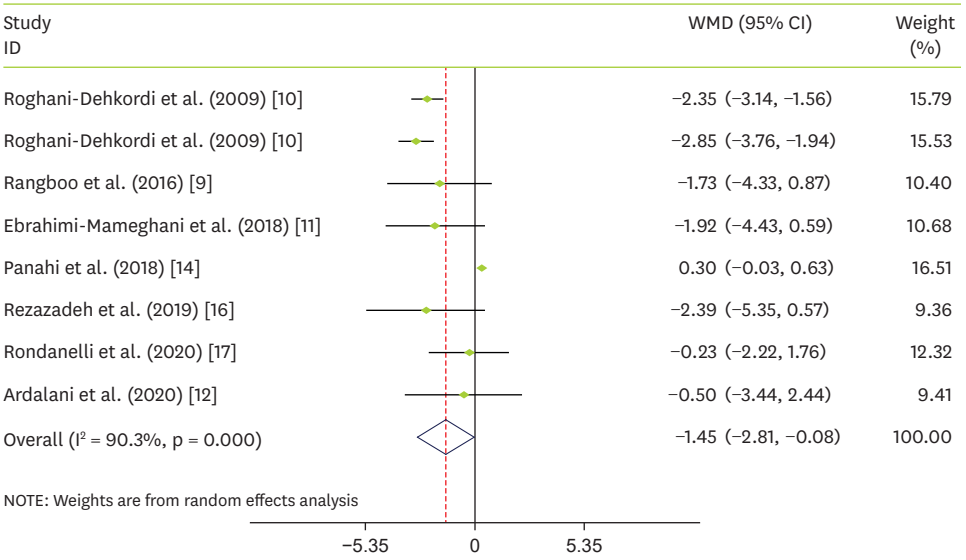

Figure 3. Forest plot detailing WMD and 95% CIs for the effect of artichoke supplementation on DBP. WMD, weighted mean difference; CI, confidence interval; DBP, diastolic blood pressure.

Effect of artichoke on DBP

Seven qualified studies including a total of 505 subjects, reported DBP as their outcome. After pooling these studies based on random-effects model, we found a significant reduction in DBP following artichoke consumption (WMD, −1.45 mmHg; 95% CI, −2.81, −0.08; p = 0.038), with a significant between-study heterogeneity (I^2= 90.3%; p < 0.001) (**Figure 3**).

Subgroup analysis

Findings from the subgroup analyses are outlined in **Table 3**. After categorizing studies on the basis of artichoke dosage, SBP was significantly decreased for ≤ 500 mg (WMD, −3.00 mmHg; 95% CI, −3.54, −2.46; p < 0.001). The subgroup analyses based on duration of intervention revealed that the effect of artichoke supplementation on SBP was significantly greater in trials lasted > 8 weeks (WMD, −3.11 mmHg; 95% CI, −3.66, −2.56; p < 0.001) than ≤ 8 weeks (WMD, 0.21 mmHg; 95% CI, −0.18, 0.60; p = 0.281). Moreover, reduction in SBP after artichoke intake was remarkable in subjects aged < 50 years' old (WMD, −3.08 mmHg; 95% CI, −3.62, −2.54; p < 0.001), but not in the elders (WMD, 0.23 mmHg; 95% CI, −0.17, 0.62; p = 0.258) and sample size ≤70 significantly changed SBP (WMD, −2.97; 95% CI, −3.65, −2.28; p < 0.001).

DBP was also reduced by using lower doses (WMD, −2.37 mmHg; 95% CI, −2.94, −1.80; p < 0.001), but not in higher ones (WMD, 0.19 mmHg; 95% CI, −0.13, 0.51; p = 0.249). The subgroup analyses based on duration of intervention revealed that the effect of artichoke supplementation on DBP was significantly greater in trials lasted > 8 weeks (WMD, −2.53 mmHg; 95% CI, −3.10, −1.96; p < 0.001). Moreover, reduction in DBP after artichoke intake was remarkable in subjects aged < 50 years' old (WMD, −2.42 mmHg; 95% CI, −2.89, −1.86; p < 0.001), and sample size ≤ 70 significantly changed DBP (WMD, −2.20; 95% CI, −2.91, −1.49; p < 0.001).

Non-linear dose-response relation between doses and duration of artichoke intake and outcomes

Following dose-response assessment, significant non-linear association between artichoke dosage and SBP ($p_{non\text{-}linearity}$ = 0.002), and DBP ($p_{non\text{-}linearity}$ = 0.005) was seen (**Figure 4**).

