Effects of Supplementation with Green Tea Catechins on Plasma C-reactive protein Concentrations: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Corina Serban, Amirhossein Sahebkar, Diana Antal, Sorin Ursoniu, Maciej Banach

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Graphical Abstract: Lack of significant effect of green tea supplementation on plasma CRP concentration (Forest plot detailing weighted mean difference and 95% confidence intervals for the impact of supplementation with green tea catechins on plasma C-reactive protein concentrations).
Effects of Supplementation with Green Tea Catechins on Plasma C-reactive protein Concentrations: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Conflict of Interest Disclosures: None

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ABSTRACT:

Introduction: Promising experimental and clinical trials suggest that green tea decrease inflammatory process in cardiometabolic diseases, but evidence from epidemiologic studies about the effects on plasma C-reactive protein (CRP) seems inconsistent and ambiguous. Therefore the aim of the meta-analysis was to evaluate the impact of green tea supplementation on plasma CRP concentrations.

Methods: We searched selected database up to October 26, 2014 to identify randomized controlled trials (RCTs) investigating the impact of green tea supplementation on plasma CRP concentrations. Two independent reviewers extracted data on study characteristics, methods and outcomes.

Results: Meta-analysis of data from 11 RCTs arms did not indicate a significant effect of supplementation with green tea catechins on plasma CRP concentrations (WMD: 0.085 mg/L, 95%CI: -0.225, 0.395, \( p=0.592 \)). This effect size was robust in sensitivity analysis and omission of each individual study did not have a significant effect. The non-significant effects of green tea catechins on plasma CRP concentrations were also observed in subgroups of studies with green tea supplementation duration of <8 weeks (WMD: 0.029 mg/L, 95%CI: -0.229, 0.286, \( p=0.828 \)) and \( \geq 8 \) weeks (WMD: 0.099 mg/L, 95%CI: -0.555, 0.754, \( p=0.766 \)). Likewise there was no significant effect in subgroups of studies with total catechins doses <400 mg/day (WMD: 0.073 mg/L, 95%CI: -0.251, 0.398, \( p=0.658 \)) and \( \geq 400 \) mg/day (WMD: 0.213 mg/L, 95%CI: -0.148, 0.574, \( p=0.247 \)). The effect size were not significant after stratification of studies to those recruiting healthy subjects (WMD: -0.028 mg/L, 95%CI: -0.216, 0.160, \( p=0.769 \)), and those recruiting subjects with cardiometabolic diseases (WMD: 0.260 mg/L, 95%CI: -0.815, 1.334, \( p=0.636 \)).

Conclusions: This meta-analysis of data from 11 RCT arms did not indicate a significant effect of supplementation with green tea catechins on plasma CRP concentrations. Further, well-designed trials are necessary to validate these results.

Keywords: green tea, C-reactive protein, inflammation, catechins

Number of words: 287
ABBREVIATIONS:

CAD = coronary artery disease
CI = confidence interval
CV = cardiovascular
CMA = Comprehensive Meta-Analysis
EGC = epigallocatechin
EGCG = epigallocatechin gallate
HDL-C = high-density lipoprotein cholesterol
HsCRP = high-sensitivity C-reactive protein
LDL-C = low-density lipoprotein cholesterol
NA = not applicable
NS = not stated
RCTs = randomized controlled trials
SD = standard deviation
SMD = standardized mean difference
WMD = weighed mean difference
INTRODUCTION

Tea, obtained from the plant *Camellia sinensis* (L.) Kuntze, is a well-known drink consumed worldwide, mainly in Japan and China, as green, black, or Oolong tea [1]. The tea varies by manufacturing process, origin of plants and bioactive chemical elements [2]. Main constituents of green tea are catechins, integrating: catechin, epicatechin, epigallocatechin (EGC), epicatechin gallate, and epigallocatechin gallate (EGCG) [3, 4]. Other compounds responsible for health benefits of green tea are flavones, flavonols, phenolic acids, amino acids (theanine), caffeine, theophylline, and theobromine [5]. It has been shown that EGCG specifically interferes with phospholipids and proteins from plasma membrane and controls transcription factors, mitochondrial function, signal transduction pathways, DNA methylation, and autophagy [6].

