Review

The effects of garlic supplementation on weight loss: A systematic review and meta-analysis of randomized controlled trials

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Abstract: Obesity is related to increase in the incidence of morbidity and mortality. Studies have suggested anti-obesity properties of garlic; however, results are inconsistent. This systematic review and meta-analysis is done to summarize the data obtained from available randomized clinical trials on the effect of garlic supplementation on body weight, Body Mass Index (BMI), and Waist Circumference (WC). The online databases of Scopus, PubMed, Google Scholar and Cochrane library were searched until March 2018 for related publications using relevant keywords. Effect sizes of eligible studies were pooled using random-effects models. Cochran's Q-test and I^2 index were used for assessing heterogeneity. We found 1241 records in our initial search, of which 13 randomized clinical trials (RCTs) with 15 treatment arms were included. Pooled analysis showed that garlic administration might significantly decrease WC (Weighed Mean Difference (WMD): −1.10 cm, 95% CI: −2.13, −0.07, P = 0.03, I^2 = 0%). However, garlic intervention had no significant effect on body weight (WMD): −0.17 kg, 95% CI: −0.75 to 0.39, P = 0.54, I^2 = 0%) and BMI (WMD: −0.17 kg/m^2, 95% CI: −0.52, 0.16, P = 0.30, I^2 = 44.5%) as compared to controls. From Subgroup analysis, it was ascertained that the effect of garlic supplementation on BMI was significant in trials with duration < 12 weeks (WMD: −0.58 kg/m^2, 95% CI: −1.08, −0.08, I^2 = 19.8%, P = 0.02) compared to those with higher duration (>12 weeks). The current meta-analysis results suggest that garlic supplementation seems to reduce waist circumference unlike body weight and BMI.

Keywords: Garlic, BMI, Weight, Obesity, Meta-analysis

Introduction

Obesity is a medical condition in which excess body fat has accumulated to the extent that it may have a negative effect on health [1, 2]. According to the World Health Organization (WHO) in 2016, more than 1.9 billion adults (≥18 years) were overweight that over 650 million of them were obese [3]. Obesity is considered as a basic risk factor for various chronic physical and mental conditions (such as cardiovascular diseases, diabetes, musculoskeletal disorders, cancer) [4, 5] which have been linked with increased hospital admissions and subsequent use of other medical services [6, 7]. Therefore, weight management approaches are imperative for both the health-care system and prevention of diseases [8, 9].

In recent years, due to the failure of traditional therapy (diet and exercise) in weight reduction, use of alternative treatments such as weight loss supplements is considered [10–12]. Garlic (*Allium sativum*) is an herbal medicine of onion vegetable category which contains about 65% water, 2% protein, 1.5% fat and 28% carbohydrate [13, 14]. Garlic contains high levels of organosulfur compounds and flavonoids which act according to their biological functions [15]. Garlic with its anti-bacterial regulatory properties seems to modify the immune system and improve cellular immune function in the defense against intracellular pathogens [16, 17]. In addition, most clinical trials have reported that garlic is safe and well-tolerated [18]. Apart from these roles, garlic has a positive effect on lipid profile, diabetes, and body weight and seems to reduce cardiovascular risks [19, 20].

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Several proposed mechanisms may determine the effect of garlic on obesity including decrease in fatty acid synthesis [21, 22], decrease in intestinal triglyceride absorption [23], increase in the oxygen consumption [24], inhibiting human preadipocyte differentiation and lipid accumulation [25], increase in apoptosis in 3T3-L1 adipocytes [26]. Meanwhile, studies on anti-obesity properties of garlic are controversial and inconsistent. Several clinical trials have suggested that garlic exerts beneficial effects on the indicators of body composition [27, 28]. On the contrary, others reported no significant effect of garlic administration on anthropometric measures [29, 30]. Despite the numerous studies performed on the effect of garlic intake on body composition, no prior study hitherto has summarized the findings in this regard. Thus, the current study was designed as a comprehensive systematic review and meta-analysis of published randomized controlled trials (RCTs) to assess the effect of garlic supplementation on body weight, body mass index (BMI), and waist circumference (WC) in adults.

Material and Methods

This meta-analysis is performed according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [31].

Search strategy

Two reviewers searched Scopus, PubMed, Google Scholar and Cochrane library to identify relevant studies up to March 2018, by using the keywords selected from Medical Subject Headings (MeSH) and other related keywords including: ("garlic" OR "allyl sulfide" OR "vinyl dithiin" OR "S –allylcysteine" OR "diallyl sulphide" OR "allyl mercaptan" OR "allixin" OR "organosulfur" OR "alliin" OR "allicin" OR "Allium sativum" OR "garlicin" OR "garlic oil" OR "garlic extract" OR "garlic oil macerates" OR "garlic cloves" OR "garlic powder" OR "aged garlic extract" OR "diallyl disulfide" OR "diallyl trisulfide" OR "triallyl trisulfide" OR "S-allylmercaptocysteine") AND ("Obesity" OR "Abdominal obesity" OR "Intra-abdominal fat" OR "Abdominal Fat" OR "body weight" OR "body mass index" OR "BMI" OR "waist" OR "WC" OR "WHR" OR "WHtR" OR "anthropometry"* OR "fatness" OR "visceral" OR "central obesity" OR "viscera" OR "lean body mass" OR "body fat" OR "fat mass" OR "metabolic syndrome" OR "body composition"* OR "Obesity/complications" OR "Waist Circumference" OR "Waist-Height Ratio" OR "Waist-Hip Ratio" OR "percentage fat mass" OR "FM" OR "%FM" OR "visceral adipose tissue" OR "overweight" OR "adiposity" OR "Body Weight Changes" OR "Body Weight Maintenance"). The literature search was performed without language or calendar date restrictions. Meantime, the reference lists of eligible articles, related review articles and meta-analyses were checked using a manual approach for finding additional relevant articles.

