

Effect of green tea on glucose control and insulin sensitivity: a meta-analysis of 17 randomized controlled trials^{1–3}

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ABSTRACT

Background: The results of studies investigating the effect of green tea on glucose control and insulin sensitivity in humans are inconsistent.

Objective: We aimed to quantitatively evaluate the effect of green tea on glucose control and insulin sensitivity.

Design: We performed a strategic literature search of PubMed, EMBASE, and the Cochrane Library (updated to January 2013) for randomized controlled trials that evaluated the effects of green tea and green tea extract on glucose control and insulin sensitivity. Study quality was assessed by using the Jadad scale. Weighted mean differences were calculated for net changes in glycemic measures by using fixed-effects or random-effects models. We conducted prespecified subgroup and sensitivity analyses to explore potential heterogeneity. Meta-regression analyses were conducted to investigate dose effects of green tea on fasting glucose and insulin concentrations.

Results: Seventeen trials comprising a total of 1133 subjects were included in the current meta-analysis. Green tea consumption significantly reduced the fasting glucose and hemoglobin A_{1c} (Hb A_{1c}) concentrations by -0.09 mmol/L (95% CI: -0.15 , -0.03 mmol/L; $P < 0.01$) and -0.30% (95% CI: -0.37 , -0.22% ; $P < 0.01$), respectively. Further stratified analyses from high Jadad score studies showed that green tea significantly reduced fasting insulin concentrations (-1.16 μ IU/mL; 95% CI: -1.91 , -0.40 μ IU/mL; $P = 0.03$).

Conclusions: This meta-analysis suggested that green tea had favorable effects, ie, decreased fasting glucose and Hb A_{1c} concentrations. Subgroup analyses showed a significant reduction in fasting insulin concentrations in trials with high Jadad scores. *Am J Clin Nutr* 2013;98:340–8.

INTRODUCTION

Diabetes mellitus is currently one of the most significant public health challenges worldwide. The number of people with diabetes mellitus has more than doubled globally over the past 3 decades. Moreover, this number is projected to rise to 439 million by 2030, representing 7.7% of the total adult population of the world aged 20–79 y (1). Nearly 90% of the cases of incident type 2 diabetes mellitus (T2DM)⁴ can be attributed to 5 major lifestyle factors: diet, physical activity, smoking, obesity, and alcohol consumption (2, 3). Individuals with impaired fasting glucose or impaired glucose tolerance are usually considered to have a high future risk of developing T2DM (4). Furthermore, lifestyle interventions in overweight individuals with impaired glucose tolerance are most effective in those with high baseline T2DM risk (5).

Tea, derived from the plant *Camellia sinensis* is consumed in different parts of the world as green, black, or oolong tea. It is estimated that ~ 2.5 million tons of tea leaves are produced throughout the world each year; 20% is produced as green tea, which is mainly consumed in Asia, some parts of North Africa, the United States, and Europe (6). The most prominent effects of tea on human health have been attributed to green tea, and the health-promoting effects of green tea are mainly attributed to catechins, which belong to a family of compounds known as flavonoid-like polyphenols or flavanols. Flavonols such as epigallocatechin gallate (EGCG), epigallocatechin, epicatechin gallate, and epicatechin are the most common catechins found in green tea extract (7). A previous meta-analysis that included 9 cohort studies found that green tea consumption ≥ 4 cups/d (~ 948 mL) was associated with a significant reduction of T2DM risk (RR: 0.8; 95% CI: 0.7, 0.93) (8). Recent in vivo and in vitro studies have shown that green tea extract can significantly decrease fasting plasma concentrations of glucose, glycated hemoglobin (Hb A_{1c}), and insulin in diabetic rats (9–13). In addition, green tea extract has been shown to enhance the capability of adipocytes for glucose uptake and increase specific insulin binding and the glucose transporter 4 content in adipocytes isolated from rats (14, 15). Moreover, catechin intake has been shown to prevent the onset of streptozotocin-induced diabetes by protecting pancreatic islets (16, 17). However, the results of human clinical trials investigating the effect of green tea and green tea extract on glucose control and insulin sensitivity have been inconsistent, and the sample sizes were relatively

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⁴ Abbreviations used: EGCG, epigallocatechin gallate; Hb A_{1c}, hemoglobin A_{1c}; RCT, randomized controlled trial; T2DM, type 2 diabetes mellitus. Received October 10, 2012. Accepted for publication May 6, 2013.