Green tea exerts protective effects in arterial hypertension [7], obesity [8-11], type 2 diabetes mellitus [12-14], metabolic syndrome [15-18], ischemic stroke [19], Alzheimer's disease [20, 21], Parkinson's disease [22], oral cancer [23] and breast cancer [24, 25]. *In vitro* it has been extensively proven that polyphenols have anti-inflammatory activities, exerted through the modulation of enzymes and mediated by antioxidative effects. In case of green tea and tea catechins, following anti-inflammatory mechanisms were identified on a molecular level: inhibition of IL-1β-induced IL-8 production [26], prevention of the induction of vascular adhesion molecule-1 by TNF α and IL-1 [27], inhibition of human inducible nitric-oxide synthase expression [28], enhancement of the production of anti-inflammatory cytokines such as IL-10 [29], reduction of COX-2 expression induced by LPS and IL-1β [30]. On the other hand, prevention of Fenton-type reactions through chelation of iron [31], scavenging of NO and other reactive oxygen species (superoxide anion, hydroxyl radical) are considered important contributors to the anti-inflammatory effect of catechins [32, 33].
The encouraging results coming from *in vitro* experiments, as well as on the lack of tea toxicity documented by a long history of use as a beverage, incited the evaluation of its anti-inflammatory effects in clinical trials. However, a quick survey of published clinical studies shows inconsistencies between results. Some studies showed positive anti-inflammatory effects of tea products [34, 35], while no changes of the inflammatory status following the administration of tea or tea catechins were observed in others [36, 37]. In these circumstances, a meta-analysis seems to be pertinent to summarize current data.

C-reactive protein (CRP), a sensitive systemic marker of inflammation was chosen to objectively evaluate anti-inflammatory effects of green tea. CRP is as well a strong predictor of cardiovascular risk in comparison to several other inflammatory markers [38, 39]. It is mainly synthesized by hepatocytes triggered by the dual activity of interleukin 6 (IL-6) and IL-1, and participates to the enhancement of the inflammatory cascade by inducing IL-6 secretion [40].

In the present study, we targeted to systematically review all released trials analyzing the impact of green tea preparations, green tea extract, purified green tea catechins or purified green tea polyphenols on CRP as a measure of the inflammatory status.

**METHODS**

*Search Strategy*

This study was designed according to the guidelines of the 2009 preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement [41]. SCOPUS (http://www.scopus.com) and Medline (http://www.ncbi.nlm.nih.gov/pubmed) databases were searched using the following search terms in titles and abstracts (also in combination with MESH terms): (C-reactive protein) AND (green tea or catechins or catechin). The wild-card term "*" was used to increase the sensitivity of the search strategy. No language restriction
was used in the literature search. The search was limited to studies in human. The literature
was searched from inception to October 26, 2014. Selected articles were hand searched to
identify further relevant studies.

**Study Selection**

Original studies were included if they met the following inclusion criteria: (i) be a
randomized clinical case-control or case-cross-over trial, (ii) investigated the impact of green
tea preparations, green tea extract, purified green tea catechins or purified green tea
polyphenols on plasma/serum CRP concentrations, (iii) presentation of sufficient information
on plasma/serum CRP levels at baseline and at the end of study in both green tea and control
groups. Exclusion criteria were (i) non-clinical studies, (ii) uncontrolled trials, (iii) trials in
which green tea was supplemented for a period of < 2 weeks, (iv) cross-over trials without a
wash-out period between interventions (in which the second period was omitted from
analysis), and (iv) lack of sufficient information on baseline or follow-up CRP concentrations.
Exclusion of an article for the latter reason was done if no feedback was received after
contacting the author(s).

**Data extraction**

Eligible studies were reviewed and the following data were abstracted: 1) first author's
name; 2) year of publication; 3) study location; 4) number of participants in the green tea and
control groups; 5) age, gender and body mass index (BMI) of study participants; 6) circulating
concentrations of CRP, total cholesterol, LDL-C, HDL-C, triglycerides and glucose; 7)
systolic and diastolic blood pressures; 8) homeostasis model assessment-estimated insulin
resistance (HOMA-IR) index; and 9) prevalence of smoking, type 2 diabetes, dyslipidemia,
hypertension and CHD. In case the values were only presented as graph, the software GetData
Graph Digitizer 2.24 (http://getdata-graph-digitizer.com/) was applied to digitize and extract the data.

