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Meta-analyses

Cinnamon supplementation positively affects obesity: A systematic review and dose-response meta-analysis of randomized controlled trials

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SUMMARY

Background & aims: Data about the effects of cinnamon supplementation on obesity measures are conflicting. This systematic review and meta-analysis of randomized controlled trials (RCTs) was conducted to summarize the effects of cinnamon intake on body weight (BW), Body Mass Index (BMI), Waist Circumference (WC), and fat mass (FM) in adults.

Methods: Online electronic search engines including PubMed, SCOPUS, Cochrane Library, and Google Scholar were searched to find pertinent articles until September 2018. Data were pooled using the random-effects method and were expressed as weighted mean difference (WMD) and 95% confidence intervals (CI). The non-linear association was assessed using fractional polynomial modeling.

Results: Out of 679 records, 12 trials that enrolled 786 subjects were included. The pooled results showed that cinnamon administration significantly decreased BW (WMD: −1.02 kg, 95% CI: −1.66 to −0.38, P = 0.002), BMI (WMD: −0.51 kg/m^2, 95% CI: −0.74, −0.28, P < 0.001), WC (WMD: −2.40 cm, 95% CI: −4.48, −0.33, P = 0.02), and FM (WMD: −1.02%, 95% CI: −1.80, −0.24, P = 0.01). Greater effects on BW were observed in subjects aged <50 years old and those with a baseline BMI of ≥30 kg/m^2. The cinnamon administrations significantly reduced FM at the dosages of ≥2 g/d, when administered for ≥12 weeks. Cinnamon administration resulted in BW and WC reduction in non-linear fashion (P = 0.04).

Conclusions: Cinnamon supplementation significantly affects obesity measures. It could be recommended as a weight-reducing supplement in obesity management.

1. Introduction

Obesity has become a global major health problem [1]. World Health Organization (WHO) defined overweight and obesity as irregular or excessive fat accumulation that poses a threat to health. According to the last WHO report in 2016, 39% of the world's adult (≥18 years) population were overweight and 13% had obesity [2]. Obesity is associated with major chronic diseases like cancer, CVD

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and, diabetes. It has also a negative effect on individuals' self-esteem due to body shape issues which finally could lead to severe depression and mental health problems [3–7].

Since conventional therapies such as restricted diet and changing lifestyle has not come out so efficacious [8], people are desperate for a new, easier and more successful methods such as supplementation with herbal remedies to reach their ideal body shape. Cinnamon is a flavor additive used to improve odor, taste, and color of meals for a long time. It is derived from the inner bark several tree species from the genus Cinnamomum widely spread in the Mediterranean region, Sri Lanka and India [9,10]. The main components exist in cinnamon are cinnamic acid, cinnamaldehyde, eugenol, and coumarin; these components were reported to have antimicrobial properties [11,12]. Cinnamon is also high in antioxidants such as polyphenols and glutathione; therefore, it could be regarded as a powerful anti-inflammatory agent and may protect against cancer [13–17]. It could lower the risk of heart diseases through reducing LDL cholesterol and increasing HDL cholesterol [18–20]. The role of cinnamon in glucose metabolism has been attributed to its effect on insulin sensitivity and stimulating cellular glucose uptake [21–24]. However, studies on anti-obesity properties of cinnamon are controversial and inconsistent. Several clinical trials have suggested that cinnamon consumption has beneficial effects on indicators of body composition [25,26]. In contrast, other did not support such finding [27,28]. To the best of our knowledge, no study has ever summarized findings on this issue. Thus, the current study was designed as a comprehensive systematic review and dose-response meta-analysis of published randomized controlled trials (RCTs) to assess the effects of cinnamon supplementation on body weight (BW), body mass index (BMI), waist circumference (WC), and fat mass percentage (FM) in adults.

2. Material and methods

The present study adhered to the Preferred Reporting Items of Systematic Reviews and Meta-Analysis (PRISMA) statement guideline for performing and reporting [29].

2.1. Search strategy

We systematically searched electronic databases including PubMed/Medline, Scopus, the Cochrane Library, and Google Scholar to identify clinical trials that examined the effects of cinnamon supplements on obesity indices from inception to September 2018; without any language restriction. The merge of MESH and non-MESH terms were used as follows: ("Cinnamomum zeylanicum" [Mesh] OR Cinnamomum [Mesh] OR Cinnamon [Title/Abstract] OR Cinnamons [Title/Abstract] OR "Cinnamomum verum" [Title/Abstract] OR Cinnamomum [Title/Abstract]) AND ("Body Weight" [Mesh] OR "Body Weight Changes" [Mesh] OR "Body Mass Index" [Mesh] OR "Weight Loss" [Mesh] OR "Obesity" [Mesh] OR "Waist Circumference" [Mesh] OR "Obesity, Abdominal" [Mesh] OR "Adipose Tissue" [Mesh] OR "Abdominal Fat" [Mesh] OR "Body Weight" [Title/Abstract] OR "Body Weight Change" [Title/Abstract] OR "Quetelet Index" [Title/Abstract] OR "Body Mass Index" [Title/Abstract] OR BMI [Title/Abstract] OR "Weight Loss" [Title/Abstract] OR "Weight Reduction" [Title/Abstract] OR "Weight Losses" [Title/Abstract] OR Obesity [Title/Abstract] OR "Waist Circumference" [Title/Abstract] OR "Abdominal Obesity" [Title/Abstract] OR "Central Obesity" [Title/Abstract] OR "Visceral Obesity" [Title/Abstract] OR obes*[Title/Abstract] OR overweight [Title/Abstract] OR "adipose tissue" [Title/Abstract] OR "fat mass" [Title/Abstract] OR adiposity [Title/Abstract] OR "Body Fat" [Title/Abstract] OR "Abdominal Fat" [Title/Abstract]). Also, we manually checked all reference lists of eligible articles, related reviews, and meta-analyses in order to avoid missing any relevant studies. The PubMed's e-mail alert service was activated to find any new articles in this area that may be published after our search.

2.2. Eligibility criteria

The following criteria were considered to select eligible articles; (1) randomized placebo-controlled trials (either parallel or cross-over design) (2) studies that were performed on adult population (≥18 years old) (3) Those that provided sufficient data on baseline and final measures of BW or/and BMI or/and WC or/and FM in both cinnamon and control groups (4) Publications that did the intervention with any cinnamon species.