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modest. Therefore, we conducted a meta-analysis of all published randomized controlled trials (RCTs) to quantitatively assess the effect of green tea on measures of glucose control and insulin sensitivity based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

METHODS

Search strategy

PubMed (updated to January 2013; <http://www.ncbi.nlm.nih.gov/pubmed/>), EMBASE (1980 to January 2013; <http://www.embase.com/>), and the Cochrane Library (1985 to January 2013; <http://www.cochrane.org/>) databases and reference lists and reviews were searched for RCTs that examined the effects of green tea on glucose control and insulin sensitivity in humans. The structured search strategies used the text key words *tea*, *tea extract*, *catechin*, *EGCG*, *Camellia sinensis*, or *tea polyphenols*, which were paired with the following words: *glucose*, *glycemic control*, *glycaemic control*, *glucose control*, *insulin*, or *insulin sensitivity*. The search was restricted to the reports of clinical trials conducted in human subjects.

Study selection

Studies were selected for analysis if they met the following criteria: 1) subjects ingested green tea beverage or extract for ≥ 2 wk; 2) the study was an RCT conducted in human subjects with either a parallel or crossover design; 3) the baseline and endpoint values for fasting glucose or insulin (or their difference) with SDs, SEMs, or 95% CIs were available for each group in the study; 4) green tea extract was not given as part of a multicomponent supplement and neither black tea or oolong tea was given in the study; and 5) the study used a concurrent control group for the green tea or green tea extract treatment group, and the difference between the control and treatment groups was green tea or green tea extract.

Quality assessment

Studies evaluated for potential inclusion in the meta-analysis were estimated for quality by using the following criteria: 1) randomization; 2) double blinding (participant masking and researcher masking); 3) reporting the number of withdrawals and reasons for withdrawal; 4) allocation concealment; and 5) generation of random numbers. RCTs scored one point for each area addressed in the study design with a possible score of between 0 and 5 (highest level of quality) (18). Studies receiving a score ≥ 4 were deemed to be of high quality, whereas those receiving a score < 4 were considered lower quality.

Data extraction

Data were collected onto a prepiloted data extraction form that included the following: 1) study characteristics, including authors, publication year, sample size, study design, study duration, dose, type of intervention, and type of diet; 2) population information, including age, and baseline healthy status; 3) net changes in fasting glucose and insulin concentrations representing the primary outcome measures, and 4) mean changes in Hb A_{1c} and 2-h glucose concentrations and the HOMA-IR

representing secondary outcome measures. All values were converted to mmol/L for glucose and $\mu\text{IU/mL}$ for insulin by using conversion factors: 1 mg/dL = 0.0556 mmol/L for glucose and 1 pmol/L = 6.945 $\mu\text{IU/mL}$ for insulin values. If primary outcome and secondary outcome concentrations were reported multiple times in different stages of trials, only values representing the final outcome concentrations at the end of trials were included in our meta-analysis.

Statistical analysis

Our meta-analysis was performed by using STATA (version 11; StataCorp). Treatment effects were defined as weighted mean differences and 95% CIs calculated for net changes in glucose and insulin values. The statistic heterogeneity was assessed by using Cochran's test ($P < 0.1$). The I^2 statistic was also calculated, and we considered $I^2 > 50\%$ to indicate significant heterogeneity across studies (19). A random-effects model was used if significant heterogeneity was shown among trials. Otherwise, results were obtained from a fixed-effects model.

Percentage changes in means and SDs were excluded when extracting SD values for an outcome. When not directly available, SDs were calculated from SEs, 95% CIs, P values, or t values. In addition, the change-from-baseline SD values were imputed as suggested by Follmann et al (20), assuming a correlation coefficient of 0.5.

Publication bias was assessed with funnel plots and the Egger's regression test. Previously defined subgroup analyses were performed to examine the possible source of heterogeneity within these studies and included healthy status, study design, type of intervention, duration, catechin dose, and Jadad score. Additional sensitivity analyses were also performed according to the Handbook for Systematic Review of Interventions of Cochrane software (version 5.0.2; The Cochrane Collaboration). Furthermore, meta-regression analyses were conducted to investigate the dose-effect relation between green tea and fasting glucose and insulin concentrations.

