

Effect of green tea supplementation on blood pressure

A systematic review and meta-analysis of randomized controlled trials

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Abstract

Background: Although evidence from animal and observational studies has supported the beneficial effects of green tea intake for lowering blood pressure (BP), randomized placebo-controlled trials (RCTs) have yielded conflicting results. In this meta-analysis of RCTs, we aimed to assess the effects of green tea supplementation on measures of BP control.

Methods: The PubMed, Embase, and Cochrane Library databases were electronically searched from inception to August 2019 for all relevant studies. The results were pooled using the generic inverse-variance method with random-effects weighting and expressed as mean differences (MDs) with 95% confidence intervals (CIs). The quality of studies was assessed using the Jadad score. Publication bias was evaluated using funnel plots, Egger test, and Begg test.

Results: Twenty-four trials with 1697 subjects were included in the meta-analysis. The pooled results showed that green tea significantly lowered systolic BP (SBP; MD: -1.17 mm Hg; 95%CI: -2.18 to -0.16 mm Hg; $P = .02$) and diastolic BP (DBP; MD: -1.24 mm Hg; 95%CI: -2.07 to -0.40 mm Hg; $P = .004$). Significant heterogeneity was found for both SBP ($I^2 = 43\%$) and DBP ($I^2 = 57\%$). In addition, no evidence of significant publication bias was found from funnel plots or Egger test ($P = .674$ and $P = .270$ for SBP and DBP, respectively).

Conclusion: Overall, green tea significantly reduced SBP and DBP over the duration of the short-term trials. Larger and longer-term trials are needed to further investigate the effects of green tea supplementation on BP control and clinical events.

Abbreviations: BP = blood pressure, CI = confidence interval, CVD = cardiovascular disease, DBP = diastolic blood pressure, EGCG = epigallocatechin gallate, MD = mean difference, PRISMA = preferred reporting items for systematic reviews and meta-analyses, RCT = randomized placebo-controlled trial, SBP = systolic blood pressure, SD = standard deviation, SE = standard error.

Keywords: blood pressure, catechin, green tea, meta-analysis

1. Introduction

Cardiovascular disease (CVD) is the leading cause of morbidity, mortality, and disability worldwide.^[1] Hypertension is 1 of the

leading causes of cardiovascular events^[2,3] and the main contributor to 7 million deaths annually worldwide.^[4] The risk of CVD doubles for each increment of 20/10 mm Hg in blood pressure (BP) from as low as 115/75 mm Hg.^[5] Almost 50% of ischemic heart disease cases and 60% of stroke cases are attributed to elevated BP.^[6] Studies have shown that even a modest reduction in BP is clinically relevant in reducing the risk of coronary heart diseases and stroke.^[7]

Lifestyle modifications have been shown to be effective in regulating BP.^[8] In particular, nutrition therapies have shown beneficial effects for the prevention and control of hypertension. Green tea, obtained from the plant *Camellia sinensis*, is a widely consumed beverage worldwide and is traditionally used in Asian countries as a medication. The mechanisms underlying the beneficial effects of green tea are mainly attributed to its flavonoid-like polyphenol contents such as catechins. Catechins mainly include epigallocatechin gallate (EGCG), epicatechin gallate, epigallocatechin, and epicatechin, which are the most common green tea extracts and have been shown to be beneficial to human health.^[9] In vitro studies have shown that green tea catechins exert a cardioprotective effect through multiple mechanisms, including the inhibition of oxidation, vascular inflammation, and thrombogenesis, as well as the improvement of endothelial dysfunction.^[10,11] Animal studies have also revealed that green tea catechins influence nitric oxide production and vasodilation, thereby improving endothelial dysfunction and hypertension in rodents.^[10]

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To date, many longitudinal observational studies and intervention trials have investigated the association between tea consumption and BP reduction; however, the results were controversial. Some studies reported that tea intake decreased BP,^[12,13] whereas others reported no significant change in BP control with tea intake.^[14] Thus, we conducted a meta-analysis of all published randomized placebo-controlled trials (RCTs) to quantitatively assess the effect of green tea on measures of BP reduction in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines.

2. Methods

2.1. Search strategy and eligibility criteria

This systematic review and meta-analysis was conducted in accordance with the PRISMA statement guidelines.^[15] We searched PubMed, Embase, and the Cochrane Library from the index date of each database through August 2019 by using the following terms: “green tea”, “green tea extract”, “tea component(s)”, “tea solid(s)”, “catechin”, “catechins”, “EGCG”, “Camellia sinensis”, “tea polyphenols”, “blood pressure”, “hypertension”, “hypertensive”, “hypotension”, “hypotensive”, “endothelium”, “endothelial function”, and “endothelial dysfunction.” The search was limited to RCTs in adults (age >18 years). Language was restricted to English. The reference sections of all articles selected for inclusion and those of previous meta-analysis were hand-searched for additional articles.