2.3. Excluded studies

Articles were excluded if they; (1) were performed on children, pregnant women or animals (2) were not placebo-controlled trials (3) did not provide sufficient information for the outcomes in cinnamon or control groups (4) investigated the effects of Cinnamon along with other ingredients. Unpublished documents and grey literature like conference papers, dissertations, and patents were excluded as well.

2.4. Data extraction

Two independent researchers (SMM and HKV) did the study selection whereas a chief investigator (AE) was also present to resolve any controversies. In case of lack of reporting data in the published paper, we contacted the corresponding author to acquire the necessary data. The following data were obtained from each study; first author's name, year of publication, study location, trial duration, type and dosage of cinnamon supplements, mean age and gender of participants, study design, health status of participants, number of subjects in each group, mean and SD of outcome measures at baseline, post-intervention and/or changes in outcome measures from baseline to the end-of-trial. If a study provided multiple data at different time points, only the latest were considered.

2.5. Quality assessment

We assessed the quality of included studies by using the Cochrane scoring system [30]. It consists of 7 criteria to assess the risk of bias which are as follows: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases. Three scores of yes, no, and unclear could be given to each aforementioned item, which are interpreted as high risk, low risk, and unknown risk respectively (Table 1).

2.6. Data synthesis and statistical analysis

Mean change and standard deviation (SD) of the relevant outcomes were used to estimate the overall effect size. Effect sizes for all variables were stated as weighted mean differences (WMDs) and 95% CI. The random-effects model by DerSimonian and Laird method [31] was used to estimate the overall effect sizes. When the within-group changes were not reported, we calculated it through subtracting baseline mean from the final mean value in each group separately. The SDs for mean differences was calculated using this formula: $SD_{change} = \text{square root } [(SD_{baseline})^2 + (SD_{final})^2 - (2 \times 0.9 \times SD_{baseline} \times SD_{final})]$ [32]. For trials that only reported standard error of the mean (SEM), SD was obtained using the

Table 1
Risk of bias assessment of the studies included in this meta-analysis.

Study. (year)	Random Sequence Generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective outcome reporting	Other sources of bias
Ziegenfuss (2006)	U	U	L	U	L	L	L
Blevins (2007)	U	L	L	L	L	L	L
Akilen (2010)	L	L	L	L	L	L	L
Haghighian (2011)	L	L	L	L	U	L	U
Wainstein (2011)	L	L	L	L	L	H	U
Vafa (2012)	U	U	L	L	L	L	L
Torabi (2016)	L	L	H	H	L	L	U
Gupta (2017)	U	L	L	L	L	L	L
Borzoei (2017)	L	L	L	L	L	L	L
Hajimonfarednejad (2018)	L	U	L	L	L	L	L
Nakhaei (2018)	L	L	H	H	L	L	L
Zare (2018)	U	L	L	L	L	L	L

U; unclear risk of bias, L; low risk of bias, H; high risk of bias.

following formula: SD = SEM × $\sqrt{n}$, where "n" is the number of subjects in each group.

Heterogeneity between studies was assessed by Cochrane's Q test (significance point at $P < 0.1$) and I^2 index. To identify potential sources of heterogeneity, a pre-defined subgroup analysis based on cinnamon dosage, duration of supplementation, mean age, sex, baseline BMI, and health status of subjects was performed. To determine the impact of each trial on the pooled effect size, a sensitivity analysis was performed. Studies were removed one by one and the analysis was repeated [33]. The non-linear potential effects of cinnamon dosage (g/day) and intervention duration (weeks) were assessed by fractional polynomial modeling [34]. Publication bias assessment was done using visual inspection of 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 statistically significant.

3. Results

3.1. Study selection

In our primary search, we detected a total of 679 records; 120 duplicates were identified and removed. After screening based on title and abstract, 42 articles were retained for further evaluation. In the next step, 30 papers were excluded based on the full-text review. These exclusions were due to the following reasons: Irrelevant (n = 4), studied adolescents (n = 1), administered cinnamon in combination with other components (n = 4), duplicate dataset (n = 3), those without a placebo group (n = 4), studies that did not provide sufficient data for outcomes (n = 14). Finally, 12 trials were included in this meta-analysis [25–28,35–42]. Of these, 10 trials reported the effect of cinnamon on BW [26–28,36–42], 11 articles on BMI [26–28,35–42], 4 articles on WC [27,28,36,38], and 5 trials on FM [25,26,37,38,41,42]. The process of study identification is presented in Fig. 1.

3.2. Characteristics of the included studies

The general characteristics of the included studies are outlined in Table 2. These studies were published between 2006 and 2018 and were carried out in the USA [25,35], United Kingdom [28], Israel [36], India [38], and Iran [26,27,37,39–42]. The follow-up period ranged from 8 to 16 weeks. Daily recommended dosage of cinnamon varied between 1 and 10 g in these studies. The design of all the included trials was parallel. All studies were done on both genders except for four trials that were done exclusively on women [27,39,41,42]. The sample size in the included trials ranged from 18 [41] to 138 [26]. In total, 786 subjects were enrolled in these studies, of which 395 individuals allocated to cinnamon supplementation group and 391 subjects to the control group. The mean age of the participants ranged from 21.8 to 63.9 years old and mean baseline BMI varied from 27.6 to 33.6 kg/m^2. Participants in these studies were patients with type 2 diabetes [26,28,35–37,40,41], pre-diabetic subjects [25], individuals with the metabolic syndrome [38], overweight women [42], and those with polycystic ovary syndrome [27,39].

Based on the present systematic review, 4 trials reported reduced body weight with cinnamon [26,37–39], while 6 studies failed to find any significant effect on BW [27,28,36,40–42]. In terms of changes in BMI, a significant reduction was observed in 4 trials [26,37–39], while 7 studies did not find such an effect [27,28,35,36,40–42]. Few studies assessed the effect of cinnamon on WC [27,28,36,38]. Based on their findings, one trial reported the favorable effect of cinnamon intake on WC reduction [38] and others found no significant effect [27,28,36]. All studies that examined the effect of cinnamon supplementation on FM found a significant reduction in FM [26,37–39] except for one publication [41].