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Table 3. Subgroup analysis of included randomized controlled trials in meta-analysis of the effect of artichoke supplementation on blood pressure

Group	No. of trials	WMD (95% CI)	p value	I^2 (%)	p-heterogeneity	p for between subgroup heterogeneity
SBP						
Dosage (mg)						< 0.001
≤ 500	2	−3.00 (−3.54, −2.46)	< 0.001	50.8	0.131	
> 500	5	0.20 (−0.19, 0.59)	0.321	56.0	0.059	
Duration (wk)						< 0.001
≤ 8	4	0.21 (−0.18, 0.60)	0.281	52.6	0.097	
> 8	3	−3.11 (−3.66, −2.56)	< 0.001	0.0	0.822	
Mean age (yr)						< 0.001
< 50	4	−3.08 (−3.62, −2.54)	< 0.001	0.0	0.810	
≥ 50	3	0.23 (−0.17, 0.62)	0.258	66.1	0.052	
Sample size						< 0.001
≤ 70	6	−2.97 (−3.65, −2.28)	< 0.001	13.0	0.331	
> 70	2	−0.34 (−0.69, 0.02)	0.067	98.0	< 0.001	
DBP						
Dosage (mg)						0.003
≤ 500	2	−2.37 (−2.94, −1.80)	< 0.001	63.7	0.063	
> 500	5	0.19 (−0.13, 0.51)	0.249	52.2	0.079	
Duration (wk)						0.003
≤ 8	5	0.24 (−0.08, 0.57)	0.138	0.0	0.425	
> 8	3	−2.53 (−3.10, −1.96)	< 0.001	0.0	0.823	
Mean age (yr)						0.003
< 50	4	−2.42 (−2.89, −1.86)	< 0.001	0.0	0.567	
≥ 50	3	0.25 (−0.07, 0.58)	0.128	40.7	0.185	
Sample size						0.003
≤ 70	6	−2.20 (−2.91, −1.49)	< 0.001	30.5	0.206	
> 70	2	−0.10 (−0.40, 0.21)	0.538	97.3	< 0.001	

SBP, systolic blood pressure; DBP, diastolic blood pressure; WMD, weight mean difference; CI, confidence interval.

Moreover, the duration of artichoke treatment showed significant non-linear association with SBP ($p_{non\text{-}linearity}$ = 0.016), and DBP ($p_{non\text{-}linearity}$ = 0.003) (**Figure 5**).

Sensitivity analysis

To explore the impact of every single trial on the pooled effect size, we removed each study from the analysis. Sensitivity analysis for SBP and DBP indicated that the overall estimates were influenced by the elimination of none of the included studies.

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 = 0.320) and DBP (p = 0.162).

DISCUSSION

This systematic review and dose-response meta-analysis of 7 clinical trials assessed available evidence about the blood pressure-lowering effect of artichoke supplementation in adults. The pooled results revealed a significant effect of artichoke in lowering SBP and DBP when compared with placebo/control. The subgroup analyses showed that SBP was reduced following artichoke supplementation in trials lasted > 8 weeks, in lower doses (500 mg or less), and subjects aged < 50 years old. There was also a similar impact of artichoke on DBP.

Over recent years, functional foods and nutraceuticals have gained attention due to their potential therapeutic effects on preventing cardiovascular risk factors [29]. Nutraceuticals, a food or part of a food that have medical or therapeutic benefits, are proposed as factors in the