2.2. Study selection

The prespecified inclusion criteria were as follows:

- (1) Adult subjects who ingested green tea beverages or extract for ≥ 2 weeks.
- (2) RCTs with either a parallel or crossover design.
- (3) The baseline and endpoint values of systolic BP (SBP) or diastolic BP (DBP), or both, with standard deviations (SDs), standard errors (SEs), or 95% confidence intervals (CIs) were available for each group in the study.
- (4) Green tea extract was not administered as part of a multicomponent supplement in either the experimental or control group.
- (5) The food intake control regimens of the experimental groups were consistent with those of the control groups, and the only difference between the control and treatment groups was green tea or green tea extract supplementation; and
- (6) Each group had > 10 subjects.

The exclusion criteria were as follows:

- (1) Trials that enrolled children or pregnant women.
- (2) Review, meta-analysis, or abstract only; and
- (3) Trials without details of the EGCG or polyphenol content of the green tea. The data of multiple published reports from the same study population were included only once.

2.3. Quality assessment

The quality of studies was assessed using the Jadad score with the following criteria:

- (1) Randomization,
- (2) Double blinding (participant and researcher masking),

- (3) Reporting the number of and reasons for withdrawal,
- (4) Allocation concealment, and
- (5) Generation of random numbers.

The trials were scored 1 point for each area addressed in the study design, with a possible score of between 0 and 5 (highest quality).^[16] The trials were categorized as high quality (Jadad score ≥ 4) or low quality (Jadad score <4).

2.4. Data extraction

Two authors (CGZ and XRF) independently extracted the data, and discrepancies were adjudicated by a third author (YK). The following information was abstracted:

- (1) Study characteristics (authors, publication year, sample size, study duration, study design, intervention dose, and type of intervention), participant characteristics (location, mean age or age range, sex, preexisting disease or condition, and
- (2) Treatment with antihypertensive medications), and details of the baseline and final SBP and DBP measurements. For multi-arm studies, only intervention groups that met the inclusion criteria were used in the analysis. If BP was reported several times in different stages of the trials, only the final BP records at the end of the trials were extracted for the meta-analysis.

2.5. Statistical analysis

Statistical analysis was performed with RevMan version 5 software (Cochrane Collaboration). The main outcome of the meta-analysis was the mean difference (MD) in BP (SBP and DBP, mm Hg) between the intervention and control groups from baseline to the end of the intervention period. When SDs were not directly available, they were calculated from SEs, 95% CIs, *P* values, or *t* values.^[17] In addition, the change-from-baseline SD values were imputed as suggested by Follmann et al, assuming a correlation coefficient of 0.5.^[18] In trials that reported more than 1 BP measure, such as nighttime and daytime ambulatory BP, we used the mean BP calculated from the greatest number of measurements.

Heterogeneity was assessed using the Cochran *Q* statistic, in which a *P* value of < .10 was considered significant; and measured inconsistency (*I*²) statistics, with *I*² > 50% considered indicative of substantial heterogeneity.^[19] We presented the results on the basis of a random-effects model when the test for heterogeneity of the total population was significant. Otherwise, the results of a fixed-effects model are presented.^[20] To identify the possible source of heterogeneity within the studies, subgroup and sensitivity analyses were performed in accordance with the Cochrane Handbook for Systematic Reviews of Interventions. The following information was abstracted in the subgroup analyses: consumption of catechins, divided into high (≥ 615 mg/d, high median) and low (<615 mg/d, low median) doses; duration of the green tea intervention, divided into long term (≥ 12 weeks) and short term (<12 weeks); type of intervention, divided into green tea beverage and capsule; ethnicity, divided into Asian and Western; study design, divided into parallel and crossover; health status, divided into healthy and with cardiovascular risks; and baseline BP status, divided into high-normal/hypertensive and normotensive. Trials were considered to be of high quality when the score was ≥ 4 and low-quality when the score was <4. Funnel plots and Egger regression test were used to assess publication bias.^[21] A *P* value of < .05 was considered statistically significant, unless otherwise specified.