3.3. Effect of cinnamon supplementation on BW

Totally, 10 eligible studies with 12 treatment arms, including a total of 707 participants, examined the effect of cinnamon intake on body weight. Combining their findings based on random-effects model, we found that body weight was significantly reduced after cinnamon supplementation (Weighted Mean Differences (WMD): −1.02 kg, 95% CI: −1.66 to −0.38, P = 0.002) compared to the control group, with a significant between-study heterogeneity (I^2 = 80.1%, P < 0.001) (Fig. 2A). Duration of intervention and participants' gender did not explain this heterogeneity. However, the mean age of study participants, and their health status and baseline BMI could explain the heterogeneity. Among subjects aged <50 years old, cinnamon administration resulted in a greater reduction in BW (WMD: −1.17 kg, 95% CI: −2.17, −0.17; P < 0.001) than older subjects (WMD: −0.85 kg, 95% CI: −1.81, 0.11; P = 0.09). Reduction in BW after cinnamon consumption was significant in subjects with baseline BMI ≥30 kg/m^2 (WMD: −1.93 kg, 95% CI: −3.76, −0.10; P = 0.03); however, it did not influence BW in overweight subjects (WMD: −0.68 kg, 95% CI: −1.39, 0.02; P = 0.06). Based on health status, the effect of cinnamon was significantly greater in women with PCOS (WMD: −0.51 kg, 95% CI: −0.83, −0.19; P = 0.002) than

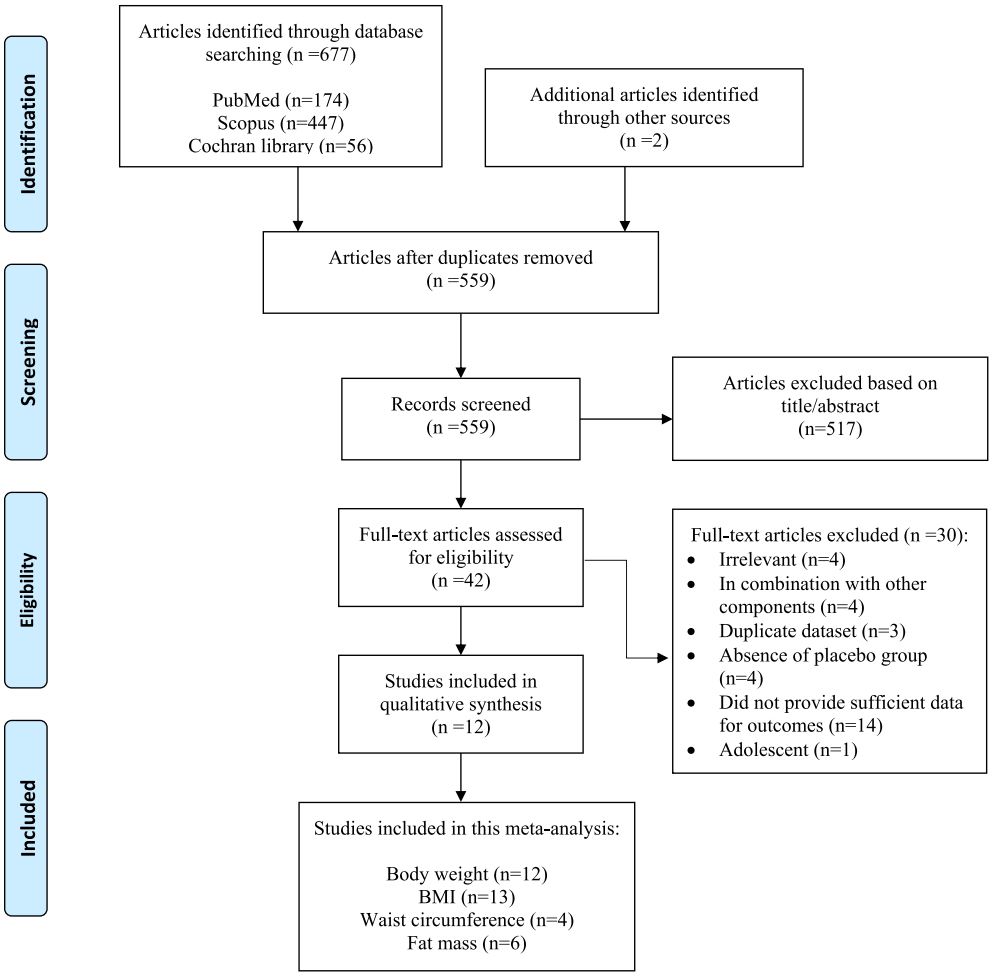

Fig. 1. Flow chart for study identification and selection into the meta-analysis.

type 2 diabetic patients (WMD: −0.85 kg, 95% CI: −1.81, 0.11; P = 0.09) and apparently healthy subjects (WMD: −1.52 kg, 95% CI: −3.23, 0.18; P = 0.08). All these findings were provided in Table 3.

3.4. Effect of cinnamon supplementation on BMI

Overall, 11 trials with 13 treatment arms, including a total of 764 subjects, reported the effect of cinnamon consumption on BMI. Pooled results from the random-effects model showed a significant effect of cinnamon intake on BMI; such that this intervention resulted in a significant reduction in BMI compared with placebo (WMD: −0.51 kg/m^2, 95% CI: −0.74, −0.28, P < 0.001). A significant between-study heterogeneity was reached (I^2 = 89.9%, P < 0.001) (Fig. 2B). In the subgroup analysis, we found that gender and health status of study participants explained this heterogeneity. Studies that were conducted on both sexes revealed a greater reduction in BMI (WMD: −0.55 kg/m^2, 95% CI: −0.86, −0.25; I^2: 92.6%, P < 0.001) than those performed on women (WMD: −0.43 kg/m^2, 95% CI: −0.92,0.05; I^2: 86.4%, P = 0.08). In addition, based on participants' health status, a significant reduction in BMI was found in trials that were performed on individuals with type 2 diabetes (WMD: −0.41 kg/m^2, 95% CI: −0.68, −0.14; I^2: 89.5%, P = 0.004) and apparently healthy individuals (WMD: −0.91 kg/m^2, 95% CI: −1.48, −0.33; I^2: 75.9%, P < 0.001) compared with those conducted on PCOS patients (WMD: −0.36 kg/m^2, 95% CI: −0.92, 0.19; I^2: 77.7%, P = 0.20).