**Quality assessment**

The quality of included studies was assessed using Jadad scale. This scale encompasses randomization (0-2 points), blinding (0-2 points), and dropouts and withdrawals (0-1 point). The overall score of a study according to this scale ranges between 0-5, with higher scores indicative of a better quality [42]. Studies with Jadad scores of $\leq 2$ and $\geq 3$ were considered as low- and high-quality, respectively [43].

**Risk of bias assessment**

According to the Cochrane Collaboration, a specific tool for assessing risk of bias in each included study comprises judgment of specific features of the study [44]. This involves assessing the risk of bias as ‘low risk’, as ‘high risk, or as ‘unclear risk’. The last category indicates either lack of information or uncertainty over the potential for bias. There are seven analyzed domains comprising: sequence generation (selection bias), allocation sequence concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective outcome reporting (reporting bias) and other potential sources of bias.

**Quantitative Data Synthesis**

Meta-analysis was conducted using the Comprehensive Meta-Analysis (CMA) V2 software (Biostat, NJ)[45]. Plasma CRP concentrations were collated in mg/L. Standard deviations (SDs) of the mean difference were calculated using the following formula: $SD = \sqrt{SD_{pre-treatment}^2 + SD_{post-treatment}^2 - (2R \times SD_{pre-treatment} \times SD_{post-treatment})}$, assuming
a correlation coefficient (R) = 0.5. In case of reporting SEM, SD was estimated using the following formula: SD = SEM × sqrt (n), where n is the number of subjects.

Net changes in measurements (change scores) were calculated for parallel and crossover trials, as follows: (measure at end of follow-up in the treatment group – measure at baseline in the treatment group) – (measure at end of follow-up in the control group – measure at baseline in the control group). A random-effects model and the generic inverse variance method were used to compensate for the heterogeneity of studies in terms of green tea supplement used (decoction, extract or purified form), green tea dose, trial design (parallel or cross-over), duration of green tea supplementation, and demographic characteristics of individual trials (underlying disease, age, gender and etc). In case of double-arm (2 × 2) crossover trials, each arm was treated as a single study. In case of no washout between the interventions periods of a crossover trial with a 2 × 2 design, only the first periods of each arm were used for analysis. In order to avoid double counting of subjects and consequent unit-of-analysis error in the trials with more than 1 treatment arm, the control group was evenly (where possible) splitted. Effect size was expressed as weighed mean difference (WMD) and 95% confidence interval (CI). In order to evaluate the influence of each study on the overall effect size, sensitivity analysis was conducted using the one-study remove (leave-one-out) approach [46, 47].

**Meta-regression**

Random-effects meta-regression was performed using unrestricted maximum likelihood method to evaluate the association between calculated WMD in plasma CRP concentrations with the catechin content of green tea supplement as well duration of green tea supplementation.
Publication bias

Potential publication bias was explored using visual inspection of Begg’s funnel plot asymmetry, and Begg’s rank correlation and Egger’s weighted regression tests. Duval & Tweedie “trim and fill” method was used to adjust the analysis for the effects of publication bias [48].

RESULTS

Search results and trial flow

The initial screening for potential relevance removed the articles in whose titles and/or abstracts were obviously irrelevant. By all 12 RCTs selected for eligibility, 3 studies were excluded because the duration of supplementation < 2 weeks [49-51] and one study because used green tea in combination with black tea, without an appropriate control group [52]. After final assessment, 8 RCTs achieved the inclusion criteria and were preferred for the final meta-analysis [34, 36, 37, 53-57]. In total, 377 participants were randomized, of whom 199 were allocated to Green tea supplementation group and 165 to control group in the selected studies. The number of participants in these trials ranged from 20 to 60. Included studies were published between 2000 and 2012, and were conducted in USA, Poland, the Netherlands, Switzerland and Japan (4 trials). Ranges of doses from 160 mg catechin/day to 2488.68 mg catechin/day were administered in the included trials. Duration of supplementation with Green tea ranged between 2 weeks and 3 months. Six trials were designed as parallel-group studies and 2 as cross-over studies, comprising a total of 12 treatment arms. Demographic and baseline parameters of the included studies are shown in Table 1.

