



Review

Effect of green tea on plasma leptin and ghrelin levels: A systematic review and meta-analysis of randomized controlled clinical trials



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ABSTRACT

Objective: The purpose of this study was to conduct a meta-analysis of randomized controlled trials (RCTs) to assess the effect of green tea on serum leptin and ghrelin concentrations.

Methods: We searched PubMed, ISI Web of Science, Scopus, and Google scholar databases up to December 2016. The searches included RCTs conducted in human adults, and studies on the effect of green tea and green tea extract on serum leptin and ghrelin concentrations as outcome variables. Weighted mean differences (WMDs) and standard errors (SEs) of changes in serum ghrelin and leptin levels were calculated. The random effects model was used to derive the summary mean estimates with their corresponding SEs.

Results: Eleven RCTs were eligible to be included in the systematic review and the meta-analysis. Our analysis indicated that green tea did not significantly affect leptin and ghrelin concentrations in comparison to placebo (WMD = 1.28 ng/mL, 95% confidence interval: −0.49 to 3.05; $P = 0.156$, and WMD = 21.49 pg/mL, 95% confidence interval: −40.86 to 83.84; $P = 0.499$, respectively). However, green tea was associated with an increase in leptin concentration in studies that lasted for more than 12 wk and an increase in ghrelin in women and non-Asians.

Conclusions: Green tea or green tea extract might not be able to change circulatory leptin and ghrelin levels, especially with short-term interventions. More RCTs with longer duration of treatment and higher doses are necessary to assess green tea's effect on fat mass and obesity hormones.

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Introduction

Obesity is the most common health problem worldwide. More than 50% of Americans are overweight [1–3]. Obesity increases the risk of many chronic diseases such as diabetes mellitus, cancer, osteoarthritis, cardiovascular disease, and hyperlipidemia [4–7]. Increased energy intake or decreased energy expenditure is the main cause for the development of obesity; therefore, reducing energy intake and sustaining energy expenditure is a solution to lose weight [8].

Losing 5% to 10% of the initial body weight leads to beneficial health effects [9,10]. For most obese subjects, modest weight loss is a realistic goal, but long-term weight maintenance might be unsuccessful, because people do not easily change their diets and activities adequately [11,12]. Therefore, finding some helpful strategies for weight maintenance is relevant. Natural herbal supplements, like green tea, may be a useful agent in this regard [13,14].

Green tea (GT) has the most significant effects on chronic diseases such as cardiovascular disease [15] because it contains antioxidants such as catechins [16]. Several studies have indicated that drinking tea, especially GT, can protect against chronic diseases like obesity [17]. GT may reduce adiposity through several mechanisms: 1) by inhibiting catechol-O-methyl transferase enzyme (COMT) and, consequently, increasing thermogenesis and fat oxidation [13]; 2) by reducing adipocyte

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differentiation and proliferation during lipogenesis [14]; and 3) by changing obesity-related hormones such as leptin and ghrelin. Leptin is produced by brown adipose tissue, skeletal muscle, ovaries, pituitary glands placenta, stomach, bone marrow, liver, and mammary epithelial cells, but is primarily secreted by the adipocytes in white adipose tissue [18]. Leptin helps to regulate energy balance by inhibiting hunger. In obesity, sensitivity to leptin decreases, resulting in an inability to detect satiety; however, recent evidence has indicated that in obese animals, leptin can increase lipolysis by promoting phosphorylation of the enzyme hormone-sensitive lipase (HSL) [19]. Furthermore, leptin can have an affect on the circulatory system, lung surfactant activity, fertility, the brain, and bones [20]. Ghrelin is another novel hormone secreted mainly by the stomach, and regulates energy metabolism, feeding behavior, and gastrointestinal function [21,22]. Ghrelin stimulates appetite, increases food intake, and promotes lipogenesis. In humans, ghrelin can increase food intake by circulating in the bloodstream at the hypothalamus [22]. Some randomized clinical trials (RCTs) have assessed the effect of GT or green tea extract (GTE) on leptin and ghrelin levels; however, the results are inconsistent. In one study, GTE intake for 16 wk increased ghrelin concentration, but leptin concentration did not change significantly [23]. In another study, 12 wk of GTE intake decreased leptin concentration significantly [8], but Westerterp-Plantenga et al. [24] reported that GTE for 48 wk did not change leptin and ghrelin concentrations.

According to our research results, no systematic review or meta-analysis has tried to assess the effect of GT consumption on ghrelin and leptin concentrations. Because the data published on such an association are conflicting, we attempted a systematic review to summarize the results from RCTs conducted on human adults. The purpose of our review was to determine whether GT or GTE protects against obesity in humans by changing obesity hormones and, if possible, to perform a meta-analysis to quantify the effects.