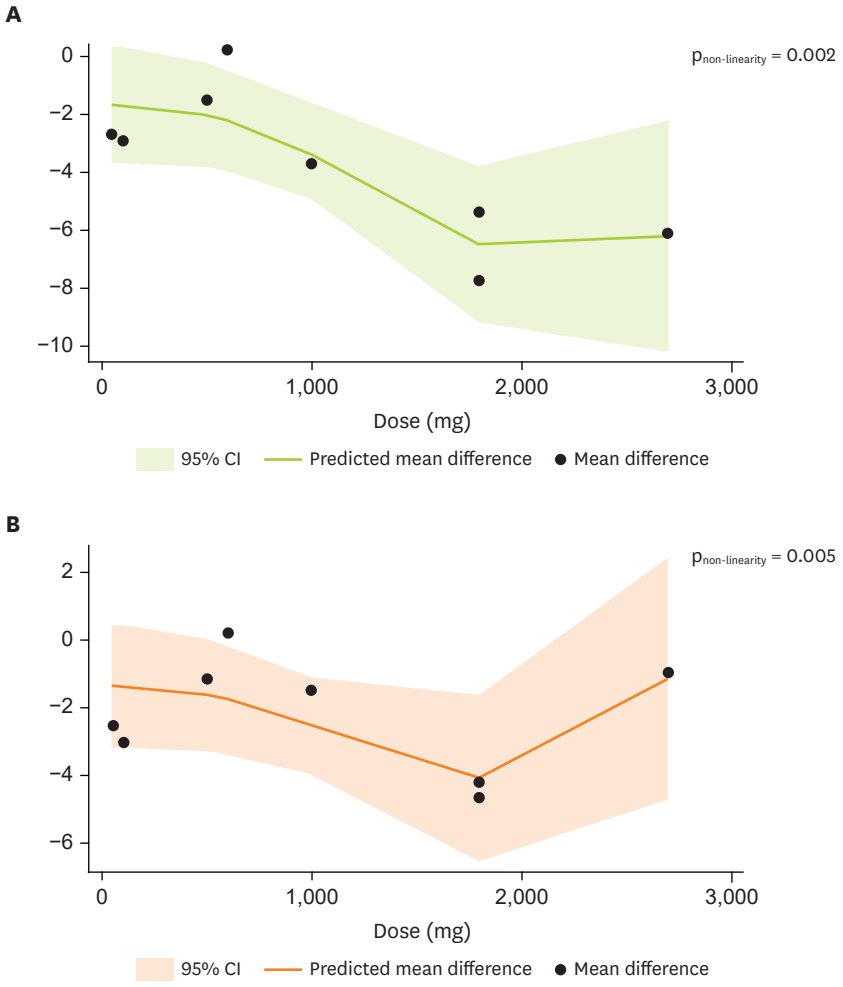

Figure 4. Non-linear dose-response relations between artichoke dosage (mg/day) and unstandardized mean difference in (A) SBP, and (B) DBP. The 95% CI is revealed in the shaded regions.
CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure.

management of chronic diseases, glycemic and lipid metabolic disorders, and component of metabolic syndrome [30,31]. Preceding meta-analysis showed that artichoke supplementation was associated with a significant reduction in both total and low-density lipoprotein cholesterol, without an effect on either triglycerides or high-density lipoprotein cholesterol levels [32]. In addition, other systematic reviews evaluating the effect of artichoke supplementation on anthropometric and glycemic indices showed the promising effect of artichoke extract on fasting blood glucose and waist circumference but without any effects on other factors [33,34]. To our knowledge, this systematic review and meta-analysis evaluated the effect of artichoke supplementation on blood pressure for the first time. In a study conducted by Roghani-Dehkordi et al. [10] either 50 mg/day or 100 mg/day artichoke for 12 weeks lowered DBP along with SBP through a dose-dependent pattern in patients with mild HTN. Also, artichoke supplementation (2,700 mg/day) for 2 months reduced SBP but did not affect DBP [9]. Findings from a study by Ebrahimi-Mameghani et al. [11] revealed that a 12-week supplementation with 1,800 mg/day artichoke did significantly affect either DBP or SBP in metabolic syndrome patients. However, another study showed that 2 months of artichoke supplementation with a dose of 600 mg/day increased SBP, while DBP did not differ between groups [14]. Moreover, it has been shown that 1,000 mg/day of artichoke had a beneficial effect on DBP but it did not affect SBP [12].