Quantitative data synthesis

Meta-analysis of data from 11 RCT arms did not indicate a significant effect of supplementation with green tea catechins on plasma CRP concentrations (WMD: 0.085 mg/L,
95% CI: -0.225, 0.395, \( p = 0.592 \) (Figure 2). This effect size was robust in sensitivity analysis and omission of each individual study did not have a significant effect (Figure 3). The non-significant effects of green tea catechins on plasma CRP concentrations were also observed in subgroups of studies with green tea supplementation duration of < 8 weeks (WMD: 0.029 mg/L, 95% CI: -0.229, 0.286, \( p = 0.828 \)) and \( \geq 8 \) weeks (WMD: 0.099 mg/L, 95% CI: -0.555, 0.754, \( p = 0.766 \)) (Figure 4). Likewise there was no significant effect in subgroups of studies with total catechins doses < 400 mg/day (WMD: 0.073 mg/L, 95% CI: -0.251, 0.398, \( p = 0.658 \)) and \( \geq 400 \) mg/day (WMD: 0.213 mg/L, 95% CI: -0.148, 0.574, \( p = 0.247 \)) (Figure 5). The effect size were not significant after stratification of studies to those recruiting healthy subjects (WMD: -0.028 mg/L, 95% CI: -0.216, 0.160, \( p = 0.769 \)), and those recruiting subjects with cardiometabolic diseases (comprising prediabetes or diabetes, obesity and metabolic syndrome) (WMD: 0.260 mg/L, 95% CI: -0.815, 1.334, \( p = 0.636 \)) (Figure 6).

Green tea was safe and well-tolerated in all of the RCTs included in this review, with no report of serious adverse events.

**Meta-regression**

Meta-regression analysis was conducted to evaluate the association between changes in plasma CRP concentrations and potential moderator variables. The impact of green tea catechins on plasma CRP levels of was found to be independent of total catechin dose (slope: 0.0004; 95% CI: -0.0004, 0.0012; \( p = 0.377 \)) and duration of supplementation (slope: -0.042; 95% CI: -0.130, 0.046; \( p = 0.351 \)) (Figure 7).

**Publication bias**

Visual inspection of the funnel plot of the study precision (inverse SEM) by effect size (mean difference) suggested a slight asymmetry that was imputed by 3 studies on the left of
the mean using trim-and-fill method. The imputed effect size was 0.031 (95% CI: -0.278, 0.340), showing lack of significant effect even after imputation of potentially missing studies. There was no sign of publication bias according to either Begg’s rank correlation (Kendall’s Tau with continuity correction = 0.327, Z = 1.401, two-tailed p-value = 0.161) and Egger’s linear regression (intercept = 1.135, 95% CI = -0.417, 2.688, t = 1.655, df = 9.00, two-tailed p = 0.132) test. Funnel plot of the impact of green tea catechins on plasma CRP concentrations is illustrated in Figure 8.

DISCUSSION

Meta-analysis of data from 11 RCT arms did not indicate a significant effect of supplementation with green tea catechins on plasma CRP concentrations. This effect size was robust in sensitivity analysis and omission of each individual study did not have a significant effect. The non-significant effects of green tea catechins on plasma CRP concentrations were also observed in subgroups of studies with green tea supplementation duration of < 8 weeks and ≥ 8 weeks. Likewise there was no significant effect in subgroups of studies with total catechins doses < 400 mg/day and ≥ 400 mg/day. The effect size was not significant after stratification of studies to those recruiting healthy subjects, and those recruiting subjects with cardiometabolic diseases (comprising prediabetes or diabetes, obesity and metabolic syndrome). Furthermore, the impact of green tea catechins on plasma CRP levels of was found to be independent of total catechin dose and duration of supplementation.