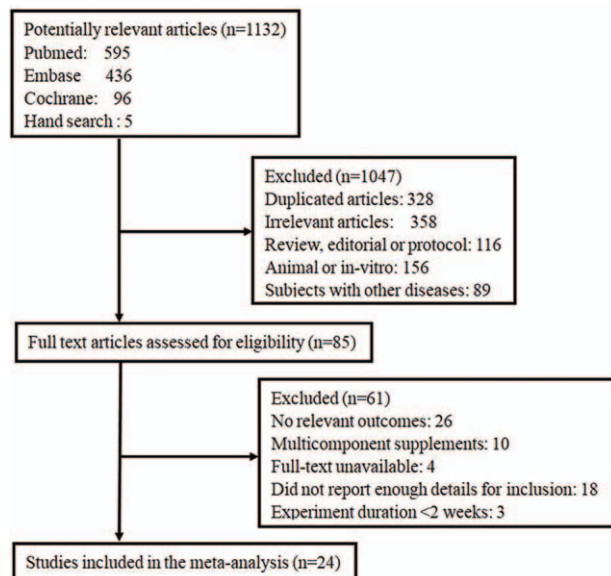


Figure 1. Flow diagram of the study selection process. From a total of 1132 potentially relevant studies, 24 randomized controlled trials that met the predefined inclusion and exclusion criteria were included in the meta-analysis.

2.6. Ethics

This is a systematic review and meta-analysis and ethical approval was not necessary.

3. Results

3.1. Results of the literature search

A total of 1132 articles were initially identified after electronic searching. Of them, 1047 articles were excluded because they were not clinical trials, the interventions were irrelevant to the current meta-analysis, or they were duplicated articles. Eighty-five articles remained for a more detailed full-text inspection. An additional 61 articles were excluded for various reasons: 26 articles were excluded because no relevant outcomes were reported; 10 articles were excluded because green tea extract was administered as part of a multicomponent supplement; 4 articles were excluded because only the abstract was available; 18 articles were excluded because they did not meet the inclusion criteria; and 3 articles were excluded because the experiment duration was <2 weeks. Finally, 24 eligible articles were considered to have met the inclusion criteria and were included in the meta-analysis (Fig. 1).

3.2. Study characteristics

Twenty-four eligible RCTs with 1697 subjects were enrolled in the meta-analysis.^[22–45] The baseline characteristics of the studies included in the meta-analysis are described in Table 1. The trial size ranged from 22 to 240 subjects. The duration of the green tea intervention varied from 3 to 16 weeks. The mean age of the trial participants ranged from 22 to 74 years. The doses of green tea catechins in the treatment group ranged from 208 to 1344 mg/d. The mean pretreatment SBP ranged from 111 to 147 mm Hg, and the mean DBP ranged from 68 to 93 mm Hg.

Table 1
Characteristics of 24 included randomized controlled trials.

