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Effects of Triphala on Lipid and Glucose Profiles and Anthropometric Parameters: A Systematic Review

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Abstract

Aim. The efficacy of triphala on lipid profile, blood glucose and anthropometric parameters and its safety were assessed. *Methods.* Databases such as PubMed, ScienceDirect, Web of Science, and Thai Library Integrated System (ThaiLIS) were systematically searched to review current evidence of randomized controlled trials (RCT) on triphala. RCTs investigating the safety and efficacy of triphala on lipid profile, blood glucose and anthropometric parameters were included. Study selection, data extraction, and quality assessment were performed independently by 2 authors. *Results.* Twelve studies on a total of 749 patients were included. The triphala-treated groups showed significantly reduced low-density lipoprotein-cholesterol, total cholesterol and triglyceride in 6 studies. Five RCTs demonstrated triphala-treated groups led to statistically significant decrease in body weight, body mass index and waist circumference of obese patients. Moreover, triphala significantly decreased fasting blood glucose level in diabetic patients but not in people without diabetes. No serious adverse event associated with triphala was reported during treatment. *Conclusions.* This review summarized a current evidence to show triphala might improve the lipid profile, blood glucose, the body weight, body mass index and waist circumference under certain conditions. However, large well-designed RCTs are required to confirm this conclusion.

Keywords

triphala, lipid profile, blood glucose, anthropometry, systematic review

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Introduction

According to estimates of current and future worldwide cardiovascular disease (CVD) prevalence have been reported by the World Health Organization (WHO), it is expected to grow by approximately 10% by 2030.[1] Hyperlipidemia, diabetes, and obesity are crucial factors potentiating the development of CVD and related morbidity and mortality.[2,3] Therefore, the risk posed by such cardiometabolic factors should be attenuated to minimize CVD prevalence.[1]

Complementary and alternative medicine (CAM) is commonly used for improving lipid profile, blood glucose, and anthropometric indices. Triphala, used in Ayurvedic and traditional Thai medicine, is a combination of dried fruits of 3 plants, *Phyllanthus emblica* Linn., *Terminalia chebula* Retz., and *Terminalia bellerica* Roxb.[4,5] The major constituents of triphala are tannins, gallic acid, ellagic acid, and chebulinic acid.[5] Previous studies indicated that triphala was multifunctional including antimicrobial,[6,7] antioxidant,[8] anti-inflammatory activities,[9,10] chemopreventive,[11] radioprotective,[12,13] and immunomodulatory.[14] The main purposes of triphala currently used as CAM are lipid-lowering, blood glucose-lowering, anti-obesity, antidiarrheal, and dental care.[15]

To date, a number of non-randomized and randomized controlled trials (RCTs) conducted to assess the antihyperlipidemic,[16,17] antihyperglycemic,[18-20] and anti-obesity effects[21,22] of triphala. Results from previous studies did not fully

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conclusive regarding the effects of triphala on lipid profile, blood glucose and anthropometric parameters.[16-22] This systematic review summarizes the RCT studies currently available to assess the effects of triphala supplements on patients with cardiometabolic risks to provide a comprehensive clinical evidence of triphala as CAM.

Methodology

This systematic review was conducted according to the Cochrane Collaboration Framework guideline[23] and the reporting complies with the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement.[24]

Search Strategies and Study Selection

The following databases were used to search for original research articles without date restrictions: PubMed, ScienceDirect, Web of Science, SCOPUS, DOAJ, JSTOR and Thai Library Integrated System (ThaiLIS). Strategic search terms used were "triphala," "hyperglycemia," "hyperlipidemia," "obesity," and "randomized controlled trial." References of papers obtained from full text review were scanned to identify potential studies not indexed in the above databases. Research articles were included if they were RCTs investigating antilipidemic, antiglycemic, or anti-obesity effects of triphala.

Inclusion criteria for this systematic review were RCT of triphala on any of lipid profile, blood glucose and anthropometric parameters, and the criteria for excluded studies were lack of sufficient information on lipid profile, blood glucose and anthropometric outcomes, and did not indicated dose or dosage form of triphala.