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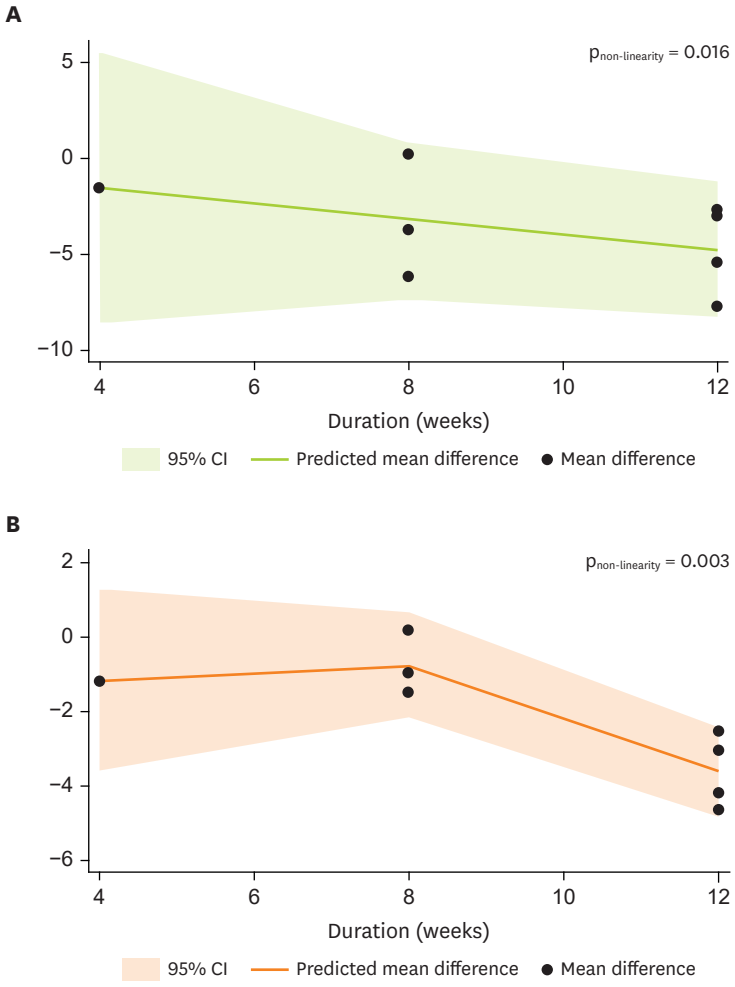

Figure 5. Non-linear dose-response relations between duration of treatment (weeks) and unstandardized mean difference in (A) SBP, and (B) DBP. The 95% CI is revealed in the shaded regions.
CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Additionally, taking 1,000 mg/day of artichoke for 8 weeks by obese and overweight patients was not associated with a significant change in SBP and DBP [17]. Different study designs, different baseline values of dependent variables, different doses of artichoke used along with characteristics of study participants might elucidate the discrepancies among included studies. In addition to human-based study, in vitro as well as experimental animals in vivo have shown a beneficial effect of artichoke on epithelial cells through its antioxidant's effects [35,36]. The biologically active compounds of the artichoke such as phenolic acids (benzoic, ellagic, and caffeic), sesquiterpenes lactones (cynaropicrin), luteolin, phytosterols (β sitosterol, stigmasterol), and dietary fibers (inulin-type fructans) could contribute to a variety of biological functions, including lipid-lowering [37], hepatoprotective [38] and reducing oxidative stress [39]. Artichoke exerts its antihypertensive effects on leaf extracts through upregulation of eNOS expression and increased NO production which enhances endothelium-dependent vasodilation [15,40]. Additionally, it has been shown that some compounds of artichoke such as cynarin might prevent the development of atherosclerotic plaques [41], taken together, this evidence emphasizes the key role of artichoke supplementation in reducing blood pressure. According to human and animal studies, physiological and pharmacological doses of artichoke supplementation in wide ranges did not show any side effects, and there is extensive consonance

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regarding its nontoxicity [42]. Therefore, due to the fact that artichoke is affordable and can be easily produced in purely pharmacological form and notably, because of its protective effect on heart damage mutilation of vital molecules by free radicals via its antioxidant effect [41], and vasodilation through increasing NO production [15], it could be considered as a preventive treatment for cardiovascular disorders.

Our systematic review and meta-analysis has several strengths. Our search strategy was very precise and covered multiple databases. Statistical examinations showed no evidence of publication bias in our analyses. Nevertheless, this study had several weaknesses, and the findings should be interpreted with caution. Randomized controlled trials (RCTs) included in our meta-analysis were represented with various health conditions and study durations, which might potentially affect the results. However, all included patients in our meta-analysis had different kind of metabolic disorders and desired outcome was blood pressure. The existence of uncontrollable factors in the 2 comparison groups, such as eating habits and lifestyle, can effect the pooled results. Considering the limitations, further studies are needed to test the effect of artichoke on stress blood pressure.

In conclusion, this meta-analysis of available RCTs suggests a significant benefit of artichoke extract supplementation in decreasing blood pressure. Hence, additional clinical studies with a large sample size, duration, dosage, and route of administration (bio-availability) among people with mild HTN are needed to be done for a better understanding of the results obtained in this current meta-analysis.

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