Reference	Study design	No. of subjects (M/F)	Country or Region	Population	Duration	Tea group	Control group	Jadad score
Basu 2011	P	25 (5/20)	USA	Obese, high-normal	8wk	decaffeinated GTE beverage (928 mg catechins)	Placebo (water)	4
Bogdanski 2012	P	56 (28/28)	Poland	Obese, hypertension	3mo	GTE capsule (208 mg EGCG)	placebo (cellulose)	4
Brown 2009	P	88 (88/0)	UK	Overweight/obese, high-normal BP	8wk	decaffeinated GTE capsule (800 mg EGCG)	Placebo (lactose)	5
Brown 2011	C	64 (64/0)	UK	Overweight/obese, high-normal BP	6wk	decaffeinated GTE capsule (800 mg catechins)	Placebo (lactose)	5
Chen 2015	P	77 (0/77)	Taiwan	Obese, high-normal BP	12wk	decaffeinated GTE capsule (1344 catechins)	placebo (cellulose)	5
Diepvens 2006	P	46 (0/46)	Netherlands	Overweight, normotensive	12wk	GTE capsule (1125 mg catechins, 225 mg caffeine)	placebo	2
Frank 2009	P	33 (33/0)	UK	Healthy, normotensive	3wk	GTE capsule (672 mg catechins, 114 mg caffeine)	Placebo (matched with caffeine)	3
Fukino 2005	P	66 (53/13)	Japan	Diabetes, high-normal BP	2mo	GTE beverage (456 mg catechins, 102 mg caffeine)	No intervention	2
Fukino 2008	C	60 (49/11)	Japan	Diabetes, high-normal BP	2mo	GTE beverage (456 mg catechins, 102 mg caffeine)	No intervention	2
Hill 2007	P	38 (0/38)	Australia	Obese, normotensive	12wk	decaffeinated GTE capsule (300 mg EGCG)	placebo (lactose)	2
Hsu 2008	P	78 (0/78)	Taiwan	Obese, high-normal BP	3mo	GTE capsule (613.5 mg cathchins, 27.3 caffeine)	Placebo	5
Hsu 2011	P	68 (24/44)	Taiwan	Obese, Diabetes, hypertension	16wk	decaffeinated GTE capsule (1344 catechins)	placebo (cellulose)	5
Kafeshani 2017	P	32 (32/0)	Iran	Healthy, normotensive	6wk	GTE capsule (240 mg catechins)	placebo (maltodextrin)	3
Liu 2014	P	77 (32/45)	Taiwan	Diabetes, obese, high-normal BP	16wk	decaffeinated GTE capsule (1344 catechins)	placebo (cellulose)	3
Lu 2016	P	64 (0/64)	Taiwan	Acne, normotensive	4wk	decaffeinated GTE capsule (1344 catechins)	placebo (cellulose)	5
Maeda-Yamamoto 2018	P	75 (30/45)	Japan	Healthy, normotensive	12wk	GTE capsule (735.3 EGCG, 202.5 caffeine)	Placebo (Barley tea extract powder with no catechins and caffeine)	5
Maeda-Yamamoto-b 2018	P	76 (31/45)	Japan	Healthy, normotensive	12wk	GTE capsule (409.3 EGCG, 184.8 caffeine)	Placebo (Barley tea extract powder with no catechins and caffeine)	5
Miyazaki 2013	P	52 (20/32)	Japan	high-normal BP	14wk	GTE beverage (630.9 mg catechins, 77 mg caffeine)	GTE beverage (88.7 mg catechins and 82.4 mg caffeine)	3
Nagao 2007	P	240 (140/100)	Japan	Overweight, high-normal BP	12wk	GTE beverage (582.8 mg catechins, 72.3 caffeine)	GTE beverage (96 mg catechins, matched with caffeine)	3
Nagao 2009	P	43 (18/25)	Japan	Diabetes, high-normal BP	12wk	GTE beverage (582.8 mg catechins, 72.3 caffeine)	GTE beverage (96 mg catechins, matched with caffeine)	3
Nantz 2009	P	111 (46/65)	USA	Healthy, normotensive	3mo	decaffeinated GTE capsule (320 catechins)	Placebo (maltodextrin)	4
Nogueira 2016	C	20 (0/20)	Brazil	Obese, high-normal BP	4wk	GTE capsule (780 mg polyphenol)	placebo (cellulose)	3
Sone 2011	P	51 (18/33)	Japan	Healthy, normotensive	9wk	GTE beverage (400 mg catechins, 105 mg caffeine)	GTE beverage (100 mg catechins; 80 mg caffeine)	5
Suliburska 2012	P	46 (23/23)	Poland	Obese, high-normal BP	3mo	GTE capsule (208 mg EGCG)	placebo (cellulose)	4
Takahashi 2014	P	22 (0/22)	Japan	Healthy, normotensive	4wk	GTE beverage (615 mg catechins, 77 mg caffeine)	Placebo beverage (5.7 mg catechin and 85.2 mg caffeine)	3

BP = blood pressure, C = crossover trial, EGCG = epigallocatechin gallate, GTE = green tea extract; mo = month, P = parallel trial, wk = week.

Of the 24 trials with 25 comparisons included in the current meta-analysis, 10 comparisons focused on adults with normotension^[27,28,31,34,36,37,41,43,45] and 15 comparisons investigated adults with high-normal or hypertensive BPs.^[22-26,29,30,32,33,35,38-40,42,44] Eight comparisons were performed in healthy subjects,^[28,34,36,37,41,43,45] and 17 comparisons were conducted in patients with cardiovascular risks.^[22-27,29-33,35,38-40,42,44] Most of the comparisons (22/25) used a parallel study design,^[22-24,26-29,31-41,43-45] whereas 3 comparisons adopted a crossover design.^[25,30,42] Eight comparisons selected green tea beverage,^[22,29,30,38-40,43,45] and 17 comparisons used green tea extract capsules.^[23-28,31-37,41,42,44] Of the included studies, 10 comparisons were performed in Western countries^[22-25,27,28,31,41,42,44] and the remaining 15 were conducted in Asian countries.^[26,29,30,32-40,43,45] Nine comparisons used decaffeinated green tea extract as supplement,^[22,24-26,31,33,35,36,41] 12 comparisons used caffeinated green tea as supplement,^[27-30,32,37-40,43,45] and 4 did not report the use of caffeinated supplements^[23,34,42,44] (Table 1).

3.3. Data quality

The results on the validity of the included trials are presented in Table 2. Twelve trials were classified as high quality (Jadad score of 4),^[23-26,32,33,36,37,41,43,44] and 12 trials were classified as low quality (Jadad score of 2 or 3).^[22,27-31,34,35,38-40,42,45] Allocation concealment was adequate in 11 trials and unclear in 13 trials. Twenty trials had a double-blinded RCT design, 1 trial had a single-blinded design, and 3 trials had an open-label design. Ten trials reported the generation of random numbers, but the other 14 trials did not. All trials except for 1 reported dropouts and the reasons for the dropouts (Table 2).