3.5. Effect of cinnamon supplementation on WC

Pooling effect sizes from 4 publications including 292 participants, we found that cinnamon administration had a significant effect on WC compared with placebo (WMD: −2.40 cm, 95% CI: −4.48, −0.33, P = 0.02), with a considerable between-study heterogeneity (I^2 = 90.7%, P < 0.001) (Fig. 2C). Subgroup analysis based on cinnamon dosage (<2 vs. ≥2 g/d), baseline BMI status (<30 vs. ≥30 kg/m^2), and mean age of the subjects (<50 vs. ≥50 years) revealed that these factors did not explain the heterogeneity.

3.6. Effect of cinnamon supplementation on FM

The impact of cinnamon supplementation on FM was assessed in 5 trials with 6 treatment arms including 349 participants. The pooled estimates revealed that in subjects who consumed cinnamon supplements, FM significantly decreased compared to those who took placebo (WMD: −1.02%, 95% CI: −1.80, −0.24, P = 0.01). There was a significant between-study heterogeneity (I^2 = 86.3%, P < 0.001) (Fig. 2D). Subgroup analysis revealed that cinnamon dosage, duration of intervention, health status of participants, subjects' age and gender explained this heterogeneity. In these analyses, we found that the effect of cinnamon administration on

Table 2
General demographic characteristics of the included studies.

Code/First Author (year)	Location	Study Design	Population	Gender	Sample size Cinnamon/ Placebo	Duration (week)	Mean age (year)	Baseline BMI (kg/m^2)	Intervention		Outcome; (yes/no)
									Treatment group	Control group	
1. Ziegenfuss (2006)	USA	Randomized, double-blind, placebo-controlled parallel trial	Pre-diabetic subjects	Both	12/10	12	46.3	32.3	250 mg capsules Cinnulin PF, equivalent to 5 g ground cinnamon. 2 capsules per day (10 g of whole cinnamon powder)	Placebo	- FM/yes
2. Blevins (2007)	USA	Randomized, double-blind, placebo-controlled parallel trial	Type 2 diabetes	Both	29/28	13	63.9	32.5	1 g cinnamon capsules	Placebo (wheat flour)	- BMI/no
3. Akilen (2010)	United kingdom	Randomized, double-blind, placebo-controlled parallel trial	Type 2 diabetic patients	Both	30/28	12	54.9	33.3	2 g cinnamon capsules	Placebo	- BW/no - BMI/no - WC/no
4. Haghighian (2011)	Iran	Randomized, double-blind, placebo-controlled parallel trial	Type 2 diabetic patients	Both	30/30	8	59.1	28	1.5 g/d of whole cinnamon powder capsules	Placebo	- BW/no - BMI/no
5. Wainstein (2011)	Israel	Randomized, double-blind, placebo-controlled parallel trial	Type 2 Diabetes	Both	29/30	12	61.7	29.8	3 capsules each contain 400 mg of freshly ground cinnamon (1200 mg total)	Placebo capsules contained 400 mg of microcrystalline cellulose	- BW/no - BMI/no - WC/no
6. Vafa (2012)	Iran	Randomized, double-blind, placebo-controlled parallel trial	Type 2 Diabetic Patients	Both	19/18	8	54.1	29.2	500 mg cinnamon capsules. 2 capsules 3 times a day (3000 mg total)	Placebo	- BW/yes - BMI/yes - FM/yes
7. Torabi (2016)	Iran	Randomized, placebo-controlled parallel trial	Type 2 diabetes	Women	9/9	8	53.6	29	500 mg cinnamon capsules 3 times a day (1500 mg)	Placebo	- BW/no - BMI/no - FM/no
8. Torabi (2016)	Iran	Randomized, placebo-controlled parallel trial	Type 2 diabetes	Women	9/9	8	51.2	29	500 mg cinnamon capsules 3 times a day (1500 mg) + exercise	Placebo + exercise	- BW/no - BMI/no - FM/no
9. Gupta (2017)	India	Randomized, double-blind, placebo-controlled parallel trial	Metabolic syndrome	Both	58/58	16	44.3	33.6	6 cinnamon capsules (3000 mg total)	Placebo (wheat flour)	- BW/yes - BMI/yes - WC/yes - FM/yes
10. Borzoei (2017)	Iran	Randomized, double-blind, placebo-controlled parallel trial	Polycystic ovary syndrome	Women	42/42	8	29.3	30.7	3 cinnamon capsules, each one contain 500 mg cinnamon (1500 mg total)	Placebo capsules (wheat flour)	- BW/yes - BMI/yes
11. Hajimonfarednejad (2018)	Iran	Randomized, double-blind, placebo-controlled parallel trial	Polycystic ovary syndrome	Women	29/30	12	28.6	27.6	500 mg cinnamon capsules 3 times (1500 mg total)	Placebo	- BW/no - BMI/no - WC/no
12. Nakhaei (2018)	Iran	Randomized, placebo-controlled parallel trial	Overweight subjects	Women	15/15	8	22.4	28.9	1 g cinnamon capsules	Placebo	- BW/no - BMI/no
13. Nakhaei (2018)	Iran	Randomized, placebo-controlled parallel trial	Overweight subjects	Women	15/15	8	21.8	28.2	1 g cinnamon capsules + exercise	Placebo + exercise	- BW/no - BMI/no
14. Zare (2018)	Iran	Randomized, triple -blind, placebo-controlled parallel trial	Type 2 diabetes	Both	69/69	13	52.1	29.9	1 g cinnamon capsules	Placebo	- BW/yes - BMI/yes - FM/yes

Abbreviations: BW; body weight, BMI; body mass index, WC; waist circumference, FM; fat mass.