RESULTS

Results of the literature search

Detailed processes of the relevant study selection are shown in **Figure 1**. A total of 252 reports were initially identified, and 225 articles were excluded either because of duplication or because they were irrelevant to the current meta-analysis after a careful review of the titles and abstracts. Thus, 27 articles remained for more detailed examination; an additional 10 articles were excluded for various reasons: 6 articles were excluded because the subjects had been treated with black tea or oolong tea (21–26), 3 studies were discarded because green tea extract was given as part of a multicomponent supplement (27–29), and 1 study was excluded because of inappropriate blinding (30). Thus, 17 articles were ultimately selected for inclusion in the meta-analysis (31–47).

Study characteristics

A summary of the study characteristics included in the meta-analysis is presented in **Table 1**. Ten studies ruled out the confounding effect of caffeine on fasting glucose and insulin



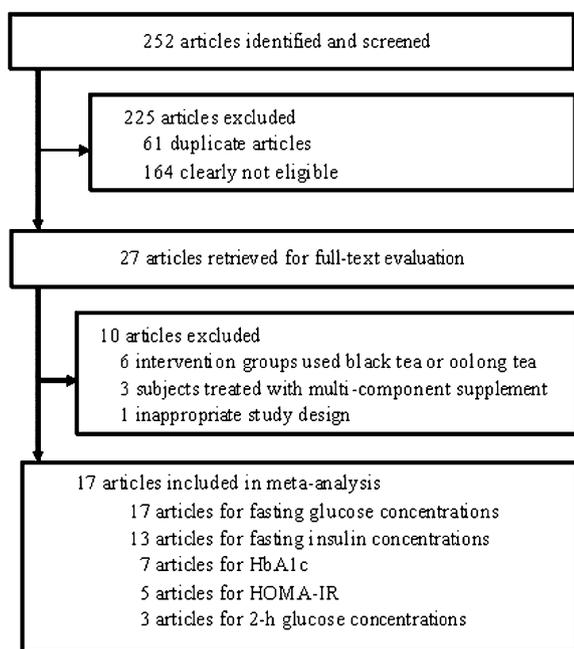


FIGURE 1. Flow diagram showing the number of citations retrieved in individual searches of articles included in the review. Hb A_{1c}, hemoglobin A_{1c}.

concentrations, whereas 7 studies used caffeinated green tea as supplements. The total number of subjects included in each study ranged from 34 to 240 subjects. The green tea catechin content ranged from 208 to 1207 mg/d (median: 457 mg/d). The study duration varied from 2 wk to 6 mo (median: 12 wk). Of the 17 trials included in the current meta-analysis, 9 trials focused on overweight to obese adults, 4 trials were conducted in patients with T2DM, 2 studies included subjects with borderline diabetes, and 2 trials investigated healthy subjects. Fifteen of the 17 studies included subjects with metabolic risk factors, such as elevated fasting glucose concentration, obesity or overweight at baseline, and the remaining 2 studies used the healthy subjects. Most studies (14 of 17) used parallel design. Of the 16 studies that suggested that subjects maintain a usual diet, 2 studies imposed restrictions on caffeine or catechin intake, and one study recommended that subjects maintain their physical activities during the study period.

Data quality

Study quality was assessed by the Jadad scale (18), and the results varied. Seven trials (40–43, 45–47) were classified as high quality (Jadad score ≥ 4), and the remaining 9 trials were low quality (Jadad score < 4). All 7 high-quality trials had an adequate allocation concealment (ie, conducted by a third-party manufacturer or data collection team or used opaque envelopes) and reported use of random-number generation or randomization list. Details related to dropouts were reported in 15 trials (32, 34–47).

