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A meta-analysis and meta-regression study of the effects of Triphala on anthropometric parameters

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ABSTRACT

Triphala is a medicinal plant that can improve anthropometric parameters. Although Triphala is widely used, especially in India and Thailand, its efficacy is still controversial. Consequently, the purpose of this meta-analysis and meta-regression analysis was to assess the safety of Triphala and its effects on anthropometric parameters. A comprehensive review and meta-analysis of randomized controlled trials assessing the safety of Triphala and its effects on anthropometric parameters were conducted by searching PubMed, ScienceDirect, Web of Science, and ThaiLIS databases. Two authors independently conducted the study selection and data extraction and evaluated the quality of the studies. The clinical therapeutic effects and adverse events of Triphala were evaluated and aggregated using a random-effects model. The chi-square and I^2 tests were used to assess heterogeneity between the studies. Seven trials with a total of 458 patients were included. The Triphala-treated groups demonstrated a considerable decrease in body weight (BW) (weighted mean difference [WMD]: −2.99 kg; 95% CI: −5.31, −0.67; P = 0.012; I^2 = 94.4%), body mass index (BMI) (WMD: −0.79 kg/m^2; 95% CI: −1.52, −0.07; P = 0.032; I^2 = 90.4%), and waist circumference (WC) (WMD: −1.86 cm; 95% CI: −3.10, −0.62; P = 0.003; I^2 = 88.8%). During the treatment period, there were no reports of serious adverse events related to Triphala. However, there was no association between the dose or duration of treatment and any of the recorded outcomes. This meta-analysis revealed that Triphala significantly improved BW, BMI, and WC. Nevertheless, substantial, well-designed randomized controlled studies are necessary to confirm this finding.

Implication for health policy/practice/research/medical education:
This meta-analysis demonstrated that Triphala could reduce anthropometric parameters.
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Introduction

The World Health Organization (WHO) has provided estimates of the existing and future global prevalences of cardiovascular diseases (CVDs), which are anticipated to increase by approximately 10% in 2030 (1). Obesity is a crucial factor known to potentiate CVD and associated morbidity and mortality (2,3). Therefore, this cardiometabolic risk factor must be mitigated to lower the prevalence of CVD (1). The typical use of complementary and alternative medicine is to improve the lipid and glycemic profiles and anthropometric parameters.

Triphala is a mixture of three plants' dried fruits, which are used in Ayurvedic and traditional Thai medicine: *Phyllanthus emblica* Linn., *Terminalia chebula* Retz., and *Terminalia bellerica* Roxb (4,5). Tannins, gallic acid, ellagic acid, and chebulinic acid are the primary components of Triphala (5). Previous studies have revealed that Triphala has antioxidant, chemopreventive, radioprotective, immunomodulatory, antimicrobial, and anti-inflammatory activities. It is used for multiple purposes, including lipid-lowering, blood glucose-lowering, anti-obesity, and anti-diarrheal activities (6).

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A previous systematic review suggested that significant improvements were observed in body weight (BW), body mass index (BMI), and WC when Triphala was administered (7).

Previous preclinical trial studies have demonstrated that Triphala supplementation for 10 weeks reduced BW and body fat in mice (8). However, the results of the different clinical trials conducted to evaluate the anti-obesity effects of Triphala were inconsistent, and these clinical trials were conducted with a small number of participants (9-11). These inconsistencies may be due to variations in research design, small sample sizes, differences in population in individual trial and intervention periods, or differences in the dosages and forms of Triphala. Moreover, according to our best knowledge, no meta-analysis and meta-regression studies have been conducted to evaluate the effect of Triphala on anthropometric parameters. Therefore, we performed this meta-analysis and meta-regression study of quantitative evidence from the available randomized controlled trials (RCTs) to evaluate the effects of Triphala supplements on anthropometric parameters.

Materials and Methods

This meta-analysis was done according to the guidelines of the Cochrane Collaboration Framework (12), and the reporting conformed with the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement (13).

Search strategies and study selection

PubMed, ScienceDirect, Web of Science, and Thai Library Integrated System (ThaiLIS) were used to search for original research publications without limits on date or language.

The strategic search terms used were "Triphala", "obesity", "weight", body mass index", "waist circumference", and "randomized controlled trial". The references of the publications retrieved from full-text reviews were further examined to identify relevant research not listed in the aforementioned databases. Included publications (RCTs) were examined for the anti-obesity benefits of Triphala. The final search was performed on 31st January 2022.