3.4. Effect of green tea on BP

Twenty-five comparisons from 24 studies including 859 subjects in the green tea group and 838 subjects in the placebo group reported the SBPs and DBPs at baseline and follow-up. Compared with the control, green tea significantly lowered both SBP (-1.17mm Hg; 95%CI: -2.18 to -0.16; $P=.02$) (Fig. 2) and DBP (-1.24mm Hg, 95%CI: -2.07 to -0.40; $P=.004$) (Fig. 3). The pooled effects on both SBP and DBP were heterogeneous ($I^2=43%$ and $P=.01$ for SBP, $I^2=57%$ and $P=.0002$ for DBP); thus, we reported the results from the random-effects models.

3.5. Subgroup analyses

Subgroup analyses were conducted to examine heterogeneity. However, substantial heterogeneity persisted in most subgroup analyses. The subgroup analyses included study duration effects, dose-effect relationship, health status effects, ethnic group variation, coffee content variation, catechin dosage variation, study design effect, and type of intervention effect (green tea beverage or capsule). The subgroup analyses showed that the effects of green tea on both SBP and DBP were greater in subjects with any of the following characteristics: from Western countries, had low catechin dosage (<615 mg/dL), from parallel trials, had high-normal or hypertensive BP, and had cardiovascular risks. The significant reductions in both SBP and DBP were not influenced by the effect of caffeine. Finally, when the studies were stratified according to Jadad score, a significant reduction in SBP was found in low Jadad scores and a significant reduction in DBP was found in high Jadad scores (Table 3).

Table 2
Validity of included studies.

References	Randomization	Allocation concealment	Masking of participants	Masking of researches	Generation of random numbers reported	Reporting of withdraws	Jadad score
Basu 2011	Yes	Adequate	Yes	No	Yes	Yes	4
Bogdanski 2012	Yes	Adequate	Yes	Yes	No	Yes	4
Brown 2009	Yes	Adequate	Yes	Yes	Yes	Yes	5
Brown 2011	Yes	Adequate	Yes	Yes	Yes	Yes	5
Chen 2015	Yes	Adequate	Yes	Yes	Yes	Yes	5
Diepvens 2006	Yes	Unclear	Yes	Yes	No	No	2
Frank 2009	Yes	Unclear	Yes	Yes	No	Yes	3
Fukino 2005	Yes	Unclear	No	No	No	Yes	2
Fukino 2008	Yes	Unclear	No	No	No	Yes	2
Hill 2007	Yes	Adequate	No	No	No	Yes	3
Hsu 2008	Yes	Adequate	Yes	Yes	Yes	Yes	5
Hsu 2011	Yes	Adequate	Yes	Yes	Yes	Yes	5
Kafeshani 2017	Yes	Unclear	Yes	Yes	No	Yes	3
Liu 2014	Yes	Unclear	Yes	Yes	No	Yes	3
Lu 2016	Yes	Adequate	Yes	Yes	Yes	Yes	5
Maeda-Yamamoto 2018	Yes	Adequate	Yes	Yes	Yes	Yes	5
Miyazaki 2013	Yes	Unclear	Yes	Yes	No	Yes	3
Nagao 2007	Yes	Unclear	Yes	Yes	No	Yes	3
Nagao 2009	Yes	Unclear	Yes	Yes	No	Yes	3
Nantz 2009	Yes	Unclear	Yes	Yes	Yes	Yes	4
Nogueira 2016	Yes	Unclear	Yes	Yes	No	Yes	3
Sone 2011	Yes	Adequate	Yes	Yes	No	Yes	5
Suliburska 2012	Yes	Unclear	Yes	Yes	Yes	Yes	4
Takahashi 2014	Yes	Unclear	Yes	Yes	No	Yes	3