Effect of green tea on glucose control and insulin sensitivity

As shown in **Table 2**, green tea significantly lowered fasting glucose concentrations and Hb A_{1c}, but did not significantly affect fasting insulin, 2-h glucose concentrations, or HOMA-IR

values. No significant heterogeneity was found for the outcomes of fasting glucose concentration, Hb A_{1c}, 2-h glucose, and HOMA-IR, and the results were reported on the basis of fixed-effects models. We observed significant between-study heterogeneity in the effects of green tea on insulin concentrations ($I^2 = 57.1\%$). For the 17 trials that reported data on fasting glucose concentrations, a significant reduction in fasting glucose concentrations was observed in subjects supplemented with green tea (-0.09 mmol/L; 95% CI: $-0.15, -0.03$ mmol/L; $P < 0.01$; **Figure 2**) as compared with control subjects. The mean difference in the change in fasting insulin concentrations was reported in 12 trials and was found to not be significantly different (-0.40 μ IU/mL; 95% CI: $-1.27, 0.46$ μ IU/mL; $P = 0.36$; **Figure 3**). Hb A_{1c} values were measured in 7 trials, and the pooled estimated net change was -0.30% (95% CI: $-0.37, -0.22\%$; $P \leq 0.01$). In addition, 5 studies examined HOMA-IR, and 3 studies detected 2-h glucose concentrations; no significant mean differences were observed for either outcome (Table 2).

Sensitivity and subgroup analysis

Subgroup analyses (**Table 3**) were performed to explore the effects of healthy status, study design, catechins dose, and study quality and to evaluate any differences between trials ruling out the confounding effect of caffeine and trials using caffeinated green tea as supplement. Catechin consumption was categorized as either high dose (≥ 457 mg/d) or low dose (< 457 mg/d). In addition, an additional subgroup analysis was conducted by dividing the follow-up duration into a longer-term subgroup (≥ 12 wk) and a shorter-term subgroup (< 12 wk). The subgroup analyses indicated that green tea had a lowering effect on fasting glucose in subjects at risk of the metabolic syndrome, but did not affect fasting glucose concentrations in healthy subjects. In parallel- and crossover-design subgroups, a significant reduction in fasting glucose concentration was observed in parallel-design subgroup. However, no effect was found in the crossover-design subgroup. When we stratified studies according to intervention type, the beneficial effects of green tea on fasting glucose concentrations could only be observed when the confounding effect of caffeine was removed. Significant reductions in fasting glucose concentrations were observed in subgroups consuming green tea for both long and short durations. In addition, green tea consumption significantly lowered fasting glucose concentrations in subgroups with higher catechin intakes, but no effect was found in the subgroup with lower catechin intakes. Finally, when studies were stratified according to Jadad score, a significant reduction in fasting glucose concentrations was found only in those trials with high Jadad scores. In total, 13 trials reported data on fasting insulin concentrations. The subgroup analyses indicated that the overall outcome of fasting insulin was not affected by study design, type of intervention, catechin dose, and intervention duration. A significant reduction in fasting glucose concentrations was found in the subgroup with a high Jadad score but not in the subgroup with a low Jadad score. The results of sensitivity analysis showed that the pooled effects of green tea on fasting glucose and insulin concentrations were not changed after imputation using a correlation coefficient of 0.5. Finally, systematically removing each trial during the sensitivity analysis did not significantly change the overall observed effects of green tea on fasting glucose and insulin concentrations.