All titles and abstracts were scanned based on inclusion and exclusion criteria. Full text articles of the studies were subsequently assessed independently by 2 of the authors researchers (Wiraphol Phimarn (WP), Bunleu Sungthong (BS)). Disagreements between the reviewers were resolved by discussion with Hiroyuki Itabe (HI).

Data Extraction and Quality Assessment

All data were independently extracted by WP and BS using a standardized extract form. The following information was sought from each article: authors, year of publication, type of study design, participant and intervention characteristics, sample size, duration of therapy, and outcome measurements.

Studies included in this review were assessed for methodological quality by WP and BS using the Jadad scale to evaluate RCT's methodological approach. Studies that met at least 3 out of the 5 criteria were classified as high quality.[25] Thereafter, we used the Cochrane Risk of bias 2.0 tool to evaluate risks of bias in individual studies.[26] This tool contains 7 domains: (1) random sequence generation (selection bias), (2) allocation concealment (selection bias), (3) blinding of participants and personnel (performance bias), (4) blinding of outcome assessment (detection bias), (5) incomplete outcome data (attrition bias), (6) selective reporting (reporting bias), and (7) other biases. The risk of bias for each domain was classified as low risk, unclear, or high risk. Disagreements between the reviewers were settled through discussion with a third party (HI).

Outcome Measurement

The primary outcomes examined were (1) lipid profile parameters (low-density lipoprotein-cholesterol [LDL-C], high-density lipoprotein-cholesterol [HDL-C], total cholesterol [TC], and triglyceride [TG]), (2) blood glucose parameters (fasting blood sugar [FBS] and hemoglobin A1c [HbA1c]) and (3) anthropometric parameters (body weight [BW], body mass index [BMI], and waist circumference [WC]). The secondary outcomes were hepatic and renal function tests and adverse events.

Results

Study Selection

The PRISMA flow diagram of the studies is shown in Figure 1. Four hundred eighty-six (486) related articles were identified through database search, and 269 articles were eligible for screening among them after removal of duplicates. Based on titles and abstracts screened, 14 articles in English and Thai were selected for full text review. Two articles were excluded after full text review: 1 article reported a non-randomized controlled trial and the other did not evaluate the outcome of interest. Therefore, 12 articles[4,16,17,19,20,22,27-32] were included in our study.

Characteristics and Methodological Quality of Selected Studies

The characteristics and methodological quality of the selected studies are summarized in Table 1. Of the 12 studies on a total of 749 patients, 6 studies were conducted in India, 3 studies in Thailand, 1 study in Sri Lanka, 1 study in Norway, and 1 study in Iran. The studies were published between 1990 and 2019. Most of the studies are relatively small-sized trials but 2 studies[16,32] enrolled more than 100 patients. Eight studies enrolled middle aged participants and 2 studies contained young participants as low as teens. Most studies treated the patients for 2 to 3 months and 1 study followed the treatment for 12 months, however, the shortest duration of the study was 25 days.

Three studies[16,17,28] were performed on dyslipidemia patients and 6 studies[4,22,27,30-32] were performed on obese patients. Two studies were performed on prediabetes[10] and diabetes type II patients.[20] Two studies[28,29] investigated triphala mixed with other herbal medicines.

With respect to the methodological quality of the studies included in the systematic review, 8/12 studies were rated to have high quality Jadad scoring ($\geq$3) and low risk of bias. Four studies[20,27,30,31] did not report information allocation concealment and 4 studies[20,29-31] did not report blinding participants and personnel (Figure 2).