A recent meta-analysis has shown that the consumption of green tea could considerably decrease plasma LDL-C and TC concentrations [58]. The other one confirmed that green tea might have a beneficial effect on glucose control in individuals [59]. Therefore, the effect of green tea or green tea catechins on inflammation, precisely on CRP, an important CV risk assessment tool due to its capacity to predict CV events [59], was a pertinent question.
The promising anti-inflammatory potential detected \textit{in vitro} for green tea or green tea catechins could not be demonstrated in the current meta-analysis of human clinical trials. Many different factors could be responsible for these results. First of all, concentrations of tea catechins differ greatly between \textit{in vitro} experiments and clinical setups: while experiments on cell cultures often employ EGCG in concentrations of 10-100 µM, the mean EGCG peak plasma level after 2 cups of tea is only situated in the low micromolar range, attaining about 0.17 µM [60]. Secondly, there exists a considerable human inter-individual polymorphism impacting on the bioavailability and metabolic fate of tea flavonoids. After administration, the absorption of polyphenols is generally low, and extensive structural changes of the unabsorbed fraction occur under the influence of colic flora. Recent metabolomics of polyphenol decay products generated in the gut sheds increasing light on the plethora of metabolites and chemical processes occurring here. Their impact is not only local, but as well relevant for distally occurring pathologic processes such as cancer and inflammation [61]. In the gut, polyphenols and their metabolites perform a selection of fermentative species, with impact on the metabolism of subsequent polyphenol intakes [62]. If polyphenols modify the ecology of the gut microbiome, then species selected during longer timespans according to dietary habits could modulate the metabolism of other food components in a way that is health promoting. This may be one of the causes why epidemiologic studies on natural compounds have different outcomes than intervention studies. For example it has been shown that serum CRP concentrations are inversely associated with the intake of dietary flavonoids in U.S. adults [63]. Tea polyphenols, and more generally catechins are important contributors to the total polyphenol intake.

However, the current meta-analysis of RCTs failed to show any conclusive benefit of green tea products on CRP. The hypothesis cannot be ruled out, that the microbiome selected by lifelong dietary habits in the population observed by epidemiologic studies has a different
composition than the one in randomly chosen individuals for intervention trials. Biological effects of secondary metabolites from plants are a result of long-achieved balance and co-evolution, and may not be apparent in rapid, punctual pharmacologic evaluations as in the case for drugs obtained by chemical synthesis. However, the green tea phytochemical compounds and their metabolites have an impact on several endogenous pathways by modulation of gene-expression [64]. Although green tea catechins have been reported to be the most efficient ingredients of green tea, there is a growing proof that these chemical substances are not the only constituents responsible for the effects of green tea [65]. In addition, kaempferol, quercetin, myricetin and caffeine from green tea have been shown to have pleiotropic effects on numerous biological pathways [65]. In human hepatoma cell lines, it has been shown that the induction of CRP by cytokines is potentiated by caffeine [66]. Therefore, the possible confounding effect of caffeine from green tea on our results should be also taken into account. Another possible explanation for the effects of green tea on CRP might be the modification of the bioavailability of catechins through interactions with many competitive nutrients at the level of absorption, metabolism, and membrane transportation [64]. It also can be speculated that the variation of habitual caffeine consume of the individuals included in these RCTs could have masked the beneficial effects of the green tea catechins [67]. This hypothesis was confirmed by a study that showed different opposite results of green tea catechins supplementation in a similar set-up in low-level caffeine consumers versus high level caffeine consumers [67].

In many epidemiological studies it has been suggested that increasing green tea intake is correlated with greater protective effects. This inconsistency between epidemiological and intervention studies needs be addressed in human intervention studies in an effort to acquire more informations regarding the dose-response relationship of green tea catechins in particular conditions [68].
status of green tea are changing within 2h of tea consumption [69, 70]. Furthermore, the results obtained in different experimental studies should be interpreted with large caution due to the pharmacokinetic and pharmacodynamics variations of the test agents in experimental studies [69, 70].

However, green tea is generally considered a healthful drink when is utilized in reasonable portions. Despite the fact that many studies have demonstrated health benefits after two or three cups of green tea daily, the ideal dose has not been identified to allow any consistent findings to be derived concerning the numerous advantages of green tea beverages or its components in individuals [71].

The most frequent side-effects generated by caffeine content of green tea are the stimulation of central nervous system and gastrointestinal upset [72]. Furthermore, hepatotoxicity related to the ingestion of green tea extract has also been documented [73]. Green tea catechins may modify the absorption and bioactivity of prescription drugs, inhibit drug-transporters and activities of drug-metabolizing enzymes, upregulate or downregulate different proteins or may induce harm when are mixed with additional popular herb treatments [74, 75].

This meta-analysis has different limitations. Most significantly, the qualified RCTs generally had modest populations and limited follow-up. Moreover, the studies involved were heterogeneous concerning the population similarities, the concept of the study (inclusion/exclusion criteria), and green tea quantity.