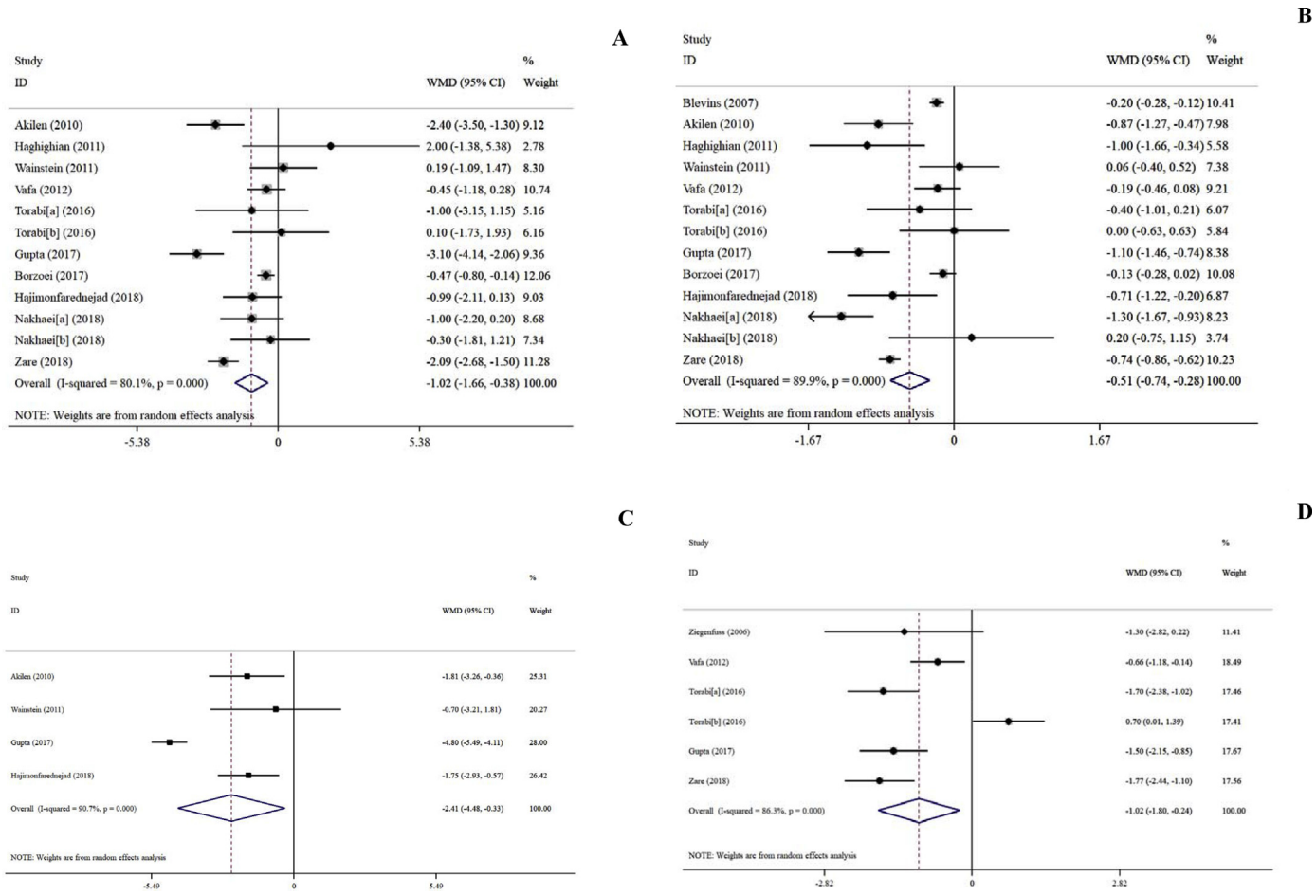

Fig. 2. Forest plot detailing weighted mean difference and 95% confidence intervals (CIs) for the effect of cinnamon supplementation on A) body weight, B) BMI, C) waist circumference, and D) fat mass.

FM was significant at the dosages of ≥2 g/d (WMD: −1.08%, 95% CI: −1.71, −0.49; P = 0.001), in trials lasting ≥12 weeks (WMD: −1.60%, 95% CI: −2.05, −1.15; P < 0.001), in studies performed on subjects with obesity (WMD: −1.46%, 95% CI: −2.06, −0.87; P < 0.001), in studies on people with a mean age of <50 years old (WMD: −1.19%, 95% CI: −2.28, −0.10; P < 0.001), and in trials conducted of both gender (WMD: −1.28%, 95% CI: −2.87, −0.69; P < 0.001).

3.7. Dose-responses association between cinnamon supplementation and outcomes

Based on the dose-response evaluation, cinnamon administration resulted in reduced BW ($P_{non\text{-}linearity} = 0.04$) and WC in a non-linear fashion ($P_{non\text{-}linearity} = 0.04$). Greater effects were seen at doses of 1.5 g/d. We did not find a significant non-linear relationship with BMI ($P_{non\text{-}linearity} = 0.18$), and FM ($P_{non\text{-}linearity} = 0.47$) (Fig. 3A-D). Moreover, the duration of cinnamon supplementation did not show a significant non-linear association with BW ($P_{non\text{-}linearity} = 0.07$), BMI ($P_{non\text{-}linearity} = 0.39$), WC ($P_{non\text{-}linearity} = 0.06$), and FM ($P_{non\text{-}linearity} = 0.50$) (Fig. 4A-D).

3.8. Sensitivity analysis

To explore the impact 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 BW, BMI, WC, and FM.

3.9. Publication bias

Visual inspection of the funnel plots indicated no evidence of asymmetry in the effects of cinnamon supplementation on anthropometric measures and body composition (Fig. 5). These observations were approved by the use of Egger's regression tests for BW (P = 0.77), BMI (P = 0.32), WC (P = 0.12), and FM (P = 0.83).

4. Discussion

In the present systematic review and meta-analysis, we summarized available records from 12 RCTs which examined the effects of cinnamon supplementation on anthropometric measures including BW, BMI, WC, and FM in adults. Our findings revealed that cinnamon supplementation can significantly reduce BW, BMI, WC, and FM. In the subgroup analyses, we found a greater reduction in BW in subjects aged <50 years old, those with a baseline BMI of ≥30 kg/m^2. The cinnamon administrations significantly reduced FM at the dosages of ≥2 g/d, when administered for ≥12 weeks.

Our findings were in agreement with a recent systematic review which proposed the potential anti-obesity effects of cinnamon supplementation [43]. In a recent meta-analysis of RCTs, flavanols, a major component of cinnamon, showed a potential role against obesity [44]. Such results were also observed for polyphenols [45].

Table 3
Subgroup analysis of included randomized controlled trials in meta-analysis of the effect of cinnamon supplementation on obesity indices.