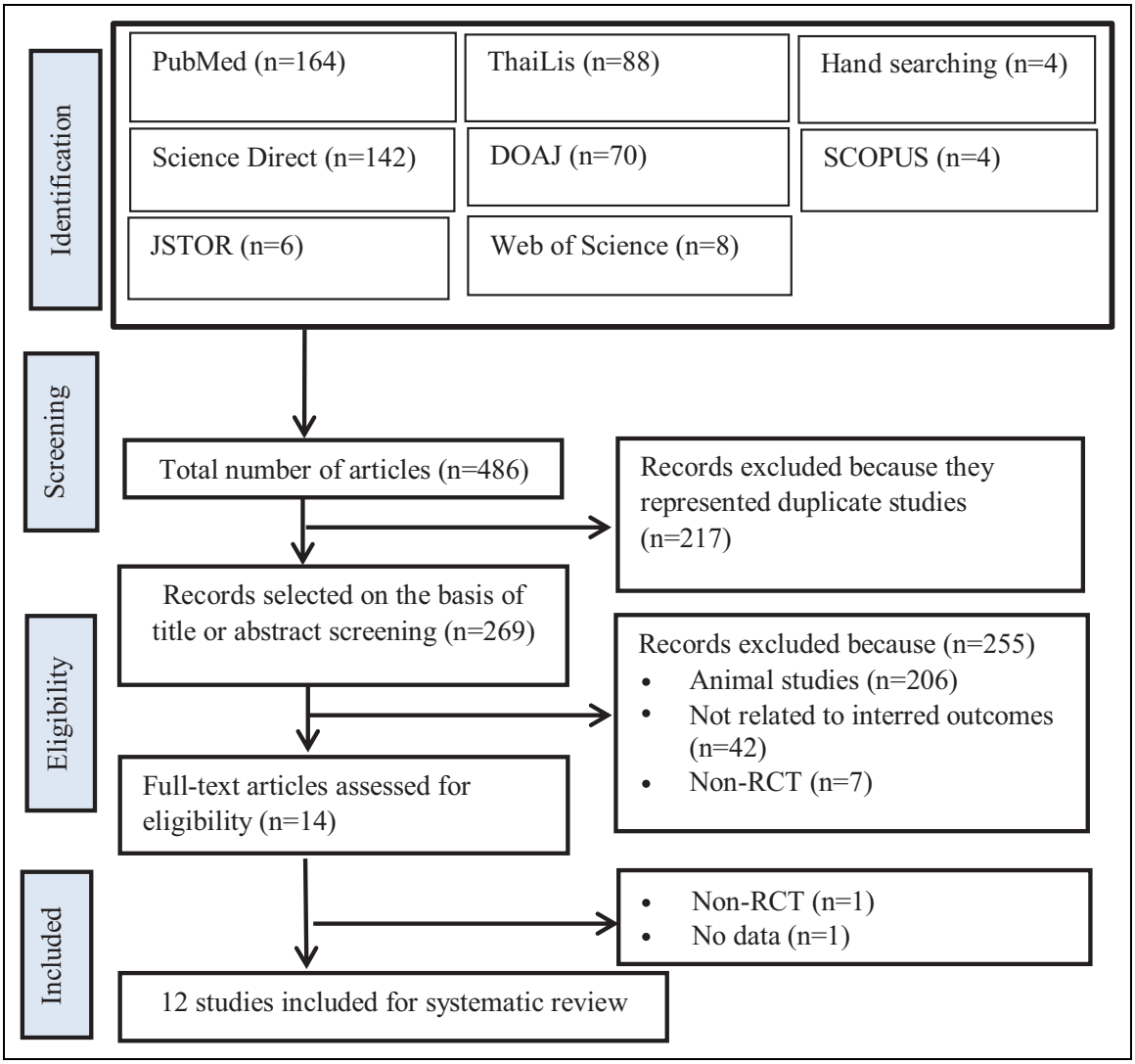

Figure 1. A PRISMA flow diagram describing the selection process for identifying studies included in the systematic review.

Primary Outcomes

Antihyperlipidemia. Nine trials[4,16,17,20,22,27-30] involving a total of 551 patients reported clinical therapeutic efficacy of triphala on lipid profile. Five studies showed patients treated with triphala experienced reduction in LDL-C, TC and TG and also increase HDL level.[4,20,27,29,30] However, Kaewtong study[22] demonstrated no effect of triphala on lipid profile. It might be because this study performed in obese participants and short duration (8 weeks). Lipid lowering effect of triphala was determined in dyslipidemia participants. Nohr's trial[28] performed 12 weeks of treatment of patients with hypercholesterolemia found triphala decreased TC significantly (3.53%, $p < 0.05$) when compared to placebo group. While 1 study in Thailand[17] showed triphala decreased LDL-C (10.89%, $p < 0.05$) and TG (14.39%, $p < 0.05$) when compared to the baseline level. Moreover, Ekanayaka study[16] undertook effect of triphala adjunct statin therapy compared placebo in hypercholesterolemia. The results found triphala treatment did not show additional lowering effect on LDL-C, TG and HDL levels in dyslipidemia patients with Atorvastatin 10 mg daily.