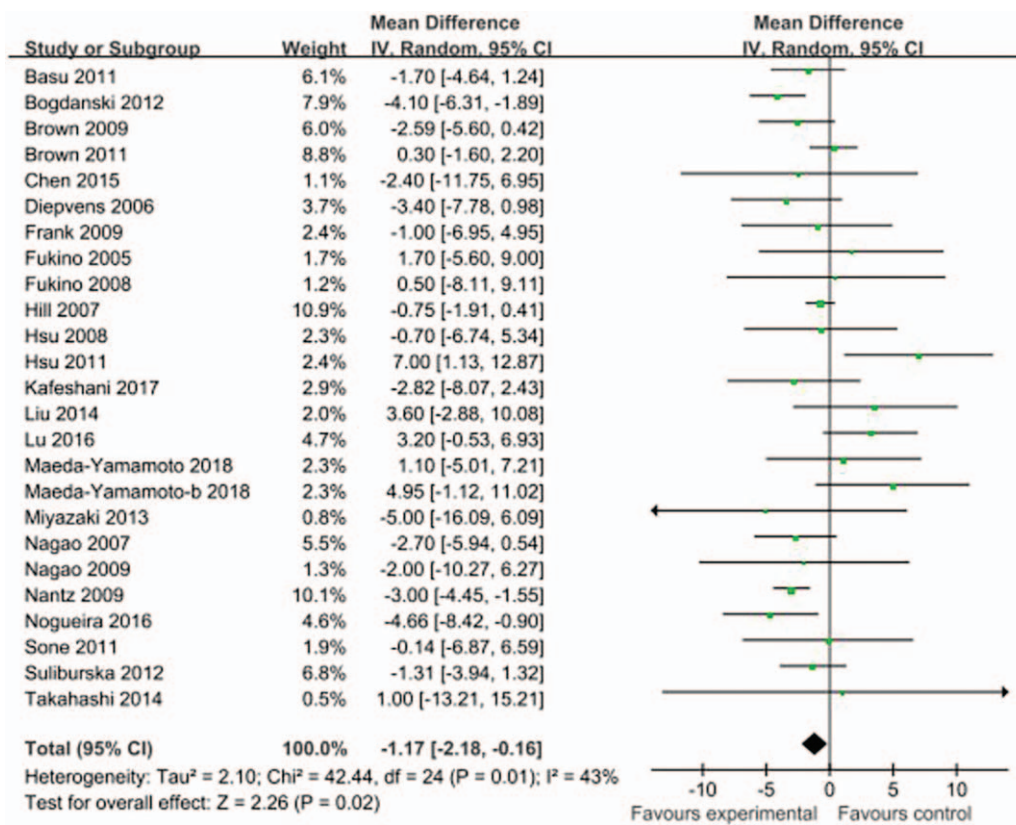


Figure 2. Net changes in systolic blood pressure in randomized trials of green tea supplementation.

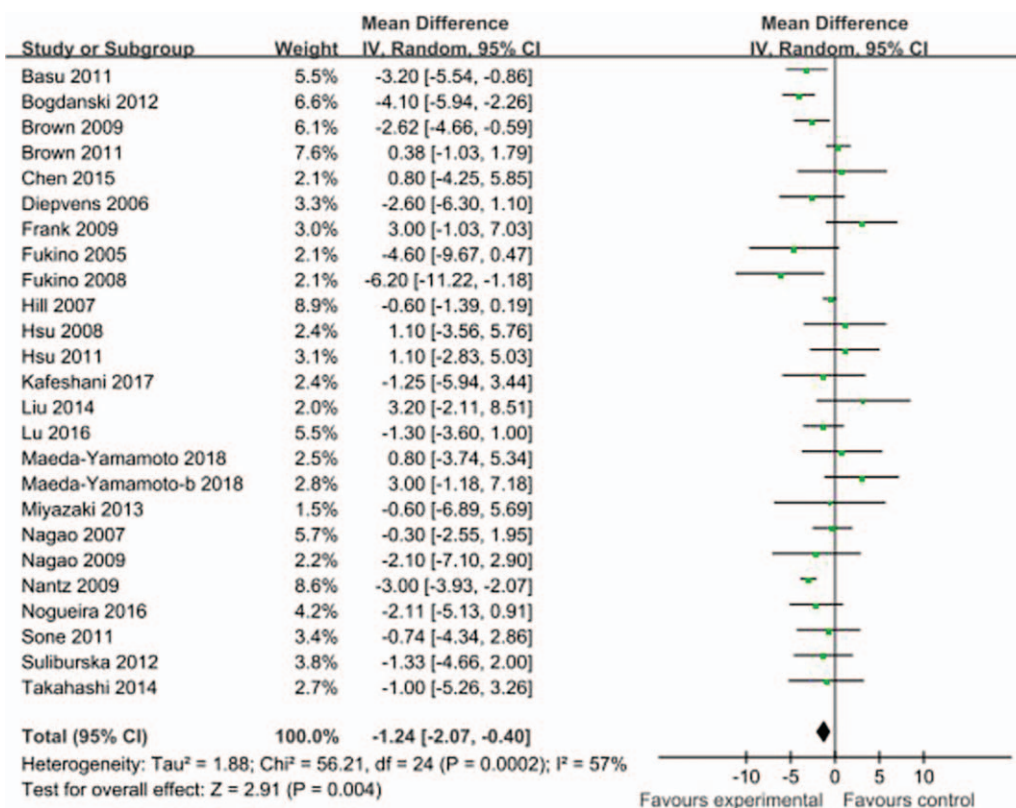


Figure 3. Net changes in diastolic blood pressure in randomized trials of green tea supplementation.