Group	No. of trials	WMD (95% CI)	P value	I^2 (%)	P-heterogeneity	P for between subgroup heterogeneity
Body weight						
Cinnamon dosage						0.009
<2 g	9	−0.69 (−1.36, −0.02)	0.04	72.2	<0.001	
≥2 g	3	−1.94 (−3.66, −0.23)	0.02	89.8	<0.001	
Duration (week)						<0.001
<12 week	7	−0.47 (−0.75, −0.18)	0.001	0.0	0.74	
≥12 week	5	−1.73 (−2.69, −0.77)	<0.001	79	0.001	
Baseline BMI						0.37
Obese (≥30)	3	−1.93 (−3.76, −0.10)	0.03	93.5	<0.001	
Overweight (25 < BMI<30)	9	−0.68 (−1.39, 0.02)	0.06	66.4	0.002	
Mean age						0.02
<50 years	5	−1.17 (−2.17, −0.17)	0.02	82.6	<0.001	
≥50 years	7	−0.85 (−1.81, 0.11)	0.09	78.0	<0.001	
Gender						<0.001
Females	6	−0.53 (−0.82, −0.23)	<0.001	0.0	0.83	
Both	6	−1.33 (−2.42, −0.24)	0.02	85.4	<0.001	
Health status						<0.001
Type 2 diabetes	7	−0.85 (−1.81, 0.11)	0.09	78.0	<0.001	
PCOS	2	−0.51 (−0.83, −0.19)	0.002	0.0	0.38	
Apparently healthy	3	−1.52 (−3.23, 0.18)	0.08	82.6	0.003	
Body mass index						
Cinnamon dosage						0.01
<2 g	10	−0.45 (−0.71, −0.18)	0.02	90.5	<0.001	
≥2 g	3	−0.70 (−1.30, −0.12)	0.01	89.0	<0.001	
Duration (week)						0.09
<12 week	7	−0.43 (−0.81, −0.04)	0.03	84.6	0.04	
≥12 week	6	−0.59 (−0.93, −0.25)	0.001	93.5	<0.001	
Baseline BMI						<0.001
Obese (≥30)	4	−0.51 (−0.84, −0.19)	0.002	91.3	<0.001	
Overweight (25 < BMI<30)	9	−0.49 (−0.80, −0.19)	0.001	81.3	<0.001	
Mean age						0.48
<50 years	5	−0.65 (−1.25, −0.06)	0.03	92.3	<0.001	
≥50 years	8	−0.41 (−0.68, −0.14)	0.003	89.5	<0.001	
Gender						0.25
Females	6	−0.43 (−0.92, 0.05)	0.08	86.4	0.03	
Both	7	−0.55 (−0.86, −0.25)	<0.001	92.6	<0.001	
Health status						<0.001
Type 2 diabetes	8	−0.41 (−0.68, −0.14)	0.004	89.5	<0.001	
PCOS	2	−0.36 (−0.92, 0.19)	0.2	77.7	0.03	
Apparently healthy	3	−0.91 (−1.48, −0.33)	<0.001	75.9	0.02	
Waist circumference						
Cinnamon dosage						<0.001
<2 g	2	−1.56 (−2.62, −0.49)	0.004	0.0	0.46	
≥2 g	2	−3.37 (−6.30, −0.45)	0.02	92.5	<0.001	
Baseline BMI						<0.001
Obese (≥30)	2	−3.37 (−6.30, −0.45)	0.02	92.5	<0.001	
Overweight (25 < BMI<30)	2	−1.56 (−2.62, −0.49)	0.004	0.0	0.46	
Mean age						<0.001
<50 years	2	−3.31 (−6.30, −0.32)	0.03	94.8	<0.001	
≥50 years	2	−1.53 (−2.78, −0.27)	0.01	0.0	0.45	
Fat mass						
Cinnamon dosage						0.82
<2 g	3	−0.92 (−2.50, 0.65)	0.25	93.8	<0.001	
≥2 g	3	−1.08 (−1.71, −0.49)	0.001	50.5	0.13	
Duration (week)						<0.001
<12 week	3	−0.55 (−1.80, 0.69)	0.38	91.5	<0.001	
≥12 week	3	−1.60 (−2.05, −1.15)	<0.001	0.0	0.78	
Baseline BMI						0.07
Obese (≥30)	2	−1.46 (−2.06, −0.87)	<0.001	0.0	0.81	
Overweight (25 < BMI<30)	4	−0.85 (−1.91, 0.19)	0.11	91.0	<0.001	
Mean age						0.07
<50 years	2	−1.19 (−2.28, −0.10)	<0.001	0.0	0.81	
≥50 years	4	−0.85 (−1.91, 0.19)	0.11	91.0	<0.001	
Gender						0.02
Females	2	−0.50 (−2.85, 1.85)	0.67	95.7	<0.001	
Both	4	−1.28 (−1.87, −0.69)	<0.001	61.3	0.05	

In addition to its effect on body weight, cinnamon supplementation has also been shown to improve weight-related disorders including blood triglycerides, total cholesterol, HDL-C levels, fasting plasma glucose, and HbA1c levels in humans [19,46,47]. The beneficial effects of cinnamon supplementation on inhibiting pancreatic α-amylase and reducing intestinal glucose absorption, stimulating cellular glucose uptake and glycogen synthesis, inhibiting gluconeogenesis, stimulating insulin receptor activity, improving weight loss, increasing insulin levels, and reducing fasting blood glucose were also seen in *in vitro* and *in vivo* studies [21]. Overall, these