Inclusion criteria

Studies were eligible for inclusion in this systematic review and meta-analysis if :(1) were randomized controlled trials (RCTs) with either parallel or crossover design; (2) subjects were human with a mean age of $\geq$ 18 years old and not pregnant women; (3) reported the effect of garlic preparations on anthropometric indices (weight, BMI, WC); (4) had a control group; (7) offered sufficient information on anthropometric indices at baseline and at the end of intervention or the net change values data in each group; (8) reported mean and standard deviation (SD) or available data (standard errors) to calculate SD; (9) written in English language. Two reviewers (MDM and JR) independently checked inclusion and exclusion criteria by reading the titles, abstracts and if necessary, the full text of the articles and disagreement was solved by discussion with a third reviewer (SMM).

Exclusion criteria

Other types of human studies (cross-sectional, cohort studies), animal and In vitro studies, grey literatures (book chapters, abstracts in conferences, interviews, comments, opinion pieces, methodological papers, editorials, letters), narrative reviews, studies which were performed on pregnant women or terminally ill patients, studies which were not randomized clinical trials and lacked sufficient information on baseline or follow-up or the net change values data of anthropometric indices, studies with concomitant intervention in the intervention group, studies about garlic which did not report anthropometric indices, studies without a control group and in a language other than English were not included.

Data extraction

A data extraction form was developed and two reviewers extracted the outcomes of interest from the selected studies independently. Eligible studies were reviewed and the following data were extracted: (1) first author's name; (2) year of publication; (3) study location; (4) study design; (5) health status; (6) number of participants in the garlic and control groups; (7) age (mean, range), gender and number of person in each sex; (8) baseline, final and change values of anthropometric indices; (9) type of garlic and placebo; (11) dose of garlic; (12) jaded score for quality assessment and (12) adjustment or matching covariates.

Quality assessment

Jadad scoring system was used to assess the quality of the included studies [32]. The Jadad scale contains questions which describe randomization, blinding and withdrawal in intervention and placebo group. In this scoring system, each study is assigned zero to five points. Studies with a score of < 2 were regarded low-quality studies and high-quality studies received a score of > 3 [33].

Data synthesis and statistical analysis

Mean change and its corresponding standard deviation (SD) in anthropometric indices within the garlic and control groups were used to calculate the unstandardized difference in means (MD) as effect size for meta-analysis. If the studies did not report net changes, they were calculated as follows: measure at end of follow-up – measure at baseline. Standard deviations (SDs) of the mean change were estimated using the following formula: SD change = square root [(SD baseline)^2 + (SD final)^2 – (2R $\times$ SD baseline $\times$ SD final)]. The correlation coefficient of the formula was determined using the data from included studies which reported baseline, final values and changes from baseline of body weight and BMI. Our estimated value of 0.90 indicated that the correlation between baseline and final values of body weight and BMI was very high. As for the studies which only reported standard error of the mean (SEM), standard deviation (SD) was calculated using the following formula: SD = SEM $\times$ sqrt (n), where n is the number of subjects. Summary mean estimates with their corresponding SDs were pooled using random effects model. Between-studies heterogeneity was examined using Cochrane's Q test (significance point at $P < 0.1$) and I^2 statistic. Subgroup analyses were performed to check for specific source of heterogeneity. Between studies, heterogeneity was evaluated using fixed-effect model. To determine the influence of each study on overall effect size, a sensitivity analysis was performed. Studies were removed one by one and the analysis was repeated [34]. Publication bias was assessed visually by funnel plots and statistically with Egger's regression test. All statistical analyses were performed using STATA software version 14 (STATA Corp, College Station, Texas). $P < 0.05$ was considered as statistically significant.

Results

Study selection

Our study selection process is presented in Figure 1.

In primary search, we detected 1241 records. A total of 248 duplicates were identified and removed. After screening based on title and abstract, 60 articles were retained for further evaluation. After full-text review, 47 articles were excluded. The reasons for exclusion were: Not English language studies (n = 3), observational studies (n = 1), studies which had no control group (n = 3), studies on pregnant women (n = 1), studies reporting not relevant outcome (n = 28), multiple treatment (n = 10), studies on terminal ill patients (n = 1). Finally, thirteen studies with 15 appropriate treatment arms were included in this meta-analysis.

Study characteristics

The general characteristics of the included studies are outlined in Table 1.

These studies are published in English between 1993 and 2017, of which three had a cross-over design [29, 35, 36] and ten had parallel design [18, 27, 28, 30, 37–42]. The follow-up period ranged from 3 to 15 weeks. All of the included studies were done on both genders except two [41, 42]. 4 studies were performed in the US [18, 30, 37, 38], 5 in Iran [27, 28, 35, 40, 42] and remaining studies were conducted in Korea [41], India [39], UK [29] and Colombia [36]. In total, 347 participants were allocated to garlic supplementation group and 333 to control group in the selected studies. Participants were in the age range of 18 to 75 years. All papers assessed the effects of garlic alone with the exception of the studies done by Kumar et al. [39] and Seo et al. [41]. These studies also recommended metformin and exercise in conjunction with garlic to both intervention and placebo groups. Included papers in this meta-analysis are performed on different populations including healthy persons [18, 30, 35, 41], patients with diabetes mellitus [29, 39], metabolic syndrome [36, 42], coronary artery disease (CAD) [40], hyperlipidemia [27, 38], hypercholesterolemia [37] and non-alcoholic fatty liver disease [28]. Daily recommended dosage of garlic varied between 80 and 6000 mg. Four studies [29, 30, 36, 41] used aged garlic extract and nine administered garlic tablets [18, 27, 28, 30, 37–40, 42]. Most studies reported crude values for the effect size, while few of them (n = 3) presented adjusted effect sizes for confounding factors [27, 28, 36].