All titles and abstracts were scanned using the inclusion and exclusion criteria. Two researchers (WP, BS) independently evaluated the full-text publications of the studies thereafter. Disagreements amongst the reviewers were addressed through discussions with CT.

Data extraction and quality assessment

WP and BS extracted all data separately using a standardized extraction form. Each trial was examined for the following information: authors, publication year, research design, participant, intervention characteristics, sample size, length of treatment, and outcome measures.

Two authors (WP and BS) evaluated the methodological quality of the included studies using the Jadad scale for assessing the methodological approach of RCTs. Studies that satisfied at least three of the five criteria were deemed to be of high quality (14).

We evaluated the risk of bias in the individual studies using the Cochrane Risk of Bias 2.0 tool (15). This tool includes the following seven domains: (i) random sequence generation (selection bias), (ii) allocation concealment (selection bias), (iii) blinding of participants and personnel (performance bias), (iv) blinding of outcome assessment (detection bias), (v) incomplete outcome data (attrition bias), (vi) selective reporting (reporting bias), and (vii) other bias. Each domain's risk of bias was graded as low, uncertain, or high. Thorough discussions with a third party (CT) were done to resolve any disagreements amongst the reviewers.

Outcomes measurement and statistical analyses

The primary outcomes studied were anthropometric variables (BW, BMI, and WC). Hepatic and renal function tests, as well as adverse events, were the secondary outcomes.

The computed and stratified pooled effects were based on the outcome data. Continuous results were presented as weighted mean differences (WMD). The chi-square test and I^2 test were used to assess statistical heterogeneity across studies. The heterogeneity test judged differences to be statistically significant when $P < 0.05$, and considerable heterogeneity was indicated by $I^2 \geq 50\%$ (16).

Egger's weighted regression approach and visual examination of funnel plots (17,18) were used to assess publication bias. All analyses were conducted using the DerSimonian and Laird random-effects model (19).

Statistical analyses were undertaken using the software STATA version 14 and Review Manager (RevMan®) version 5.3.

Sensitivity and subgroup analysis

The fixed effects model was used for sensitivity analysis to confirm the robustness of the findings (20). In addition, subgroup analyses were conducted depending on treatment duration and participant type.

Meta-regression

Meta-regression analysis was conducted to assess relationships between the effect magnitude and potential moderator factors, such as dosage and duration of Triphala administration. We conducted a weighted fixed-effect meta-regression using the maximum likelihood model without restrictions.

Results

Study selection

The studies' PRISMA flowchart is shown in Figure 1. After removing duplicates, a database search yielded a total of 269 screening-eligible articles out of 406 recognized articles. On the basis of the titles and abstracts,

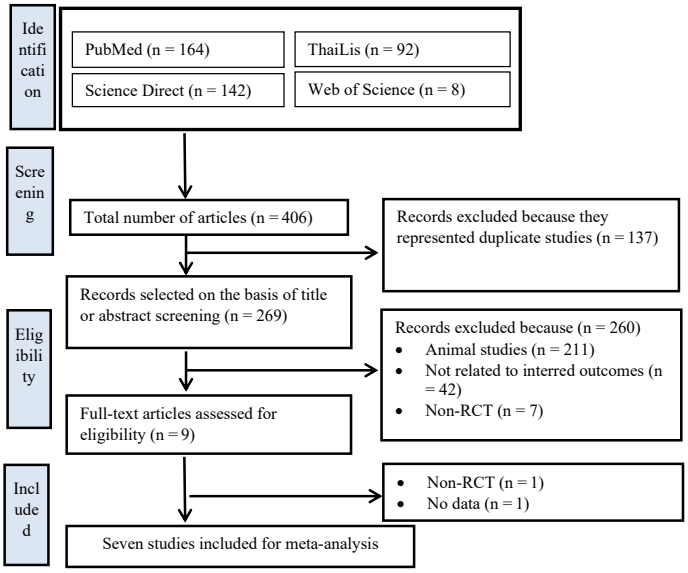

Figure 1. A PRISMA flowchart depicting the process of selecting articles for inclusion in the meta-analysis.

nine English and Thai articles were chosen for full-text review. The full-text review resulted in the exclusion of two articles: one was a non-RCT, and the other did not assess the outcomes of interest. Therefore, seven English and Thai articles (4,9,11,21-24) were considered in our research.