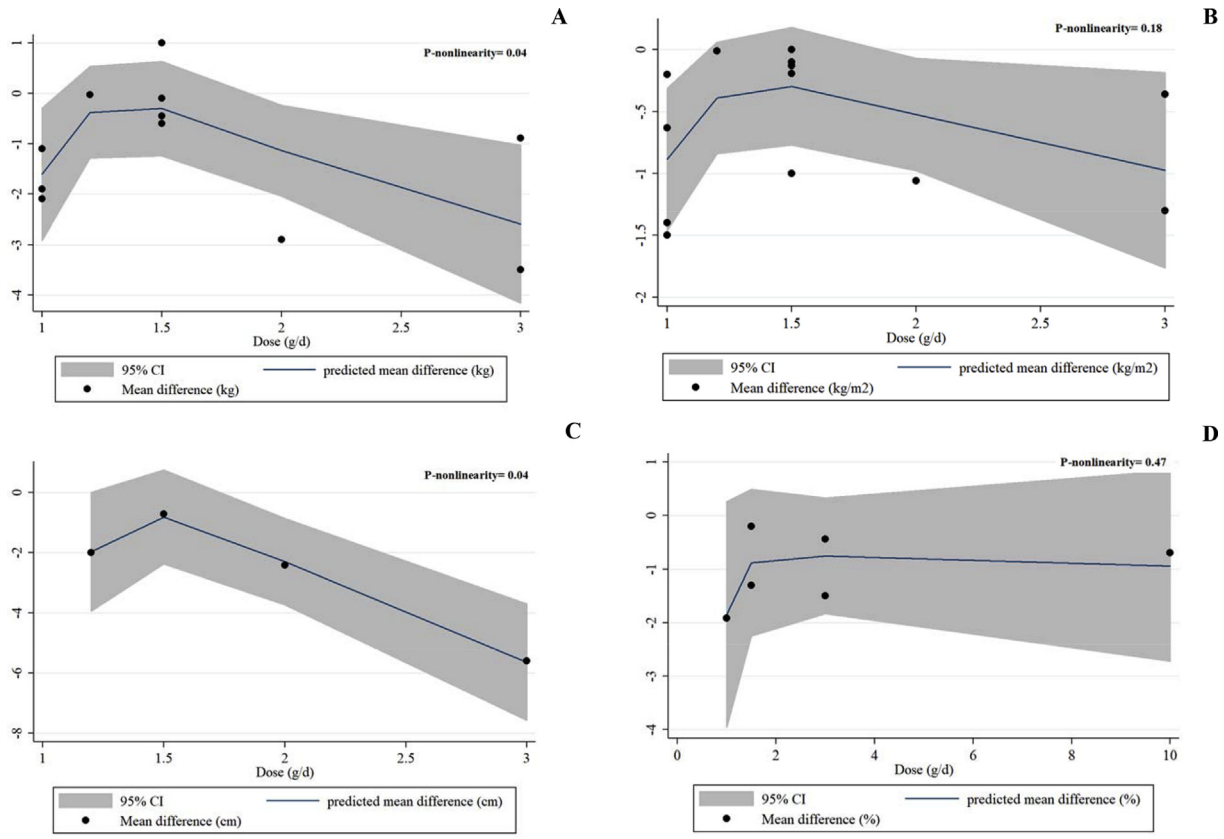

Fig. 3. Non-linear dose-response relations between cinnamon dosage (g/d) and unstandardized mean difference in (A) BW, (B) BMI, (C) WC, and (D) FM. The 95% CI is demonstrated in the shaded regions.

findings indicate that cinnamon supplementation could be regarded as a potential healthy spice for human body.

Cinnamon can delay gastric emptying, increase glucosidase enzymes and inhibit ATPase of intestinal brush borders; so it can reduce glucose absorption in the small intestine [48–50]. Furthermore, cinnamon increases glucose transporter 4 (GLUT4), activates glycogen synthase and inhibits glycogen synthase kinase-3 β [12,49]. All these actions are decreasing glucose levels and in turn its conversion to glycogen. Methyl Hydroxy chalcone polymers (MHCP) in cinnamon make adipose cells more reactive to insulin by activating the insulin-receptor kinase and inhibiting the insulin-receptor-phosphatase, which increases insulin sensitivity and helps increasing body metabolism [51,52]. Flavonoids and phenolic complexes like epicatechin, catechin, and procyanidin B2 in cinnamon can decrease the absorption of glucose in the intestine, decrease glycogenolysis, and increase glycogen synthesis. Furthermore, these actions can decrease chylomicron absorption [48]. Reducing glucose and chylomicron absorption leads to reduction in the synthesis and storage of fat and improvement in anthropometric measures [53].

Our meta-analysis indicated that cinnamon supplementation is more effective when it was administered to young adults, subjects with obesity, at higher dosages and longer duration. Serban et al. in a meta-analysis in 2017 showed that increasing duration of cinnamon administration has a significant effect on reduced blood triglycerides and cholesterol [48]. In general, the antioxidant effects of these supplements is improved when it is prescribed in higher dosage for longer duration [54]. Furthermore, Kim et al. in an animal study indicated that high doses of cinnamon extract (200 mg/kg) was most effective in decreasing the blood glucose levels compared with low doses [55]. With regards to age, it must be taken into account that age-related obesity plays an important role in the dysregulation of inflammatory cytokine production. It is possible that elevated inflammation in older people might hinder observing the effects of cinnamon [56]. The anti-inflammatory protein, tristetraprolin (TPP) is reduced in people with obesity, but it is increased by cinnamon. TPP plays an important role in insulin signaling, glucose transport, and gluconeogenesis [57]. So increasing TTP in people with obesity can explain greater weight change in these participants by cinnamon intake.

4.1. Strengths and limitations

To the best of our knowledge, this is the first meta-analysis on the effects of cinnamon supplementation on obesity measures. This study included an adequate number of trials on the effects of cinnamon intake on BW and BMI, while the number of trials about waist circumference and fat mass might be insufficient. Therefore, our findings of the latest two measures should be interpreted with caution. Although in some cases, some sort of between-study heterogeneity was found, we found potential sources of this heterogeneity in our analyses. Despite this, some limitations should be noted. First, included studies have used different spices of cinnamon, which might influence our findings. Future studies are recommended to focus on the most effective spice of cinnamon. Second, these studies were carried out on participants with different health conditions and various age groups. Although we considered these factors in our subgroup analyses, this must be considered in the interpretation.