Based on the current systematic review, three studies reported a positive effect of garlic on BMI reduction [27, 41, 42]. In contrast, four studies found that considerable reduction in BMI cannot be achieved with garlic

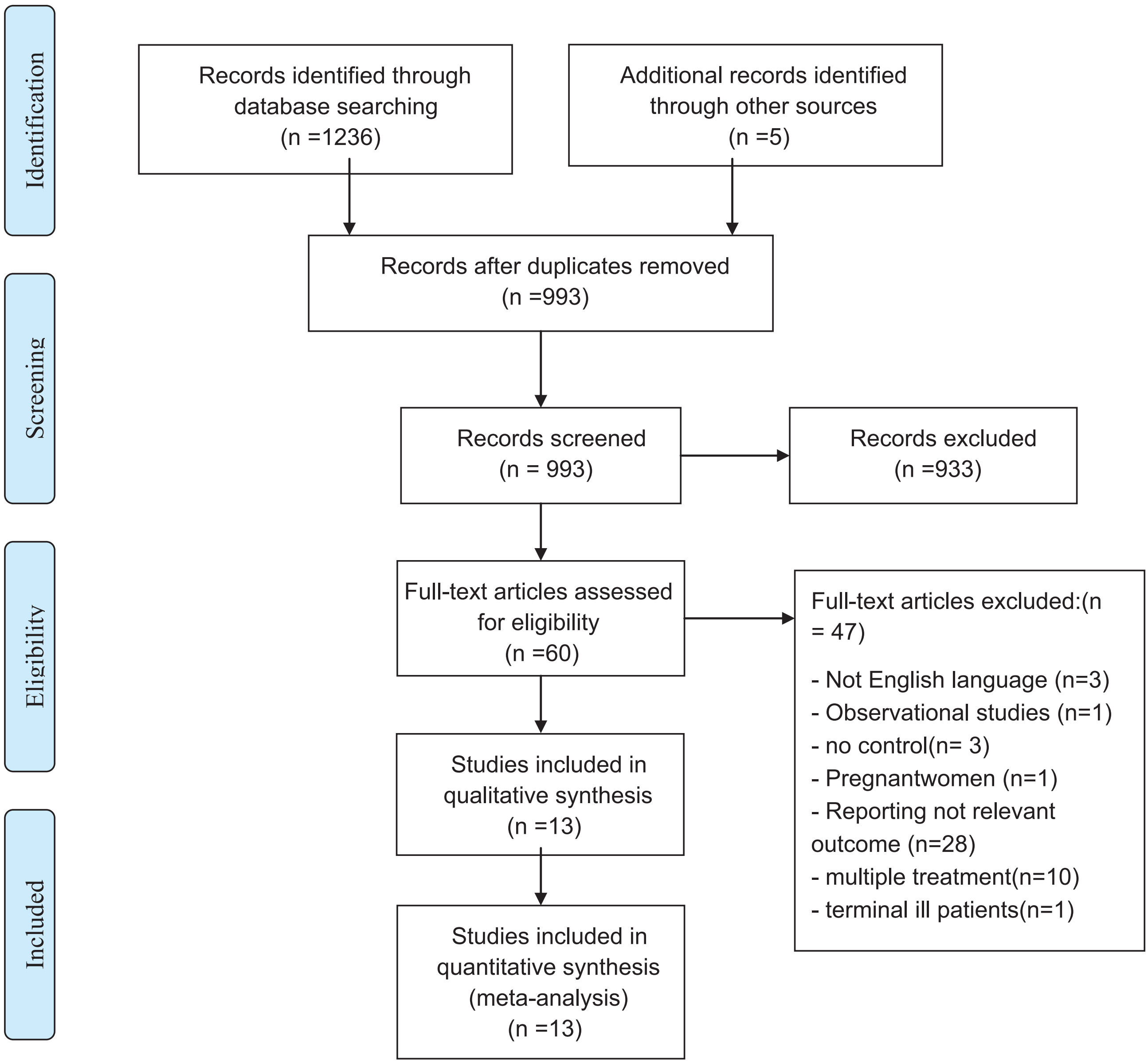

Figure 1. Flow diagram of study selection.

supplementation [30, 36, 38, 39]. Concerning weight changes, a significant reduction in body weight in the garlic group compared to the placebo group was reported in two studies [28, 41]; nevertheless, body weight changes in several trials were not significant [18, 29, 30, 35, 37, 40]. Few studies assessed the effect of garlic on WC [30, 36, 42]. Among them, one trial reported the favorable effect of garlic on WC reduction [42] and others found no significant effect on this variable [30, 36].

Study quality

The eligible papers had the quality score of 1 to 5 out of 5. Of 13 trials, 10 studies had high quality (score ≥ 3) [18, 27–30, 36–38, 40, 42]. All studies were randomized, and the randomization method is explained in seven studies [27, 28, 30, 36, 37, 40, 42]. Blindness was reported in eight studies [18, 28–30, 36–38, 42], and according to the presented information in two studies [30, 37], blinding was sufficient. Twelve studies reported the number of participants that dropped out with their corresponding reasons [18, 27–30, 36–42].

Meta-analysis results

Eight eligible studies with 10 treatment arms including a total of 407 participants examined the effect of garlic

Table 1. Demographic characteristics of included studies.