Characteristics and methodological qualities of the selected studies

Table 1 provides a summary of the selected studies' characteristics and methodological quality. Four of the seven included studies were performed in India, while one each was conducted in Thailand, Iran, and Italy. The

Table 1. Characteristics of the included studies in the meta-analysis

Articles	Year	Country	Study design	Participants	Age range or average	Treatment duration	Groups (n)		Outcomes measurement	Jadad Scale
							Intervention	Comparators		
Paranjpe et al (21)	1990	India	DRCT	Obese patients	N/A	3 months	Triphala 250 mg (16)	Placebo 250 mg (22)	BW, WC	3
Kamal et al (4)	2012	Iran	DRCT	Obese patients (BMI between 30 to 50 kg/m^2)	16-60 y	3 months	Triphala 10 g (30)	Placebo (30)	BW, BMI, WC	5
Kaewtong et al (9)	2018	Thailand	DRCT	Obese patients (BMI between 25 to 29.99 kg/m^2)	20-60 y	8 weeks	Triphala 600 mg tid (20)	Placebo tid (20)	BMI, WC	5
Pai et al (22)	2018	India	RCT	Obese patients (BMI > 30 kg/m^2)	16-60 y	48 days	Triphala 24 g bid (30)	Life style change (30)	BW, BMI, WC	2
Chaitralakshmi et al. (23)	2019	India	RCT	Obese patients (BMI > 25 kg/m^2)	18-60 y	25 days	Triphala (20)	Herbal formula (20)	BMI, WC	2
Salunke et al (24)	2019	India	DRCT	Obese patients (BMI > 25 kg/m^2)	18-60 y	3 months	Triphala extract 1000 mg bid for overweight and 1500 mg bid for obese participants (66)	Placebo (64)	BW, WC	5
Donato et al (11)	2021	Italy	DRCT	Asymptomatic hypercholesterolemic patients	35-69 y	3 months	Triphala 450 mg tid (44)	Placebo (46)	BMI, WC	5

N/A: Not available; RCT: randomized controlled trial; DRCT: double-blind, randomized, controlled trial; BW: body weight; BMI: body mass index; WC: waist circumference

studies were published between 1990 and 2021. Five out of the seven studies (5/7) were double-blind RCTs. Only one study (24) enrolled more than 100 patients. The age of the study participants ranged from 16 to 69 years. Six studies (4,9,21-24) were performed on obese patients, and one study (11) was performed on asymptomatic hypercholesterolemic patients. The treatment duration varied between 25 days and three months.

Regarding the methodological qualities of the studies included in the meta-analysis, five of the seven studies were rated to have a high-quality Jadad score (≥3) and a low risk of bias. Three studies (21-23) did not report information allocation concealment, and two studies (22, 23) did not report blinding of participants and investigators (Figure 2).

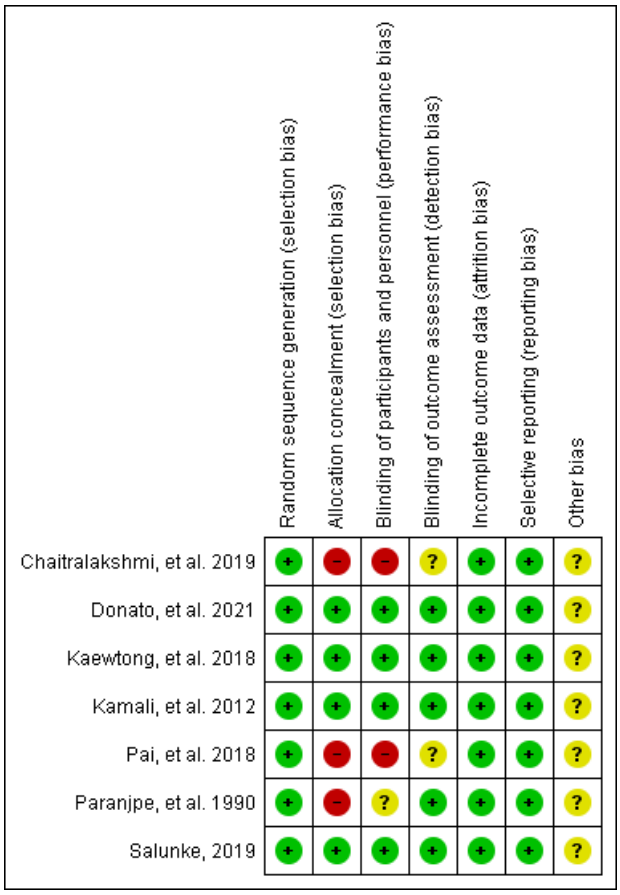

Figure 2. Summary of the risks of bias from the individual studies (+ = low risk; − = high risk; ? = unclear).