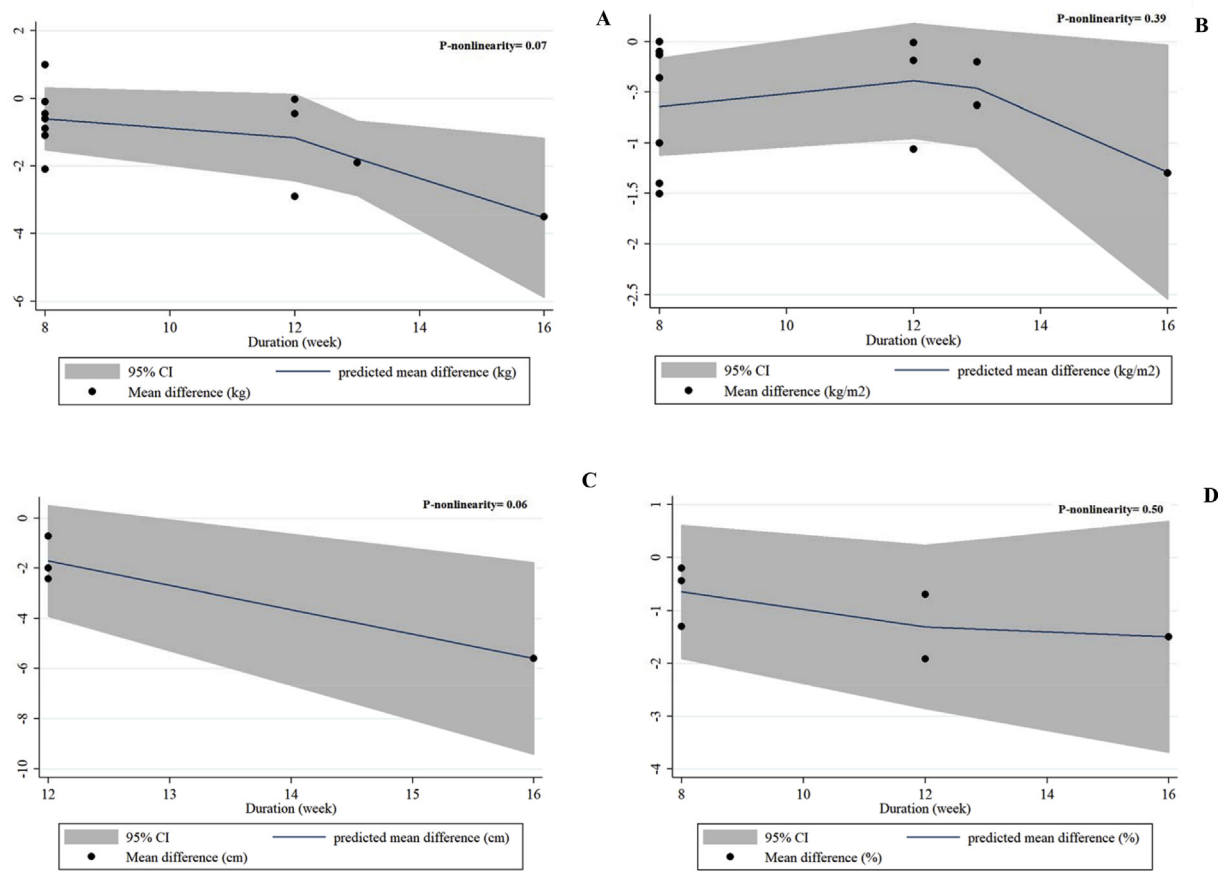

Fig. 4. Non-linear dose-response relations between duration of intervention (weeks) and unstandardized mean difference in (A) BW, (B) BMI, (C) WC, and (D) FM. The 95% CI is demonstrated in the shaded regions.

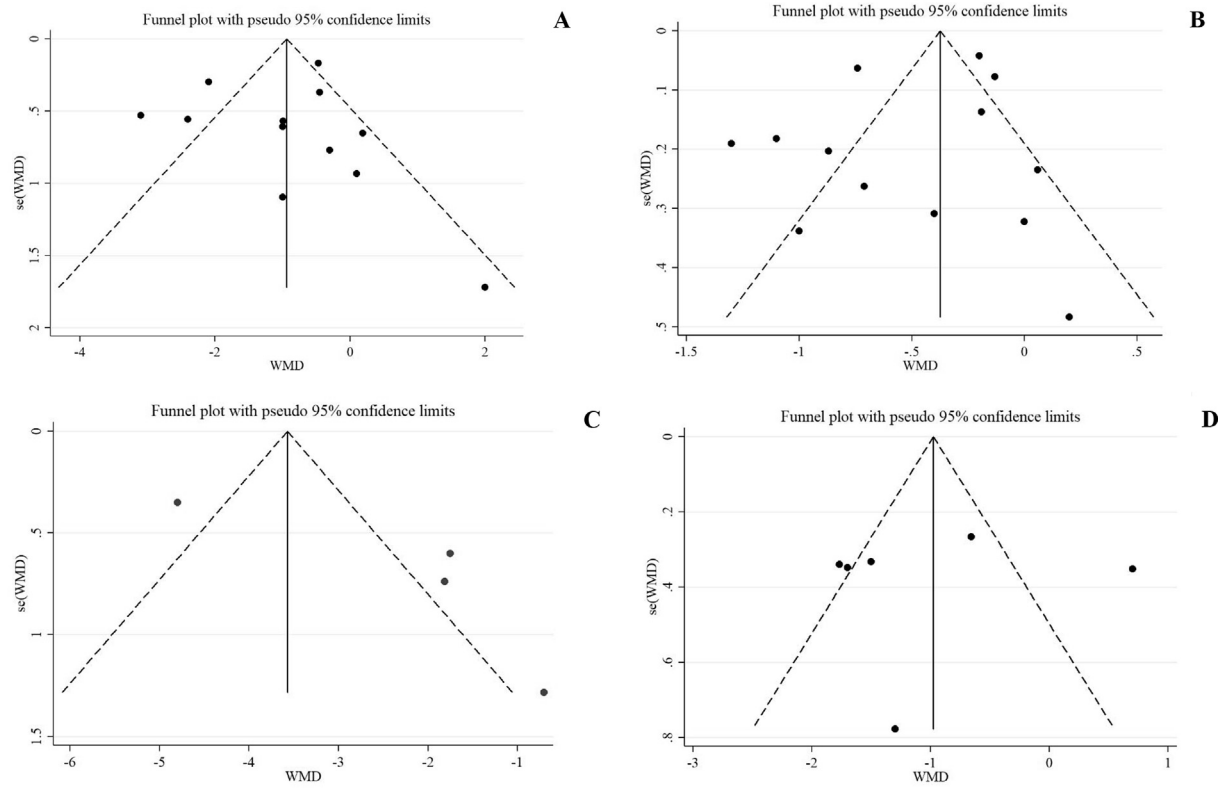

Fig. 5. Funnel plot representing publication bias in the studies reporting the effect of cinnamon supplementation on (A) BW, (B) BMI, (C) WC, and (D) FM.

5. Conclusion

The current meta-analysis pooled results from 12 RCTs including 786 participants. Our findings indicated that cinnamon supplementation can significantly reduce BW, BMI, WC, and FM. Greater effects on BW were observed in subjects aged <50 years old, those with a baseline BMI of ≥30 kg/m^2. The cinnamon administrations significantly reduced FM at the dosages of ≥2 g/d, when administered for ≥12 weeks.

Author contributions

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

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Conflicts of interest

The authors declared no conflicts of interest.

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