TABLE 1
Characteristics of 17 randomized controlled trials included in analysis¹

Author, publication year (reference no.)	No. of subjects	Study design	Population	Duration	Tea group	Control group	Jadad Score	Type of diet ²
Fukino, 2005 (31)	66	Parallel	Borderline diabetes, 32–73 y of age	2 mo	GTE beverage (456 mg catechins; 102 mg caffeine)	NR	<4	Usual diet
Chan, 2006 (32)	34	Parallel	Obese, 25–40 y of age	3 mo	GTE capsule (457.89 mg catechins; 105.8 mg caffeine)	Placebo capsules	<4	Usual diet, caffeine-free
Ryu, 2006 (33)	55	Crossover	T2DM, 53.9 ± 7.7 y of age	4 wk	GTE beverage (9 g green tea)	Water	<4	Usual diet
Diepvens, 2006 (34)	46	Parallel	Overweight, 19–57 y of age	87 d	GTE capsule (1207 mg catechins; 236.7 mg caffeine)	Placebo (maltodextrin capsule)	<4	Low-energy diet
Nagao, 2007 (35)	240	Parallel	Obese, 25–55 y of age	12 wk	GTE beverage (582.8 mg catechins; 75 mg caffeine)	GTE beverage (96 mg catechins; 72.3 caffeine)	<4	Usual diet with physical activity
Hill, 2007 (36)	38	Parallel	Overweight/obese, 45–70 y of age	12 wk	DGTE capsule (300 mg EGCG)	Placebo (lactose capsules)	<4	Usual diet with exercise
Fukino, 2008 (37)	64	Crossover	Borderline diabetes, 32–73 y of age	2 mo	GTE beverage (456 mg catechins; 102 mg caffeine)	Water	<4	Usual diet
Nagao, 2009 (38)	43	Parallel	T2DM	12 wk	GTE beverage (582.8 mg catechins; 75 mg caffeine)	GTE beverage (96.3 mg catechins; 72.3 mg caffeine)	<4	Usual diet
Mirzaei, 2009 (39)	72	Parallel	T2DM patients, ≥40 y of age	8 wk	GTE capsule (240 mg polyphenols; 150 mg caffeine)	Placebo (cellulose capsules)	<4	Usual diet
Brown, 2009 (40)	88	Parallel	Overweight/obese, 40–65 y of age	8 wk	DGTE capsule (800 mg EGCG)	Placebo (lactose capsules)	≥4	Usual diet
Stendell-Hollis, 2010 (41)	34	Parallel	Overweight/obese, 18–80 y of age	6 mo	DGTE beverage (364.48 mg catechins)	Placebo (herbal tea)	≥4	Usual diet
Hsu, 2011 (42)	68	Parallel	T2DM, 20–65 y of age	16 wk	DGTE capsule (856 mg catechins)	Placebo (cellulose capsules)	≥4	Usual diet
Brown, 2011 (43)	66	Crossover	Overweight and obese, 40–69 y of age	6 wk	DGTE capsule (800 mg catechins)	Placebo (lactose capsules)	≥4	Usual diet
Some, 2011 (44)	51	Parallel	Healthy, 20–70 y of age	9 wk	GTE beverage (400 mg catechins; 105 mg caffeine)	GTE beverage (100 mg catechins; 80 mg caffeine)	<4	Usual diet, limit catechins
Wu, 2012 (45)	66	Parallel	Healthy, >45 y of age	2 mo	DGTE capsule (800 mg catechins)	Placebo	≥4	Usual diet
Bogdanski, 2012 (46)	56	Parallel	Obese hypertensive patients, 30–60 y of age	3 mo	GTE capsule (208 mg EGCG)	Placebo capsules (cellulose)	≥4	Usual diet
Suliburska, 2012 (47)	46	Parallel	Obese, 30–60 y of age	3 mo	GTE capsule (208 mg EGCG)	Placebo capsules (cellulose)	≥4	Usual diet

¹ DGTE, decaffeinated green tea extract; EGCG, epigallocatechin gallate; GTE, green tea extract; NR, not reported; T2DM, type 2 diabetes mellitus.

² A usual diet was similar to a conventional diet; a low-energy diet contained less amounts of energy than a usual diet.

TABLE 2
Pooled effects of green tea on glucose control and insulin sensitivity

Variable	No. of studies	Sample size (treatment/control) ¹	Net change (95% CI)	Test of heterogeneity ²		
				<i>P</i>	<i>I</i> ²	<i>P</i> ³
Fasting glucose (mmol/L)	17	627/624	-0.09 (-0.15, -0.03)	0.73	0.001	<0.01
Fasting insulin (μIU/mL)	13	436/434	-0.40 (-1.27, 0.46)	0.01	57.1	0.36
Hb A _{1c} ⁴ (%)	7	225/235	-0.30 (-0.37, -0.22)	0.1	44.2	<0.01
2-h glucose (mmol/L)	3	88/101	-0.20 (-0.51, 0.11)	0.20	0.36	2.0
HOMA-IR (units)	5	171/165	-0.04 (-0.67, 0.59)	0.13	43.8	0.90

¹ Numbers of subjects in the treatment and control groups.

² *P* for heterogeneity was assessed by using Cochran's test, and *P* < 0.1 was considered to indicate significant heterogeneity across studies. The *I*² statistic was calculated by using Cochran's test, and an *I*² > 50% was considered to indicate significant heterogeneity across studies.

³ *P* for meta-analysis: *P* < 0.05 was considered to indicate significant effect of green tea on fasting glucose and insulin concentrations by using a fixed-effects or random-effects model.

⁴ Hb A_{1c}, glycated hemoglobin.