In conclusion, this meta-analysis of data from 11 RCT arms did not indicate a significant effect of supplementation with green tea catechins on plasma CRP concentrations. Further, well-designed trials are necessary to validate these results.
DECLARATION OF INTEREST

This meta-analysis was written independently; no company or institution supported it financially. No professional writer was involved in the preparation of this meta-analysis.
FIGURE LEGENDS

Figure 1. Flow diagram of the study selection procedure

Figure 2. Forest plot detailing weighted mean difference and 95% confidence intervals for the impact of supplementation with green tea catechins on plasma C-reactive protein concentrations.

Figure 3. Leave-one-out sensitivity analysis of the impact of supplementation with green tea catechins on plasma C-reactive protein concentrations

Figure 4. Forest plot detailing weighted mean difference and 95% confidence intervals for the impact of green tea catechins on plasma C-reactive protein concentrations in trials with supplementation durations of < 8 weeks (left) and ≥ 8 weeks (right).

Figure 5. Forest plot detailing weighted mean difference and 95% confidence intervals for the impact of green tea catechins on plasma C-reactive protein concentrations in trials with supplemental doses of green tea catechins < 400 mg/day (left) and ≥ 400 mg/day (right).

Figure 6. Forest plot detailing weighted mean difference and 95% confidence intervals for the impact of green tea catechins on plasma C-reactive protein concentrations in trials with healthy subjects (left) and subjects with cardiometabolic diseases (right).

Figure 7. Meta-regression plots of the association of mean changes in plasma C-reactive protein concentrations with duration of green tea supplementation (left) and dose of catechins (right). The size of each circle is inversely proportional to the variance of change

Figure 8. Funnel plot detailing publication bias in the studies selected for analysis. Trim and fill method was used to impute for potentially missing studies. Open circles represent observed published studies; closed circles represent imputed unpublished studies.

Figure 9. Risk of bias assessment of studies included in the meta-analysis using the Cochrane assessment tool
REFERENCES


Table 1. Demographic characteristics of the included studies

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<td>Randomized placebo-controlled, double-blind parallel-group study</td>
<td>Randomized single-blind, placebo-controlled parallel-group study</td>
<td>Double-blind placebo-controlled crossover design</td>
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<td>Smoking healthy volunteers recruited by newspaper advertisements</td>
<td>Young male endurance-trained cyclists volunteers</td>
<td>Patients who had a fasting blood glucose level of ≥110mg/dL or a nonfasting blood glucose level ≥140mg/dL.</td>
<td>Volunteers who had a fasting blood glucose level of &gt;46.1 mmol/l or a nonfasting blood glucose level of &gt;47.8 mmol/l in a recent health checkup.</td>
<td>Healthy male smokers</td>
<td>Persons who participated in a weight loss program aged between 20 and 70 y</td>
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<td>Freeze-dried extracts of green tea bags/capsules of green tea polyphenol isolate</td>
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* p < 0.05, ** p < 0.01, *p < 0.001
Values are expressed as mean ± SD or *mean ± SEM. ABBREVIATIONS: BMI: body mass index; NS: not stated; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; SBP: systolic blood pressure; DBP: diastolic blood pressure; hs-CRP: high-sensitivity C-reactive protein; CAD: coronary artery disease; CCS: Canadian Cardiovascular Society; CV: cardio-vascular; BMI: body mass index; HOMA-IR: homeostasis model assessment-estimated insulin resistance; # triacylglycerol (mg/dl); a denotes green tea group; b denotes green tea extract group; c denotes black tea group; d denotes green tea group; e denotes green tea polyphenol isolate; f denotes medium-dose group; g denotes high-dose group.
Published studies identified through PUBMED and SCOPUS search (n=180)

Records screened (n=45) → Records excluded (n=33)

Full text articles assessed for eligibility (n=12) → Articles excluded (n=4)

Studies included in the systematic review and meta-analysis (n=8)
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<th>Variance</th>
<th>Lower limit</th>
<th>Upper limit</th>
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Favours green bee calathine
Favours control

Difference in means and 95% CI
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**Diagram:**
- Study A: Mean change 0.1, SE 0.05, p = 0.05
- Study B: Mean change 0.1, SE 0.06, p = 0.06
- Study C: Mean change 0.1, SE 0.07, p = 0.07
• Some studies suggest that green tea decreases inflammatory process in CV diseases.
• We aimed to evaluate the impact of green tea supplementation on CRP concentrations.
• We did not indicate a significant effect of green tea on plasma CRP levels.
• These have been confirmed irrespectively on study duration and dose of green tea.
• Further, well-designed trials are necessary to validate these results.