Code/Author (year)/Study location	Subjects and gender	Age range (y) and mean	Design	Intervention type: Intervention (name and composition)	Intervention type: Control (name and composition)	Duration (week)	Outcomes	Outcome: Intervention mean ± sd	Outcome: Control mean ± sd	Any other intervention (from)	Notes about subjects	Outcome(s) (yes/no)	Outcome kind
1. Xu (2017)/ US (23)	F: 33 M: 15 Both: 48 garlic: 24 (16/7) Cont: 24 (17/8)	25–65 yrs gar: 45.7 ± 12.3 Cont: 42.4 ± 10.7	Parallel	AGE (0.6 g/capsule) three capsules with food, twice a day	Placebo capsules	6	– BMI – weight – WC	BMI (kg/m^2): Before: 36.5 ± 6.6 After: 36.5 ± 6.8 Weight (kg): Before: 103.8 ± 21.5 After: 103.5 ± 21.9 WC (cm): Before: 113.2 ± 13.9 After: 114.1 ± 15.4	BMI (kg/m^2): Before: 36.3 ± 6.0 After: 36.2 ± 5.8 Weight (kg): Before 104.2 ± 17.5 After: 104.0 ± 17.6 WC (cm): Before: 114.0 ± 13.2 After: 114.5 ± 13.2	No	44 healthy adults with obesity	– BMI (no) – weight (no) – WC (no)	Secondary
2. Soleimani (2016)/Iran (21)	F: 59 M: 39 Both: 98 garlic: 47 Cont: 51	20–70 yrs gar: 46.4 ± 11.3 Cont: 44.1 ± 11.8	Parallel	Garlic powder tablets (0.4 g/tablet) twice a day	Placebo tablet (starch and microcrystalline cellulose)	15	– weight	Weight (kg): Before: 82.45 ± 14.2 After: 80.42 ± 14.02	Weight (kg): Before 80.24 ± 15.17 After: 79.27 ± 14.21	No	98 subjects with NAFLD	– weight (yes)	Primary
3. Atkin (2016)/ UK (22)	F: 7 M: 19 Both: 26 garlic: 26 Cont: 26	18–70 yrs gar: 49.8 Cont: 49.8	Cross over	AGE(kyolic) (0.3 g/capsules) 4 times a day	Placebo capsules	4	– weight	Weight (kg): Before: 98.2 ± 18.2 After: 98.7 ± 18.2	Weight (kg): Before: 98.7 ± 18.5 After: 98.8 ± 18.4	No	26 diabetic patients	– weight (no)	Secondary
4. Mahdavi-Roshan (2016)/ Iran (26)	F: 6 M: 6 Both: 12 garlic: 6 Cont: 6	25–55 yrs gar: 38.0 ± 1.86 Cont: 38.0 ± 1.86	Cross over	Garlic powder tablets (0.4 g/tablet) twice a day	Placebo tablets	3	– weight	Weight (kg): Before: 69.7 ± 9.55 After: 69.9 ± 9.3	Weight (kg): Before: 70 ± 9.3 After: 70 ± 9.06	No	12 healthy adults	– weight (no)	Secondary
5. Aslani (2016)/Iran (20)	F: 25 M: 30 Both: 55 garlic: 27 (13/14) Cont: 28 (12/16)	30–60 yrs Gar: 45. 3 ± 9.3 Cont: 39.3 ± 6.2	Parallel	Garlic powder(6 g/d) once a day	Placebo	8	– BMI	BMI (kg/m^2): Before: 28.1 ± 5.9 After: 27.4 ± 5.6	BMI (kg/m^2): Before: 27.2 ± 3.2 After: 27.5 ± 3.3	No	55 hyperlipidemic patients	– BMI (yes)	Primary

Continued

Table 1. *(Continued)*

Code/Author (year)/Study location	Subjects and gender	Age range (y) and mean	Design	Intervention type: Intervention (name and composition)	Intervention type: Control (name and composition)	Duration (week)	Outcomes	Outcome: Intervention mean ± sd	Outcome: Control mean ± sd	Any other intervention (from)	Notes about subjects	Outcome(s) (yes/no)	Outcome kind
6. Mahdavi-Roshan (2013)/ Iran (31)	F: 13 M: 43 Both: 56 garlic: 27 (7/20) Cont: 29 (6/23)	25–75 yrs Gar: 56.88 ± 8.67 Cont: 61.68 ± 9.9	Parallel	Garlic powder tablets (0.4 g/tablet) twice a day	Placebo (corn starch)	13	– weight	Weight (kg): Before: 74.7 ± 15.06 After: 74.3 ± 14.54	Weight (kg): Before: 69.7 ± 10.77 After: 69.9 ± 10.77	No	56 patients with CAD	– weight (no)	Secondary
7. Kumar (2013)/India (30)	F: M: Both: 60 garlic: 30 Cont: 30	40–75 yrs Gar: 52.8 ± 11.0 Cont: 53.8 ± 12.2	Parallel	Garlic capsules (250 mg/capsules) twice a day + metformin tablets (500 mg/ tablet) twice a day (BD) or three times a day (TDS)	Metformin tablets (500 mg/tablet) twice a day (BD) or three times a day (TDS) after meals	12	– BMI	BMI (kg/m^2): Before: 27.72 ± 1.74 After: 25.97 ± 10.7	BMI (kg/m^2): Before: 27.23 ± 2.77 After: 26.86 ± 12.69	Yes	60 patients having type 2 diabetes mellitus and obesity	– BMI (no)	Secondary
8. Gomez-Arbelaez (2013)/ Colombia (27)	F: M: Both: 43 garlic: 43 Cont: 43	≥18 yrs Gar: 44.75 ± 10.5 Cont: 37.34 ± 9.8	Cross over	AGE (kyolic) (0.6 g/capsules) twice a day	Placebo capsules	12	– BMI – WC	BMI (kg/m^2): Change: 0.01 ± 1.37 WC (cm): Change: −0.99 ± 3.08	BMI (kg/m^2): change: −0.11 ± 1.11 WC (cm): Change: 0.32 ± 3.27	No	43 subjects with metabolic syndrome	– BMI (no) – WC(no)	Secondary
9. Seo (2012)/ Korea (32)	F: 14 M: 0 Both: 14 garlic: 8 (8/0)	Gar: 51.8 ± 1.7 Cont: 54.4 ± 5.4 Cont: 6 (6/0)	Parallel	AGE packs (80 ml/pack) five times a week	Placebo packs	12	– BMI – weight	BMI (kg/m^2): Before: 23.1 ± 3.1 After: 21.8 ± 2.9 Weight (kg): After: 55.3 ± 5.2	BMI (kg/m^2): Before: 25.5 ± 1.4 After: 24.9 ± 1.3 Weight (kg): Before: 58.3 ± 5.2 After: 59.8 ± 7.8	No	14 healthy post-menopausal women	– BMI (yes) – weight (yes) Before: 61.7 ± 7.5	Secondary