Table 3
Subgroup analyses of mean change in BP.

Subgroup	Trials (n)	Change in SBP			Change in DBP			I ²
		Net change mm Hg (95%CI)	P	I ²	Trials (n)	Net change mm Hg (95%CI)	P	
Type of intervention								
Green tea beverage	8	-1.26 (-2.89, 0.36)	.05	0%	9	-1.90 (-3.10, -0.71)	.002	0%
Green tea capsule	17	-0.91 (-2.22, 0.40)	.17	62%	16	-0.88 (-1.92, -0.16)	.1	69%
Duration								
≥12 wk	13	-0.90 (-2.50, 0.70)	.27	49%	13	-0.64 (-1.82, 0.54)	.29	45%
<12 wk	12	-1.32 (-2.72, 0.07)	.27	77%	12	-1.78 (-2.96, -0.6)	.003	60%
Country								
Western	10	-2.02 (-3.10, -0.95)	.0002	50%	10	-1.78 (-2.95, -0.60)	.003	72%
Asian	15	0.69 (-1.06, 2.45)	.44	17%	15	-0.51 (-1.55, 0.53)	.33	5%
Catechins dose								
≥615 mg/dL	13	-0.48 (-2.21, 1.24)	.58	46%	13	-0.79 (-1.89, 0.31)	.16	37%
<615mg/dL	12	-1.79 (-2.94, -0.63)	.002	34%	12	-1.69 (-2.93, -0.45)	.008	68%
Caffeine								
With caffeine	12	-1.02 (-2.74, 0.69)	.24	0%	12	-0.65 (-2.07, 0.77)	.37	29%
Without caffeine	9	-0.35 (-1.94, 1.24)	.67	68%	9	-1.16 (-2.37, 0.04)	.06	74%
unclear	4	-3.19 (-4.75, -1.64)	<.0001	7%	4	-2.93 (-4.37, -1.49)	<.001	6%
Study design								
Parallel	22	-1.16 (-2.25, -0.06)	.04	42%	22	-1.23 (-2.11, -0.35)	.006	54%
Crossover	3	-1.47 (-5.24, 2.31)	.45	63%	3	-1.94 (-5.23, 1.34)	.25	73%
Health status								
Healthy	8	0.01 (-2.58, 2.59)	1.00	56%	8	-0.49 (-2.26, 1.28)	.59	62%
Cardiovascular risk	17	-1.44 (-2.57, -0.32)	.01	39%	17	-1.47 (-2.44, -0.50)	.003	53%
Baseline BP status								
High-normal or hypertensive	15	-1.40 (-2.80, -0.01)	.04	43%	15	-1.53 (-2.72, -0.33)	.01	54%
Normotensive	10	-0.75 (-2.38, 0.88)	.37	50%	10	-0.82 (-2.11, 0.47)	.21	65%
Jadad score								
High (≥4)	13	-0.61 (-2.17, 0.95)	.44	64%	13	-1.26 (-2.43, -0.09)	.04	66%
Low (<4)	12	-1.25 (-2.20, -0.31)	.01	0%	12	-1.00 (-2.08, 0.09)	.07	24%

BP = blood pressure, CI = confidence interval, DBP = diastolic blood pressure, SBP = systolic blood pressure.

3.6. Publication bias

The funnel plots of the studies were symmetrical for SBP and DBP. Furthermore, the results of Egger regression test suggested no significant asymmetry for the overall effect estimation of SBP ($P = .674$) and DBP ($P = .270$).

4. Discussion

Our meta-analysis of 24 observational studies with 1697 subjects showed that green tea consumption significantly lowered both SBP and DBP. In addition, the results of the subgroup analyses suggested that the beneficial effect of green tea (ie, with respect to lowering both SBP and DBP) might be more pronounced in subjects with high-normal BP/hypertension, or other CVD risks. These findings are generally consistent with the results from previous meta-analyses of RCTs in the general population or in participants with cardiovascular risks and provide additional evidence supporting the beneficial effect of green tea supplementation in reducing BP.^[12,46]

Observational prospective cohort and case-control studies have been performed to determine the effect of green tea on CVD; however, the results were conflicting. A large population-based study involving 40,000 middle-aged Japanese individuals revealed that compared with non-drinking of tea, habitual green tea consumption (an average of >2 cups [almost 17oz]/d for 10 years) was associated with a lower risk of death from CVDs.^[47] Some studies have revealed that green tea intake significantly lowered BP.^[2,3,41] By contrast, several other studies reported no

positive correlations between green tea intake and BP reduction.^[26,34] To clarify the precise effect of green tea on BP control, we conducted the current meta-analysis of published RCTs.