Primary outcomes

The results of this meta-analysis showed that Triphala significantly decreased body weight (WMD: −2.99 kg; 95% confidence interval [CI]: −5.31, −0.67; $P = 0.012$; $I^2 = 94.4\%$), BMI (WMD: −0.79 mg/dL; 95% CI: −1.52, −0.07; $P = 0.032$; $I^2 = 90.4\%$), and WC (WMD: −1.86 mg/dL; 95% CI: −3.10, −0.62; $P = 0.003$; $I^2 = 88.8\%$). Heterogeneity was observed among these outcomes (Table 2).

Secondary outcomes

Only two studies (4,11) reported the results of other laboratory investigations following Triphala administration. These two studies monitored liver function tests (including aspartate aminotransferase [ASP], alanine aminotransferase [ALT], and alkaline phosphatase [ALP]), renal function tests, electrolytes, and complete blood count. The findings of all these tests were normal. However, Kamali et al (4) observed a substantial reduction in ALT levels in Triphala-treated patients; however, Donato et al (11) found no significant difference in ALT levels between Triphala-treated patients and controls at the end of the study.

Only one study reported serious adverse effects from the use of Triphala. This was a hypersensitivity rash observed in two participants in the Triphala-treated group. This phenomenon occurred a few minutes after the administration of Triphala, and one of the two affected participants developed facial edema. The patients stopped treatment and were treated with oral steroids for two days, and the rash disappeared. Additional adverse effects found in other participants included loose stools or moderate diarrhea; however, these symptoms were moderate and well-tolerated (11).

Subgroup analysis

Table 3 shows the results of the subgroup analyses, which revealed statistically significant improvements in BW and WC with Triphala treatment wherein the duration of the treatment was longer than three months (WMD: −3.85 kg; 95% CI: −7.34, −0.37; $P = 0.03$ and WMD: −3.81 cm; 95% CI: −6.22, −1.40; $P = 0.03$, respectively). We noted a significant reduction in BW and WC for Triphala doses ≥ 2000 mg/day (WMD: −1.94 kg; 95% CI: −3.68, −0.20; $P = 0.03$ and WMD: −2.37 cm; 95% CI: −4.53, −0.21; $P = 0.03$, respectively). Additionally, a significant lowering in BW and WC was seen in studies with Jadad scale ≥ three points (WMD: −3.85 kg; 95% CI: −7.34, −0.37; $P = 0.03$

Table 2. Results of the main and sensitivity analyses

Outcomes	Main analysis WMD (95% CI; *P* value); I^2	Sensitivity analysis WMD (95% CI; *P* value); I^2	References
BW	-2.99 (-5.31, -0.67; *P* = 0.012); 94.4%	-1.17 (-1.26, -1.08; *P* < 0.05); 94.4%	(4, 21, 22, 24)
BMI	-0.79 (-1.52, -0.07; *P* = 0.032); 90.4%	-0.83 (-1.03, -0.62; *P* < 0.05); 90.0%	(4, 9, 11, 22, 23)
WC	-1.86 (-3.10, -0.62; *P* = 0.003); 88.8%	-1.13 (-1.44, -0.81; *P* = 0.032); 88.8%	(4, 9, 11, 21, 23, 24)

BW: body weight; BMI: body mass index; WC: waist circumference; WMD: weighted mean differences.

Table 3. Subgroup analysis of RCTs investigating the influence of the different variables on the clinical outcomes of Triphala treatment