Publication bias

Funnel plots and Egger's tests found no significant publication bias in the current meta-analysis of fasting glucose, fasting insulin, Hb A_{1c}, and 2-h glucose concentrations and HOMA-IR (Egger's test: *P* = 0.64, 0.91, 0.25, 0.49, and 0.60, respectively).

DISCUSSION

Our meta-analysis showed that green tea consumption significantly lowered fasting glucose and Hb A_{1c} concentrations. Meanwhile, subgroup analyses using the data extracted from high-quality trials showed that green tea consumption significantly reduced fasting insulin concentrations. Our assessment of the effects of green tea on 2-h glucose concentrations and

HOMA-IR was limited by the small number of trials available for analysis.

The current analyses showed slight inconsistencies in the effects of green tea on glycemic measures in the subgroup analyses. Green tea consumption significantly decreased fasting glucose concentrations only in studies that included subjects with risk of the metabolic syndrome. This suggested that the beneficial effect of green tea (ie, lowering fasting glucose concentrations) might be more pronounced in subjects with factors that increase their risk of the metabolic syndrome. Three recent studies have shown that green tea extract supplementation significantly decreased fasting blood glucose and improved oral glucose tolerance in mice (4, 48, 49). In addition, green tea extract ameliorated the diabetes-induced oxidative stress in diabetic rats (50) and enhanced the capacity of adipocytes and skeletal muscle for glucose

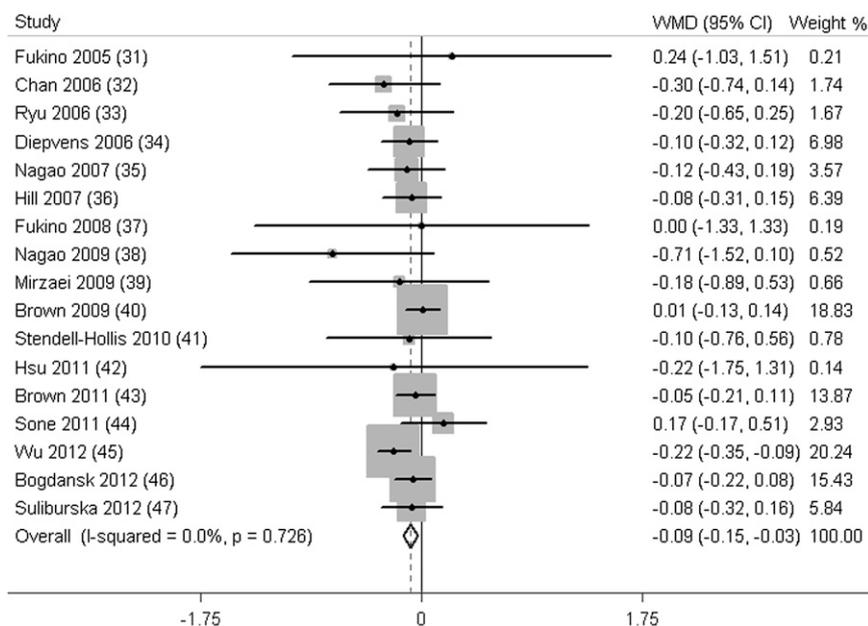


FIGURE 2. Meta-analysis of the effects of green tea on fasting glucose concentrations. Weight was assigned with STATA (version 11; StataCorp) by using the number of subjects and the SD. Sizes of the data markers indicate the weight of each study in this analysis. The diamond represents the overall estimated effect, and the result was obtained from a random-effects model. WMD, weighted mean difference.