Continued

Table 1. *(Continued)*

Code/Author (year)/Study location	Subjects and gender	Age range (y) and mean	Design	Intervention type: Intervention (name and composition)	Intervention type: Control (name and composition)	Duration (week)	Outcomes	Outcome: Intervention mean ± sd	Outcome: Control mean ± sd	Any other intervention (from)	Notes about subjects	Outcome(s) (yes/no)	Outcome kind
10. Seo (2012)/ Korea (32)	F: 16 M: 0 Both: 16 garlic: 8 (8/0) Cont: 8 (8/0)	Gar + Ex: 56.2 ± 6.2 Cont + Ex: 54.8 ± 7.7	Parallel	AGE packs (80 ml/pack) five times a week + exercise three times per week	Placebo packs + exercise three times per week	12	– BMI – weight	BMI (kg/m^2): Before: 23.6 ± 1.7 After: 23.2 ± 1.5 Weight (kg): Before: 59.2 ± 5.9 After: 57.8 ± 6.1	BMI (kg/m^2): Before: 24.1 ± 2.5 After: 23.2 ± 2.4 Weight (kg): Before: 62.1 ± 8.6 After: 60.2 ± 8.1	Yes	16 healthy post-menopausal women	– BMI (yes) – weight (yes)	Secondary
11. Sharifi (2010)/Iran (33)	F: 40 M: 0 Both: 40 garlic: 20 (20/0) Cont: 20 (20/0)	> 18 yrs Gar: 50.5 ± 12.96 Cont: 47.9 ± 13.1	Parallel	Garlic powder tablets (0.3 g/tablet) two tablets three times a day	Placebo tablets	6	– BMI – WC	BMI (kg/m^2): Before: 29.6 ± 3.57 After: 29 ± 4.02 WC (cm): Before: 103.9 ± 8.94 After: 102 ± 8.94	BMI (kg/m^2): Before: 29.1 ± 4.02 After: 29 ± 3.57 WC (cm): Before: 103.3 ± 12.07 After: 103 ± 12.07	No	40 women with metabolic syndrome	– BMI (yes) – WC (yes)	Primary
12. Gardner (2001)/US (28)	F: 15 M: 19 Both: 34 garlic: 16 (6/10) Cont: 18 (9/9)	30–65 yrs Gar: 50.2 ± 8.3 Cont: 51.6 ± 8.1	Parallel	Garlic powder tablets (0.333 g/ tablet) three times a day	Placebo tablets	12	– weight	Weight (kg): Change: 0 ± 1.6	Weight (kg): Change: 0.8 ± 1.6	No	34 moderately hyperc-holesterolemic adults	– weight (no)	Secondary
13. Gardner (2001)/US (28)	F: 19 M: 16 Both: 35 garlic: 17 (10/7) Cont: 18 (9/9)	30–65 yrs Gar: 53.4 ± 8.9 Cont: 51.6 ± 8.1	Parallel	Garlic powder tablets (0.167 g/ tablet) three times a day	Placebo tablets	12	– weight	Weight (kg): Change: 0 ± 1.6	Weight (kg): Change: 0.4 ± 1.6	No	35 moderately hyperc-holesterolemic adults	– weight (no)	Secondary
14. Isaacshon (1998)/US (29)	F: 23 M: 27 Both: 50 garlic: 28 (16/12) Cont: 22 (7/15)	Gar: 58 ± 14 Cont: 57 ± 13	Parallel	Garlic powder tablets (Kwali) (0.3 g/ tablet) three times a day	Placebo tablets	12	– BMI	BMI (kg/m^2): Change: 0.03 ± 0.6	BMI (kg/m^2): Change: 0.08 ± 0.6	No	50 hyperlipidemic patients	– BMI (no)	Secondary
15. Jain (1993)/ US (17)	F: 23 M: 19 Both: 42 garlic: 20 (9/11) Cont: 22 (14/8)	Gar: 48 ± 15 Cont: 55 ± 9	Parallel	Garlic powder tablets (Kwali) (0.3 g/ tablet) three times a day	Placebo tablets	12	– weight	Weight (kg): Before: 79 ± 17 After: 79 ± 17	Weight (kg): Before: 77 ± 14 After: 77 ± 15	No	42 healthy adults	– weight (no)	Secondary

F: female; M: male; Cont: control; gar: garlic; AGE: aged garlic extract; BMI: body mass index; WC: waist circumference; NAFLD: nonalcoholic fatty liver disease; US: united states; UK: United Kingdom; CAD: coronary artery disease.