Outcomes	No. of trials	Effect size	95% CI	I^2 (%)	*P* for effect size	*P* for heterogeneity
BW						
Duration (mon)						
< 3	1	−0.55	−1.88, 0.78	N/A	0.42	N/A
≥ 3	3	−3.85	−7.34, −0.37*	96.0	0.03	<0.0001
Triphala Do						
< 2000 mg/d	1	−5.80	−7.24, −4.36*	N/A	< 0.0001	N/A
≥ 2000 mg/d	3	−1.94	−3.68, −0.20*	86.0	0.03	0.0008
Jadad Scale						
Low (< 3)	1	−0.55	−1.88, 0.78	N/A	0.42	N/A
High (≥ 3)	3	−3.85	−7.34, −0.37*	96.0	0.03	<0.0001
BMI						
Duration (mon)						
< 3	3	−0.63	−1.70, 0.45	89.0	0.25	<0.0001
≥ 3	2	−0.86	−2.12, 0.41	94.0	0.18	<0.0001
Triphala dosage						
< 2000 mg/d	3	−0.62	−1.68, 0.44	94.0	0.25	<0.0001
≥ 2000 mg/d	2	−0.89	−2.32, 0.54	88.0	0.22	0.003
Jadad Scale						
Low (< 3)	2	−0.86	−2.12, 0.41	94.0	0.18	<0.0001
High (≥ 3)	3	−0.63	−1.66, 0.41	82.0	0.23	0.03
WC						
Duration (mon)						
< 3	3	−0.43	−1.57, 0.71	67.0	0.46	0.05
≥ 3	4	−3.81	−6.22, −1.40*	81.0	0.0009	0.001
Triphala dosage						
< 2000 mg/d	4	−1.60	−3.29, 0.09	99.0	0.1	<0.0001
≥ 2000 mg/d	3	−2.37	−4.53, −0.21*	56.0	0.03	0.10
Jadad scale						
Low (< 3)	2	−0.44	−1.75, 0.88	83.0	0.52	0.01
High (≥ 3)	5	−2.79	−4.42, −1.15*	75.0	0.008	0.003

BW: body weight; BMI: body mass index; WC: waist circumference.

and WMD −2.79 cm; 95% CI: −4.42, −1.15; $P=0.008$, respectively).

Sensitivity analyses

Sensitivity analyses of all the parameters were performed by changing the model of analysis to a fixed model approach. The pooled effects did not differ from the main outcomes.

Meta-regression

Meta-regression was utilized to examine the relationship between the main outcomes and the dose of Triphala administered. The results from the random effect meta-regression revealed no significant associations between the dose and the primary outcomes, including BMI (slope = −0.41; 95% CI: −1.17, 0.36; $P=0.077$), BW (slope = −2.18; 95% CI: −12.33, 7.96; $P=0.363$), and WC (slope = −1.68; 95% CI: −4.36, 0.99; $P=0.090$).

In addition, there was no association between the duration of Triphala treatment and the BMI (slope = 0.79; 95% CI: −3.53, 1.93; $P=0.423$), BW (slope = 1.41; 95% CI: −30.28, 27.46; $P=0.679$), and WC (slope = −0.24; 95% CI: −6.25, 6.73; $P=0.205$) (Figure 3).

Publication bias

Publication bias regarding the clinical therapeutic efficacy was analyzed using Begg's and Egger's tests. Both tests did not show any publication bias with respect to BW (intercept: −3.23; SE = 2.23; 95% CI: −12.85, 6.38; t = −1.45; $P=0.285$), BMI (intercept: 0.46; SE = 3.79; 95% CI: −11.60, 12.52; t = 0.12; $P=0.911$), and WC (intercept: -1.80; SE = 1.87; 95% CI: −6.60, 3.00; t = −0.96; $P=0.379$).