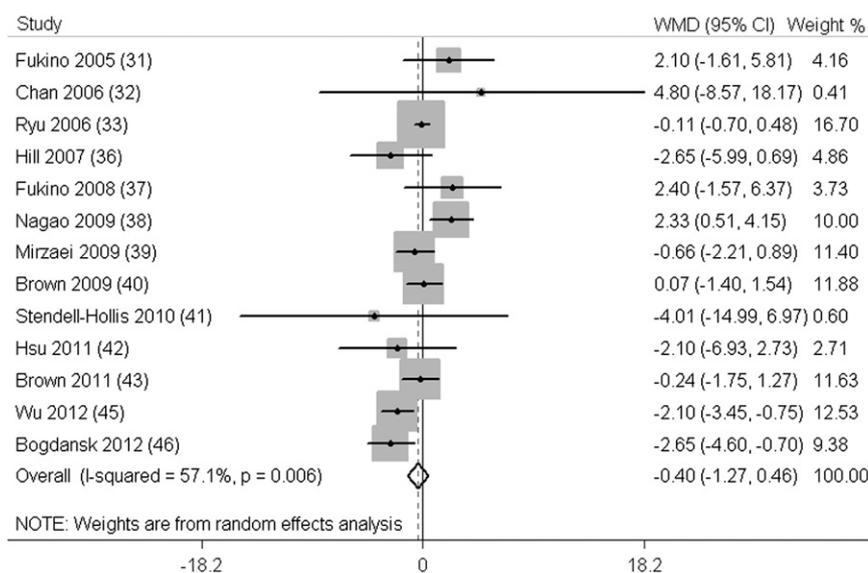


FIGURE 3. Meta-analysis of the effects of green tea on fasting insulin concentrations. Weight was assigned with STATA (version 11; StataCorp) by using the number of subjects and the SD. Sizes of the data markers indicate the weight of each study in this analysis. The diamond represents the overall estimated effect, and the result was obtained from a random-effects model. WMD, weighted mean difference.

uptake by increasing the protein content and translocation of glucose transporter 4 (15, 51). Furthermore, green tea extract regulated the expression of genes related to gluconeogenic enzymes and protein-tyrosine phosphorylation by modulating the redox state of rat hepatoma cells (52). Stratification according to study design indicated significant reductions in fasting glucose concentrations in the parallel-design subgroup, but no reductions were found in the crossover-design subgroup. This difference may have been because of the small number of crossover-design RCTs. In addition, the significant lowering effect of green tea on fasting glucose concentrations was found in the subgroup with a higher catechin consumption, but not was detected in the subgroup with a lower catechin consumption. The results of our study were consistent with a recently published meta-analysis that included 324,141 participants and 11,400 incident cases of T2DM with follow-up duration ranging from 5 to 18 y. Results of this study indicated that participants who drank ≥ 4 cups tea/d had a 20% lower risk of T2DM compared with those who drank less or none (8). When we stratified studies according to type of intervention, a significant lowering effect of green tea on fasting glucose concentration was only detected in trials ruling out the confounding effect of caffeine. This may have been attributed to study quality, because all 7 studies that used caffeinated green tea as a supplement showed a lower Jadad score. A significant reduction in fasting glucose concentration was found in the subgroup with a high Jadad score, but not in the subgroup with a low Jadad score. Moreover, the Hb A_{1c} results indicated that green tea has a significant long-term glucose-lowering effect. Consistent with our study, a recent crossover study showed that consumption of 1.0 L oolong tea (45 mg EGCG in 245 mg total catechins) for 30 d decreased Hb A_{1c} (24).

Meanwhile, a significant reduction in fasting insulin concentrations was found only in high-quality trials in this meta-analysis. This suggests that the quality of the studies might account for the differences found in the subgroup analyses related to fasting insulin concentrations. Thus, it is reasonable to conclude that green tea may lower fasting insulin concentrations

because the studies with high Jadad scores would have less bias and provide a stronger evidential basis for this effect. This finding is also supported by previous studies that found that rats maintained on normal diets supplemented with green tea extract via drinking water (370 mg/kg for 12 wk) had significantly reduced fasting insulin concentrations and enhanced insulin sensitivity (14, 15). The observed decrease in fasting insulin concentrations may have been a result of alterations in specific insulin binding and protein expression of peroxisome proliferator-activated receptor when green tea extract is consumed (14, 15, 53). Green tea extract may also decrease fasting insulin concentrations by increasing tyrosine phosphorylation of the insulin receptor and insulin receptor substrate-1 and by reducing phosphoenolpyruvate carboxykinase gene expression in a phosphoinositide 3-kinase-dependent manner (52).