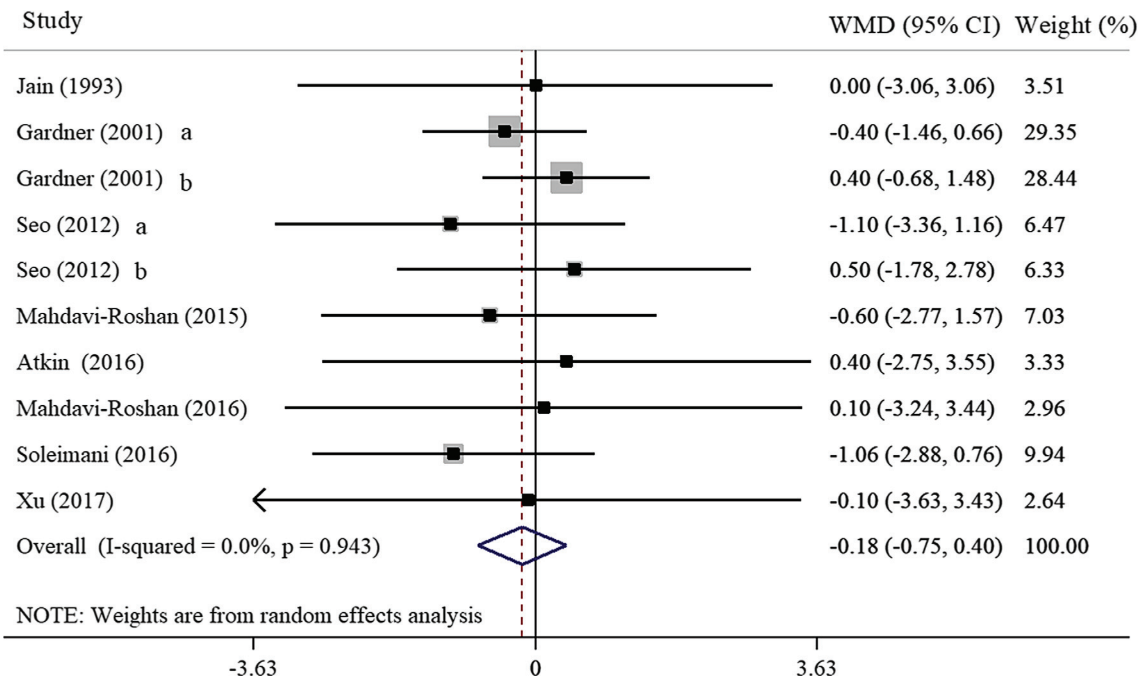

Figure 2. Forest plot of randomized controlled trials examining the effects of garlic on body weight.

consumption on body weight. Combining results from the random-effects model showed that garlic consumption had no significant effect on body weight (Weighted Mean Differences (WMD): −0.17 kg, 95% CI: −0.75, 0.39, P = 0.54) as compared to controls, with no significant between-study heterogeneity (I^2 = 0.0%, P = 0.94) (Figure 2).

None of our subgroup analyses showed a significant effect of garlic supplementation on body weight (Table 2).

Seven trials with 8 treatment arms including a total of 369 participants reported the effect of garlic consumption on BMI. Pooled results from the random-effects model indicated that garlic administration, as compared to placebo, was not associated with a significant reduction in BMI

Table 2. Results of subgroup analysis of included randomized controlled trials in meta-analysis of garlic supplementation and anthropometric measures.

	Dose (mg/d)		Duration (week)		Health status		Mean age (year)		Gender	
Variable	< 800	≥ 800	< 12	≥ 12	Healthy	Patient	< 50	≥ 50	Both	Female
Body weight										
No. of comparison	3	7	3	7	5	5	5	5	8	2
WMD (95% CI)	−0.37 (−1.25, 0.51)	−0.03 (−0.79, 0.72)	0.15 (−1.77, 2.07)	−0.20 (−0.81, 0.39)	−0.17 (−1.40, 1.04)	−0.17 (−0.82, 0.47)	−0.41 (−1.62, 0.80)	−0.11 (−0.76, 0.54)	−0.15 (−0.77, 0.45)	−0.30 (−1.91, 1.29)
p value	0.41	0.92	0.87	0.49	0.77	0.59	0.50	0.74	0.61	0.7
I^2 (%)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
p-heterogeneity	0.61	0.90	0.97	0.77	0.90	0.65	0.92	0.67	0.92	0.32
BMI										
No. of comparison	3	5	3	5	3	5	3	5	5	3
WMD (95% CI)	−0.03 (−0.52, 0.46)	−0.14 (−0.38, 0.10)	−0.58 (−1.08, −0.08)	−0.009 (−0.25, 0.23)	0.002 (−0.45, 0.45)	−0.15 (−0.40, 0.09)	−0.18 (−0.59, 0.22)	−0.09 (−0.35, 0.16)	−0.10 (−0.36, 0.15)	−0.15 (−0.57, 0.26)
p value	0.90	0.26	0.02	0.94	0.99	0.22	0.38	0.48	0.42	0.47
I^2 (%)	65.4	40.1	19.8	34.2	63.8	40.7	64.1	42.2	34.2	69.3
p-heterogeneity	0.05	0.15	0.28	0.19	0.06	0.15	0.06	0.14	0.19	0.03

BMI: body mass index, WMD: weight mean difference.

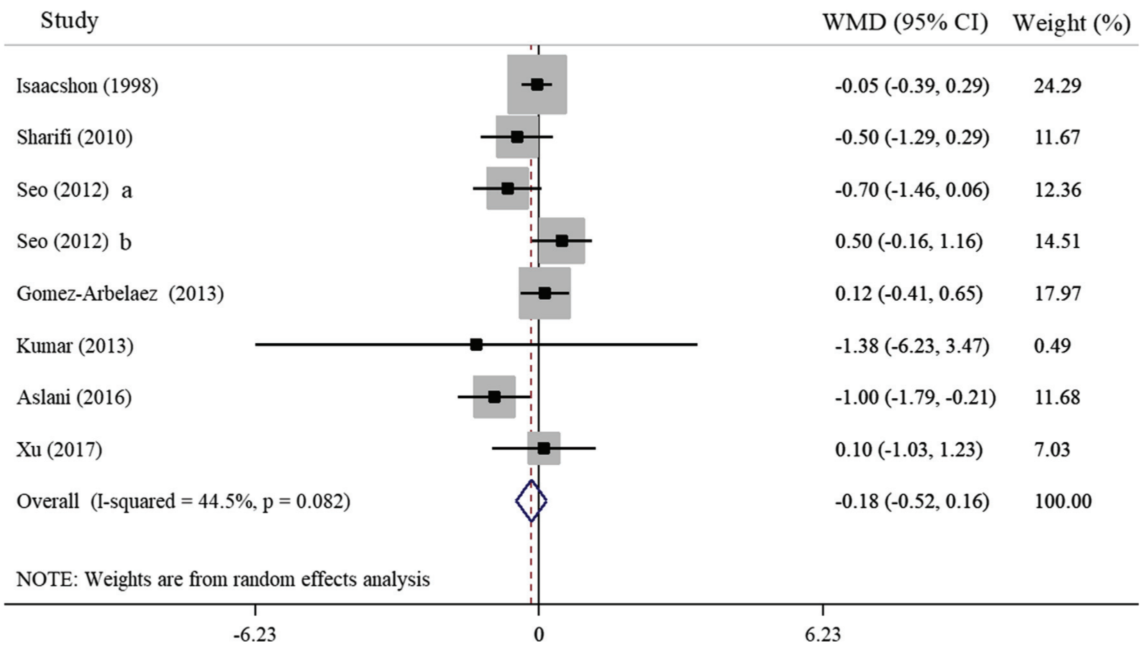

Figure 3. Forest plot of randomized controlled trials examining the effects of garlic on Body mass index (BMI).