Antihyperglycemia. Administration of triphala had positive effect on long term blood glucose control. A 1 year study of triphala on diabetic patients suppressed FBS level significantly (20.96%; $p < 0.05$).[20] Moreover, an 8 week trial (Prommart, 2014)[19] was studied at a dose of 1,000 mg triphala capsule in prediabetic participants. Triphala-treated group reduced FBS and HbA1c levels significantly compared to baseline level, however, there were no significant difference in both FBS and HbA1c levels between triphala-treated and placebo groups.[4,16,19,29] One study[22] investigated effects of triphala formula on blood glucose in obese patients. This study found triphala formula 1,800 mg/day was not significantly decreased HbA1c level compare to placebo group. This might be because the duration of triphala treatment was too short (8 weeks) for HbA1c monitoring.

Table 1. Characteristics of Studies Included in the Systematic Review.

No	Author	Year	Country	Study design	Participants	Age range or average	Duration	Groups (n)		Outcomes measurement	Jadad scale
								Intervention	Comparators		
Lipid profile											
1	Paranjpe et al[27]	1990	India	DRCT	Obese patients (ave BMI: N/A)	N/A	3 months	Triphala 250 mg (16)	Placebo 250 mg (22)	HDL, TC, TG	3
2	Nohr et al[28]	2009	Norway	DRCT	Hypercholesterolemia (ave LDL = 203.08 ± 28.5mg/dL)	27-70 yrs	12 weeks	Triphala plus other herb 1080 mg/day (18)	Placebo (16)	LDL-C, HDL-C, TC, TG	5
3	Kamali et al[4]	2012	Iran	DRCT	Obese patients (BMI between 30 to 50 kg/m^2)	16-60 yrs	3 months	Triphala 10 g (30)	Placebo (30)	LDL-C, HDL-C, TC, TG	5
4	Wichiansaen[17]	2012	Thailand	DRCT	Dyslipidemia patients	35-65 yrs	4 weeks	Triphala 500 mg bid (20)	Placebo bid (20)	LDL-C, TG	4
5	Singh et al[20]	2015	India	RCT	DM type 2 patients	54.3 ± 1.75 yrs	12 months	Triphala powder 5 g bid (20)	Placebo bid (20)	LDL-C, HDL-C, TC, TG	1
6	Chaudhary and Rohila[29]	2015	India	RCT	Hypertensive patients	60-90 yrs	30 days	Triphala powder 6 g/day plus other herb (20)	Placebo (20)	LDL-C, HDL-C, TC, TG	2
7	Ekanayaka et al[16]	2017	Sri Lanka	DRCT	Dyslipidemia patients with Atorvastatin 10 mg daily	35-75 yrs	12 weeks	Triphala 634 mg 3 tablets/ day (101)	Placebo (97)	LDL-C, HDL-C, TC, TG	4
8	Kaewtong and Sugraroek[22]	2018	Thailand	DRCT	Obese patients (BMI between 25 to 29.99 kg/m^2)	20-60 yrs	8 weeks	Triphala 600 mg tid (20)	Placebo tid (20)	LDL-C, TG	5
9	Pai et al[30]	2018	India	RCT	Obese patients (BMI > 30 kg/m^2)	16-60 yrs	48 days	Triphala 24 g bid (30)	Life style change (30)	LDL-C, HDL-C, TC, TG	2
Blood glucose											
1	Kamali et al[4]	2012	Iran	DRCT	Obese patients (BMI between 30 to 50 kg/m^2)	16-60 yrs	3 months	Triphala 10 g (30)	Placebo (30)	FBS, HbA1C	5
2	Prommart[19]	2014	Thailand	DRCT	Prediabetes patients	25-65 yrs	8 weeks	Triphala capsule 500 mg bid (15)	Placebo bid (14)	FBS, HbA1C	4
3	Singh et al[20]	2015	India	RCT	DM type 2 patients	54.3 ± 1.75 yrs	12 months	Triphala powder 5 g bid (20)	Placebo bid (20)	FBS, HbA1C	1
4	Chaudhary and Rohila[29]	2015	India	RCT	Hypertensive patients	60-90 yrs	30 days	Triphala powder 6 g/day plus other herb (20)	Placebo (20)	FBS	2
5	Ekanayaka et al[16]	2017	Sri Lanka	DRCT	Dyslipidemia patients with Atorvastatin 10 mg daily	35-75 yrs	12 weeks	Triphala 634 mg 3 tablets/ day (101)	Placebo (97)	FBS	4
6	Kaewtong and Sugraroek[22]	2018	Thailand	DRCT	Obese patients (BMI between 25 to 29.99 kg/m^2)	20-60 yrs	8 weeks	Triphala 600 mg tid (20)	Placebo tid (20)	FBS, HbA1C	5
Anthropometry parameters											
1	Paranjpe et al[27]	1990	India	DRCT	Obese patients	N/A	3 months	Triphala 250 mg (16)	Placebo 250 mg (22)	BMI, WC, HC	3
2	Kamali et al[4]	2012	Iran	DRCT	Obese patients (BMI between 30 to 50 kg/m^2)	16-60 yrs	3 months	Triphala 10 g (30)	Placebo (30)	BMI, WC, HC	5
3	Kaewtong and Sugraroek [22]	2018	Thailand	DRCT	Obese patients (BMI between 25 to 29.99 kg/m^2)	20-60 yrs	8 weeks	Triphala 600 mg tid (20)	Placebo tid (20)	BMI, WC	5