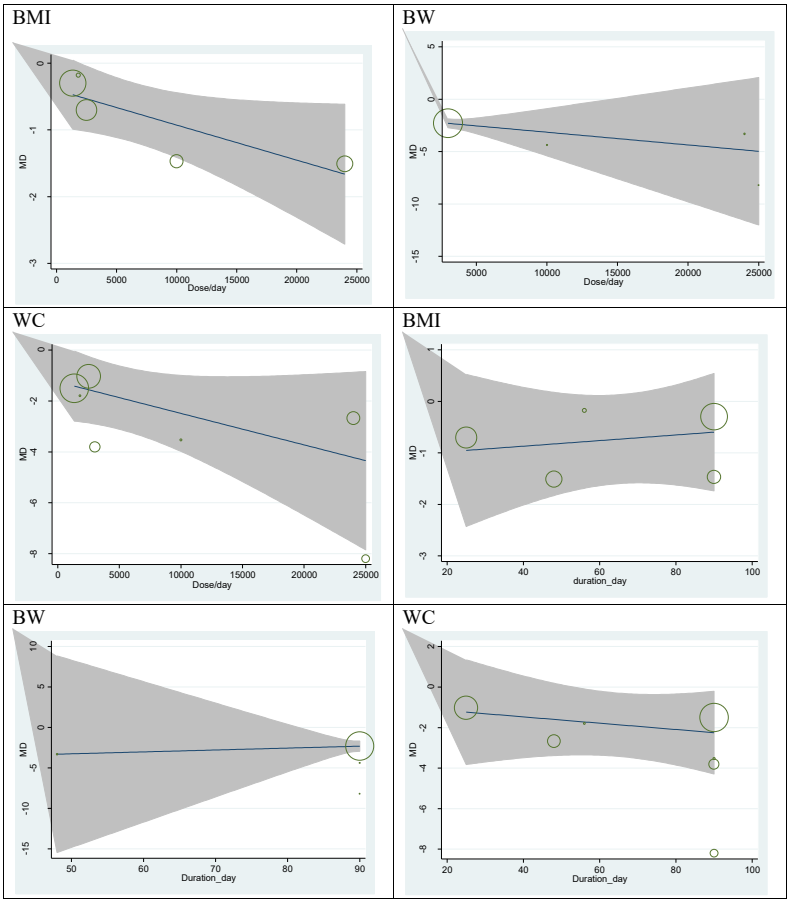

Figure 3. The meta-regression analysis of Triphala efficacy on primary outcomes. Abbreviations: BW: body weight; BMI: body mass index; WC: waist circumference.

Discussion

The purpose of this meta-analysis was to assess the safety and effects of Triphala on the anthropometric parameters. Our meta-analysis showed that Triphala, taken either as a monotherapy or in combination with other therapies, may substantially improve BW, BMI, and WC. The results showed a few adverse effects associated with the administration of Triphala; however, neither the liver nor the kidneys were affected. The meta-regression revealed that there was no association between the Triphala dose and duration with BMI, BW, and WC. Obesity is an important risk factor for CVD (3). According to reports, an improvement in anthropometric parameters is associated with a decreased risk of coronary and vascular events (25,26). Triphala has been shown to decrease anthropometric parameters and, subsequently, the risk of cardiometabolic events.

According to our findings, Triphala supplementation decreased BW, BMI, and WC; however, the mechanisms underlying these findings are still unclear. A 10-week in vivo investigation (27) on the effects of the Triphala diet on mice revealed a reduction in body weight, body fat, and calorie consumption. The suggested mechanisms underlying these observed effects of Triphala were regulation of the expression of CCAAT/enhancer-binding proteins (C/EBP) and PPAR and inhibition of adipogenesis by boosting Wnt/-catenin signaling (8).

Our subgroup analysis suggested that Triphala treatment with a duration of ≥3 months and a dosage of ≥ 2000 mg/d were more effective in reducing BW and WC than a treatment duration of <3 months and a dosage of <2000 mg/d. A better reduction in BW and WC was noted in the high-quality article (Jadad scale ≥3). However, these subgroup analysis findings should be interpreted with caution due to the limited number of studies included in the meta-analysis.

In addition, this meta-analysis found that Triphala had no impact on liver and renal function tests. In addition, only one trial (11) identified a small number of individuals who suffered adverse effects (e.g., diarrhea); nonetheless, the symptoms were mild and well tolerated. Utilizing a methodological methodology is the key strength of our meta-analysis. To the best of our knowledge, this is the first complete systematic review and meta-analysis on the impact and safety of Triphala on obesity.

The quality of studies included in the meta-analysis was further evaluated using the Jadad scale and the Cochrane Risk of Bias Assessment Tool (ACROBAT). Two of the

trials were not double-blinded trials; they were performed without proper concealment or blinding. However, the overall risk of bias was low, and the quality was high.

A significant weakness of this meta-analysis is the potential for bias owing to the small study effects of the majority of included studies. The majority of studies did not specify whether Triphala was administered in the form of an extract or a capsule containing powder; hence, the included trials indicated a broad variety of Triphala formulations.

Our meta-analysis revealed that Triphala was safe for consumption up to three months. All the studies included in our meta-analysis provided insufficient information on the long-term safety of Triphala; thus, the long-term safety of Triphala should be investigated. Well-designed, large, multicenter, randomized, placebo-controlled studies exploring the long-term effects of Triphala are required to support our existing findings.

Conclusion

Based on the current evidence, Triphala is effective against obesity. The meta-analysis showed that Triphala was effective in reducing BMI, BW, and WC. It is also worth noting that there were no reports of severe adverse effects in both Triphala- treated and control groups. However, future large-scale and long-term RCT studies on the effects of Triphala on the anthropometric parameters are recommended.

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Authors' contributions

WP, CT, and BS reviewed and contributed to data collection and preparation of the manuscript. The first draft was prepared by WP, PK, CT, KS, and BS. All authors read the final version and confirmed it for publication.

Conflict of interests

None to declare.

Ethical considerations

To avoid plagiarism, data fabrication, falsification, duplicate, or misconduct, the authors tried to monitor and document these ethical concerns.

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