(WMD: −0.17 kg/m^2, 95% CI: −0.52, 0.16, P = 0.30) (Figure 3), with a significant between-study heterogeneity (I^2 = 44.5%, P = 0.08).

Subgroup analysis on the basis of dose of intervention (I^2 = 40.1%, P = 0.150.65), duration of treatment (< 12 wk: I^2 = 19.8%, p = 0.28 & ≥ 12 wk: I^2 = 34.2%, p = 0.19), health status (I^2 = 40.7%, P = 0.15), participants' age (I^2 = 42.2%, P = 0.14), and participants gender (I^2 = 34.2%, P = 0.19) nullified the heterogeneity (Table 2). However, the effect of garlic supplementation on BMI was significant in trials with duration < 12 weeks (WMD: −0.58 kg/m^2, 95% CI: −1.08, −0.08, P = 0.02) versus those lasting ≥ 12weeks.

Three studies including a total of 174 subjects reported WC as an outcome measure. Pooling effect sizes from the random-effects model revealed that WC was significantly reduced after garlic consumption (WMD: −1.10 cm, 95% CI: −2.13, −0.07, P = 0.03) (Figure 4) in comparison to the control group, with no significant heterogeneity between the studies (I^2 = 0.0%, P = 0.44).

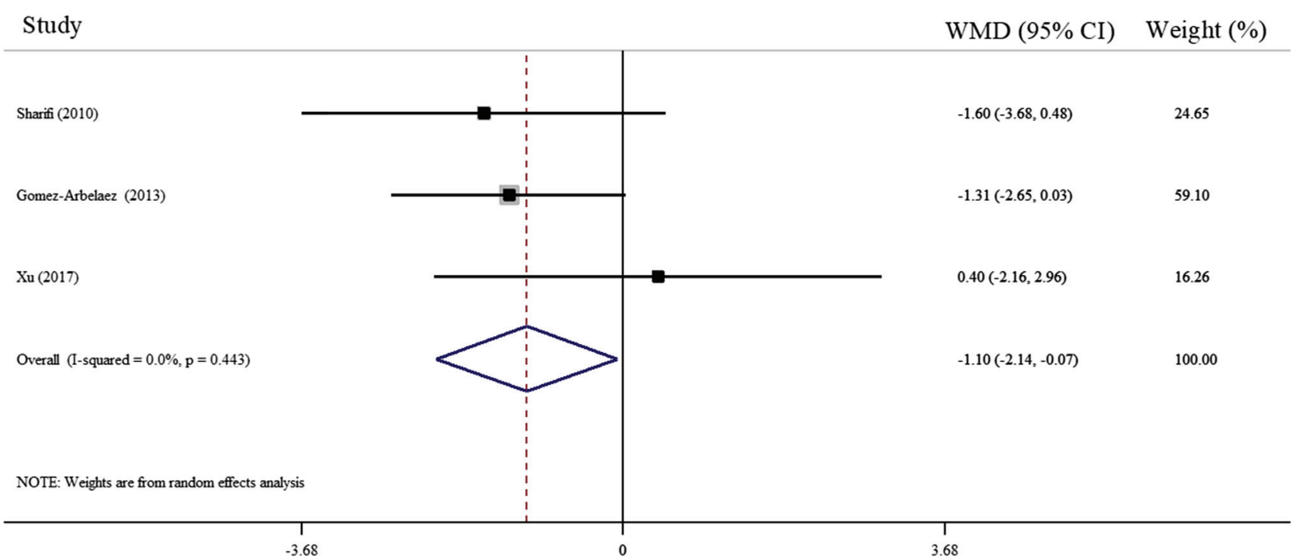

Figure 4. Forest plot of randomized controlled trials examining the effects of garlic on waist circumference (WC).

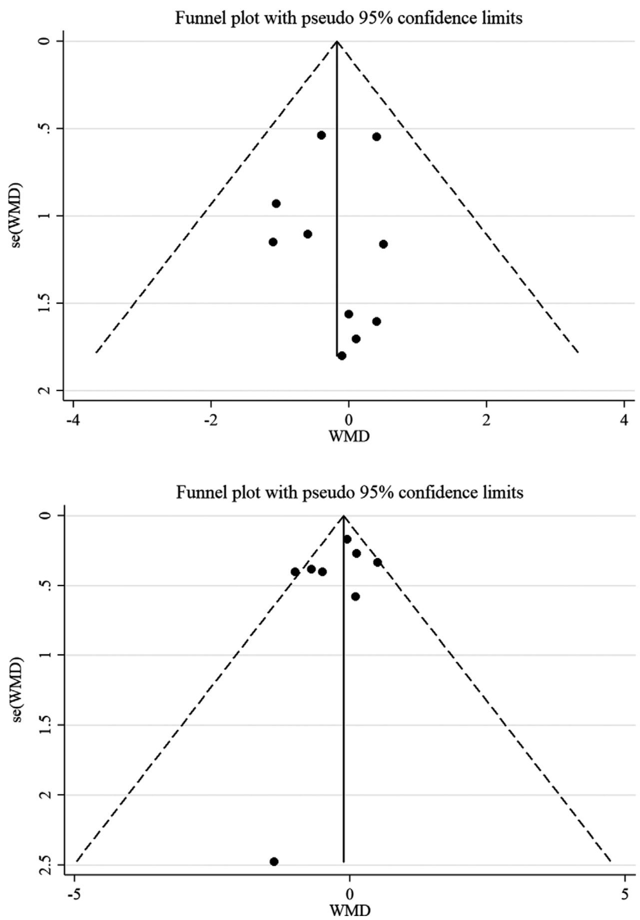

Figure 5. Funnel plot detailing publication bias in the studies reporting the effect of garlic on a) body weight and b) body mass index.