(continued)

Table 1. (continued)

No	Author	Year	Country	Study design	Participants	Age range or average	Duration	Groups (n)		Outcomes measurement	Jadad scale
								Intervention	Comparators		
4	Pai et al[30]	2018	India	RCT	Obese patients (BMI > 30 kg/m^2)	16-60 yrs	48 days	Triphala 24 g bid (30)	Life style change (30)	BMI, WC	2
5	Chaitralakshmi and Basarigidad[31]	2019	India	RCT	Obese patients (BMI > 25 kg/m^2)	18-60 yrs	25 days	Triphala (20)	Herbal formula (20)	BMI, WC	2
6	Salunke et al[32]	2019	India	DRCT	Obese patients (BMI > 25 kg/m^2)	18-60 yrs	3 months	Triphala extract 1000 mg bid for overweight and 1500 mg bid for obese participants (66)	Placebo (64)	BW, WC	5

Remark: N/A: Not available; yrs: years; RCT: randomized controlled trial; DRCT; double-blind randomized controlled trial; DM, diabetes mellitus; LDL-C: low-density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol, TC: total cholesterol, TG: triglyceride; FBS, fasting blood sugar; BW, body weight; BMI, body mass index; WC, waist circumference.

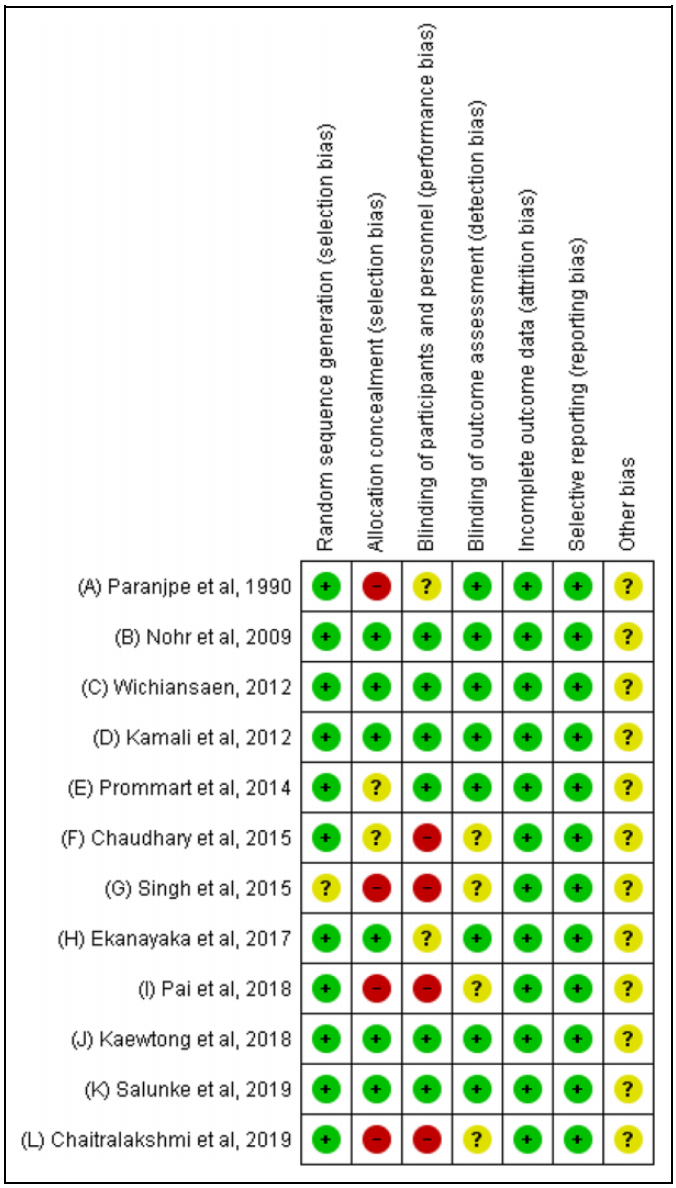

Figure 2. Risk of bias summary from individual studies (+ = low risk, − = high risk, and? = unclear).

Anti-obesity. Six studies[4,22,27,30-32] on a total of 357 participants reported on anthropometric parameters. All of the studies performed triphala effect on obese participants. Five studies[4,27,30-32] showed that triphala significantly decreased body weight, body mass index and waist circumference. However, Kaewthong study[22] found that triphala formula did not improve anthropometric parameters when compared with baseline.

Secondary Outcomes

Results of renal function test for 388 participants in 5 trials were reported and showed that triphala had no effect on serum creatinine (SCr) or blood urea nitrogen (BUN). Furthermore, all the 5 trials showed that changes in aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) levels were not significant in the triphala group compared to those in the control group.[4,16,17,20,29]