The beneficial effects of green tea on cardiovascular health may be related to the high concentration of green tea catechins. Green tea catechins have numerous biological activities that can possibly provide antihypertensive benefits, such as:

- (1) Increasing the plasma nitric oxide concentration, which can inhibit proinflammatory cytokines and platelet aggregation and lead to improvement of endothelial dysfunction;^[48]
- (2) Exerting an antiinflammatory effect through the suppression of several inflammatory factors, such as cytokines, nuclear factor-kappa B, and adhesion molecules;^[49,50]
- (3) Suppressing the contractile response by inhibiting the mRNA expression of both endothelial nitric oxide synthase and endothelin-1 at the physiological concentration, which results in vasodilation and subsequent reduction in BP;^[51,52] and
- (4) Improving calcium signals in the regulation of phosphorylation levels of inositol triphosphate, calmodulin-dependent protein kinase II, and calmodulin antibodies, particularly EGCG, which possesses a strong antihypertensive activity.^[53]

In this meta-analysis, subgroup analyses were performed on the basis of our predefined variables to identify sources of heterogeneity. Our findings indicated that subjects with high-normal BP/hypertension, and CVD risks would obtain the maximum benefit from green tea with respect to SBP and DBP reduction, perhaps through the inhibition of oxidation, vascular

inflammation, and thrombogenesis, and by improving endothelial dysfunction in patients with poor BP control and other CVD risks.^[51–53] In addition, the subgroup analyses revealed that green tea supplementation had a more pronounced effect on both SBP and DBP in subjects from Western countries than in subjects from Asian countries, which is consistent with the findings of an earlier meta-analysis by Liu et al.^[13] Our meta-analysis demonstrated that the BP reduction effect was greater in the low catechin dosage group than in the high catechin dosage group. This result was possibly due to differences in green tea composition and preparations, as well as ethnicity variations among the subjects.

We observed that the effect of caffeine was not significant for both SBP and DBP. As tea naturally contains caffeine in addition to catechins and other compounds, whether caffeine intake influences the BP-lowering effects of tea is another potential issue and is still controversial. Some studies have shown that caffeine alone could increase BP by increasing arterial stiffness and influencing arterial compliance.^[54,55] However, other studies indicated that the dosage of caffeine in green tea is relatively lower than the dosage of catechins; thus, the negative effect of caffeine on BP may not overcome the positive effect of tea and catechins.^[13]

This meta-analysis had several significant strengths. First, the trials included in this meta-analysis were all RCTs, which ensured relatively high quality and accurate information. Second, the results were unlikely to be influenced by publication bias. The results of Egger regression test suggested no significant asymmetry of the funnel plot for the overall effect estimation of MDs in SBP or DBP. Furthermore, subgroup analyses were performed to detect the sources of heterogeneity in outcomes.

The potential limitations should also be considered. First, our meta-analysis did not identify an optimal dosage of green tea that would best improve BP. The variations in characteristics among the included trials, such as the wide range of catechin dosages (from 208 to 1344 mg/d), made it difficult to assess the true dose-response relationship between tea intake and BP-reducing effects. In addition, the safety margin has not been revealed because no serious adverse effects were reported in the included trials. However, concerns have been raised about the safety of high-dose green tea catechin supplementation. Animal trials reported that intraperitoneal injection of green tea catechins increased the plasma concentrations of alanine transaminase.^[56] Clinical trials have also indicated that green tea was the major dietary source of oxalate in some patients with kidney oxalate stones.^[57] Second, we identified large variations in trial duration, trial participants, green tea catechin dose, ethnic group, green tea intervention type, and baseline health status. Some of these variations may be significant sources of heterogeneity, which may limit the validity of the overall pooled results. Third, the studies included in the meta-analysis were generally conducted over a short duration, ranging from 3 to 16 weeks, and it is crucial to know the long-term effect of green tea intake on BP. Fourth, the quality of the included studies varied from low to high. Of the 24 studies, 11 were of high quality and the remaining 13 were of low quality, which may have affected the confidence level of the meta-analysis.

In conclusion, evidence from randomized controlled trials to date suggests that green tea supplementation may have a role in lowering both SBP and DBP. However, before green tea supplementation can be recommended for the prevention of hypertension or as an adjuvant antihypertensive therapy, additional trials with larger sample sizes, longer duration,

various catechin dosages, and high quality are needed in the future.

Author contributions

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