Sensitivity analysis

To identify the influence of each single study on the overall effect size, we omitted each trial from the analysis, step by step. We found no significant effect of any individual study on the overall effect sizes of body weight, BMI and waist circumference.

Publication bias

Visual inspection of the funnel plots of standard error versus effect size (WMD) for body weight and BMI did not indicate any evidence of asymmetry (Figure 5). These findings were approved by the use of Egger's regression tests for body weight (P = 0.79), BMI (P = 0.40), and WC (P = 0.55).

Discussion

In the present systematic review and meta-analysis, we summarized the available data from thirteen trials (with 15 treatment arms) which investigated the Effect of garlic consumption on anthropometric measures including body weight, body mass index, and waist circumstance. As the main result, participants ingesting garlic had lower Waist circumstance after the intervention than controls. But garlic consumption had no significant effect on BMI and body weight. However, subgroup analysis revealed that BMI was decreased when the duration of garlic consumption was less than 12 weeks compared to higher than 12 weeks.

In this meta-analysis of 3 RCT arms, we observed reductions in waist circumstances with garlic consumption. Waist circumstance is a better indicator of body fat mass and may herald chronic diseases [43, 44]. All in all, waist circumference among others is more affected by garlic and other studies confirm this finding. Eidi et al. showed that garlic consumption improves FBG, lipid profile, cholesterol and triglyceride levels [45]. Furthermore, other studies show that administration of fresh garlic decreases white adipose tissue cell size, LDL, and cholesterol and increases HDL. It also restores adiponectin and leptin to near normal levels [46–48].

Garlic contains at least 33 organosulfur compounds with their specific biological activities as well as anti-obesity properties [49, 50]. Thiacremonone is sulfur compound isolated from garlic that has an effect on adipocyte [49]. Thiacremonone activates AMP-activated protein kinase, which leads to a decreased expression of acetyl CoA carboxylase-1. acetyl CoA carboxylase-1 is an essential enzyme for regulating the cycle of fatty acid synthesis [21, 22]. Moreover, a study in 2013 showed that garlic tends to decrease intestinal triglyceride absorption resulting in an increased triglyceride level in stool [51]. Another mechanism by which garlic seems to have a role in controlling body fat may be due to its thermogenic properties and its related derivatives which increase the oxygen consumption [24]. 1,2-vinyl-dithiin (a garlic-derived organosulfur) suppresses gene expression of peroxisome proliferator-activated receptor gamma in differentiated preadipocyte which leads to inhibiting differentiation of human preadipocyte [25]. Yang et al. indicated that another garlic-derived organosulfur, ajoene, activates mitogen-activated protein kinases and fragmentation of DNA [26], which increases apoptosis in 3T3-L1 adipocytes.

No effect of garlic supplementation was found on body weight and BMI in this systematic review and meta-analysis. There was insignificant heterogeneity in the responses. The anti-obesity effects of garlic are mediated through the down-regulation of Acetyl-CoA carboxylase and fatty acid synthase as well as stimulation of carnitine palmitoyltransferase-1 [52]. Therefore, mostly the indicators associated with body fat are affected. Dae Yun Seo et al. showed that aged garlic extract did not have a significant effect on the body weight of rats, whereas a significant decrease in rats' visceral fat was noted [53]. In fact, more change in body fat indicators is observed than in indirect indicators except in short periods of intervention. Accordingly, subgroup analysis showed that BMI was decreased when the garlic intake period was less than 12 weeks. In line with our findings, another study showed that the effect of aged garlic extract on total cholesterol decreased by prolonging the duration of intervention [54]. It seems that studies with lower duration (< 12 weeks) were consuming garlic supplements in higher doses. In addition, previous studies have shown garlic supplementation safety in commonly used doses; such that, it has been classified as Generally Recognized as Safe (GRAS) by the United State food and drug administration [55].

The present systematic review has several advantages. The main strength of the current study is the low evidence of heterogeneity for body weight, BMI and WC values and the lack of publication bias. All of the studies which included in this review are randomized controlled clinical trials. Garlic supplements have a high safety profile and are generally well tolerated. Also, this is the first systematic review that examined the effect of garlic supplementation on weight loss in humans.

The present meta-analysis has several limitations that must be taken into account. It was not feasible to examine the effects of garlic on other anthropometric indices due to insufficient dataset. Studies about the effect of garlic supplementation on WC were low. So, more clinical trials are needed to confirm our findings about WC. Furthermore, in most included studies, anthropometric indices were secondary outcomes. So, they could not elucidate the details about the measurements that can affect the results. The chemical composition of the used garlic preparations was also different which might contribute to the discrepancies in weight loss effect. Also, the number of studies and included participants were small.

Conclusion

The current meta-analysis study pooled results from 15 RCTs regarding the effects of garlic consumption on body weight, BMI, and Waist circumstance; Our findings show that garlic consumption might reduce Waist circumstance. In contrast, it seems that garlic consumption is not a good strategy for decreasing body weight and BMI. However, more researches are needed to confirm the beneficial effects of garlic on body compositions.

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Conflict of interest statement
The authors declared no conflicts of interest.

Author contributions
SMM and MDM conceived the study. The literature search and screening data were done by SMM and JR. Data extraction and quality assessment were performed independently by HKV, MDM, and SMM. MDM, SMM, and JR analyzed and interpreted data and wrote the manuscript. SMM supervised the study. All authors read and approved the final manuscript.

Ethical approval
Since this study is a secondary study and will be based on the results of published studies does not contain any studies with human participants or animals performed by any of the authors.

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