Despite the inevitable limitations of our meta-analysis, we believe that this study provides useful information. First, although the catechin dose among the 17 trials included in the current meta-analysis ranged from 208 to 1207 mg/d (median: 457 mg/d), the wide range of green tea doses did not lead to significant heterogeneity and affect the overall outcome of the analyses. Unfortunately, the results of the meta-regression analysis did not show a significant dose-response effect between green tea and fasting glucose (P -trend = 0.75) or fasting insulin (P for trend = 0.70) concentrations. Thus, it is difficult to determine the optimal dose for a dietary program as part of a health policy aimed at improving diabetic health. Second, studies included in the meta-analysis were generally of short duration, ranging from 2 wk to 6 mo, and the quality of the trials varied from low to high. Of the 17 studies, 7 studies (40–43, 45–47) were high-quality studies, whereas the remaining 10 studies were of low quality. The inconsistent results of subgroup analyses conducted to explore the effects of green tea on fasting insulin concentrations may be mainly attributed to differences in study quality and an overall limited number of higher-quality studies. Third, measures for glucose control or insulin sensitivity were not primary outcomes in most of the trials selected in this meta-analysis, and the

TABLE 3
Subgroup analyses of fasting glucose and insulin concentrations stratified by previously defined study characteristics

Variables	Fasting glucose					Fasting insulin				
	No. of trials	Net change (95% CI)	<i>P</i>	<i>I</i> ²	<i>P</i> ²	No. of trials	Net change (95% CI)	<i>P</i>	<i>I</i> ²	<i>P</i> ²
		mmol/L		%			μIU/mL		%	
Healthy status	15	-0.06 (-0.13, -0.001)	0.97	0.001	0.046	12	-0.13 (-0.58, 0.31)	0.04	46.8	0.55
Metabolic syndrome risk	2	-0.06 (-0.44, 0.32)	0.04	77.4	0.76	1	-2.10 (-3.45, -0.75)	—	—	<0.01
Healthy	14	-0.10 (-0.16, -0.03)	0.55	0.001	<0.01	10	-0.66 (-1.96, 0.65)	0.004	63.1	0.32
Study design	3	-0.07 (-0.21, 0.08)	0.82	0.001	0.38	3	-0.08 (-0.63, 0.47)	0.46	0.001	0.78
Parallel	10	-0.09 (-0.16, -0.03)	0.72	0.001	<0.01	8	-0.87 (-2.24, 0.50)	0.003	68.1	0.21
Crossover	7	-0.08 (-0.23, 0.08)	0.48	0.001	0.31	5	-0.08 (-0.62, 0.47)	0.42	0.001	0.80
Type of intervention	8	-0.08 (-0.16, -0.01)	0.26	21.6	0.03	7	-0.31 (-0.76, 0.14)	0.09	45.7	0.18
Trials ruling out confounding effect of caffeine	9	-0.10 (-0.19, -0.01)	0.92	0.001	0.03	6	-1.00 (-3.79, 1.78)	0.01	70.4	0.48
Trials using green tea containing caffeine	8	-0.05 (-0.16, 0.05)	0.95	0.001	0.31	6	-0.10 (-2.07, 0.02)	0.09	48.1	0.06
Duration	8	-0.11 (-0.18, -0.04)	0.24	23.2	0.03	6	-0.15 (-0.70, 0.48)	0.01	69.0	0.85
<12 wk (lower than median)	10	-0.10 (-0.21, -0.02)	0.74	0.001	0.10	7	0.41 (-0.80, 1.62)	0.05	52.3	0.50
≥12 wk (higher than median)	7	-0.09 (-0.16, -0.02)	0.40	3.7	<0.01	6	-1.16 (-1.91, -0.40)	0.13	42.0	<0.01
Catechins dose										
<457 mg/d (lower than median)										
≥457 mg/d (higher than median)										
Jadad score										
Low (<4)										
High (≥4)										

¹ *P* for heterogeneity was assessed by using Cochran's test, and *P* < 0.1 was considered to indicate significant heterogeneity across studies. The *I*² statistic was calculated by using Cochran's test, and *I*² > 50% was considered to indicate significant heterogeneity across studies.

² *P* for meta-analysis: *P* < 0.05 was considered to indicate a significant effect of green tea on fasting glucose and insulin concentrations by using a fixed-effects or random-effects model.

null findings of secondary outcomes may not have always been published.

In conclusion, green tea significantly lowered fasting glucose and Hb A_{1c} concentrations, and the results of our stratified analyses suggested that green tea may also reduce fasting insulin concentrations. Additional long-term and high-quality RCTs specifically designed to evaluate the effects of green tea on glucose control and insulin sensitivity are needed to further evaluate and confirm these findings.

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