Materials and methods

Systematic searches using PubMed, EMBASE, Scopus, and Google scholar were conducted for the period up to October 2016 using the following key words: "green tea," "green tea extract," "green tea extract AR25," "catechin," "catechins," "EGCG," "Camellia sinensis," "tea polyphenols," "Catechinic Acid," "Acid, Catechinic," "sinenses, Camellia," "Thea sinensis," "sinenses, Thea," "tea polyphenols," "Adipokines," "leptin," "adipocytokines," and "ghrelin." For searching exact terms and group search terms, quotation marks and parentheses were used, respectively. Asterisks were used to search all words deriving from one key word, and Boolean operators (AND and OR) were used for designing search strategies. To find additional relevant articles, reference lists of related studies were also checked. Our objective was to determine the potential effect of taking GT or GTE on leptin and ghrelin. We did not have any restrictions on language, publication time, and study design. To find relevant studies, M.H. and F.N. screened titles and abstracts; M.H., F.N., and F.H. solved discrepancies through group discussions.

Inclusion criteria

The included studies met the following criteria: 1) original article, 2) clinical trial, 3) adult subjects, 4) use of GT or GTE as an intervention, and 5) assessment of serum ghrelin and leptin levels as outcome measures.

Exclusion criteria

Articles with at least one of the following characteristics were excluded: 1) unclear data, 2) use of other food or food supplements with GT or GTE, and 3) studies of short duration (<1 wk).

Quality assessment

The quality of articles was scored on a 5-point Jadad scale [25]. Clinical trials were evaluated on randomization, double blinding, and reporting of withdrawals and dropouts with numbers and reasons. With a maximum possible score of 5,

articles with scores >2 were defined as high quality, and those with scores ≤2 were defined as low quality.

Data extraction

We extracted the names of the lead authors, sample size, study design (randomized parallel, crossover, or non-randomized intervention trial), participants' sex, age, body mass index (BMI), numbers of subjects in intervention and control groups, study duration, and means ± SD of ghrelin and leptin for intervention and control groups before and after the intervention period. One study reported the mean with standard error (SE), and we calculated the SD values by multiplying the SE by the square root of the sample size in each group [26]. Two studies expressed the results as means with 95% confidence intervals [27,28].

Statistical analysis

We performed this meta-analysis on the mean difference of changes and their corresponding SE values for leptin and ghrelin. To calculate the summary mean estimates and SE, we used the DerSimonian and Laird random effects model, which takes in account between-study variations [29]. To examine the heterogeneity between studies, we used Cochran's Q test and I² [30]. Subgroup analysis was done to identify the source of heterogeneity. The heterogeneity of subgroups was evaluated by using the fixed effect model. Sensitivity analysis was performed to explore the extent to which inferences might be attributed to a particular study or a group of publications. Publication bias was assessed by visual inspection of funnel plots [31]. Egger's regression asymmetry test and Begg's adjusted rank correlation test were used to carry out formal statistical examination of funnel plot asymmetry [30]. We performed all statistical analyses using Stata, Version 11.2 (Stata, College Station, TX, USA). P values <0.05 were considered to indicate significance.

Results

Our search retrieved 607 articles, and 366 were duplicate articles. After removing the duplicate articles, there remained 241 articles, 19 of which were selected after screening titles and abstracts [8,23,24,26–28,32–44] (Fig. 1). After reading the full texts, we excluded 8 articles because they did not meet the inclusion criteria: Six articles used other supplements or diets besides GT and GTE [38,39,41–44], and 2 articles had unclear data [37,40]. Eleven articles were eligible to be included in the systematic review and meta-analysis. Eleven articles assessed the effect of GT on leptin, and 7 articles assessed the effect of GT on ghrelin (Table 1). The studies included 927 adults ages

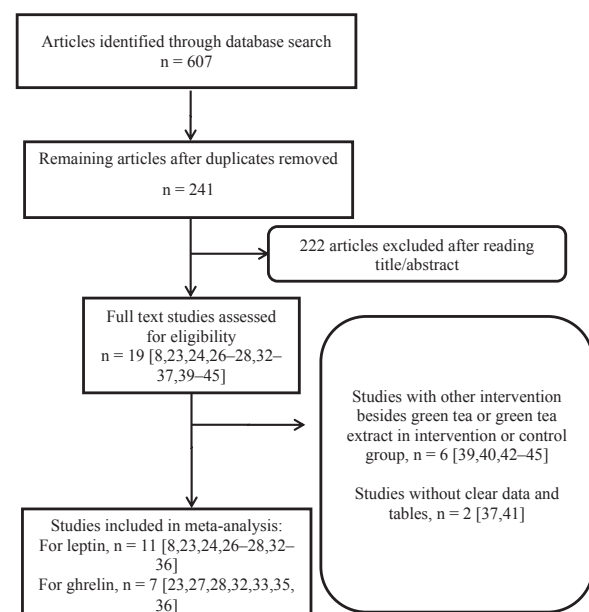


Fig. 1. Study selection process.

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