Only 1 study[28] reported adverse effects in the triphala-treated group. These adverse events were loose stools (n = 4), obstipation (n = 1), changed sense of taste (n = 1), dermatological effects (n = 1), and tiredness (n = 1).

Discussion

This study is a systematic review to summarize currently available RCT evidences on the efficacy and safety of triphala for hyperlipidemia, hyperglycemia, and obesity. The current study showed Triphala combined with antibiotics has synergistic activity against the multidrug resistant bacteria.[7] However, there were no evidence for Triphala combined with modern medicine on lipid profile, blood glucose and anthropometric parameter.

From these data, it is suggested that triphala used as monotherapy could significantly improve the blood glucose, lipid profile and anthropometric parameters.[4,20,28,32] There were a few adverse effects related to triphala administration but there were no effects on liver and renal function.

Hyperlipidemia, hyperglycemia, and obesity are crucial risk factors for CVD.[3,33,34] Reports suggest that improvement in lipid profile and blood glucose and anthropometric parameters is associated with reduced risk of coronary and vascular events.[35,36] Triphala has been reported to lower lipid and anthropometric parameters, which could reduce cardiometabolic risk.

The effects of triphala on the lipid profile suggest that triphala is effective in decreasing LDL-C, TC, and TG. The lipid-lowering properties of triphala have been explained by triphala that might decrease cholesterol absorption,[37,38] inhibit HMG-CoA reductase[39] and regulate lipid accumulation by downregulation of adipogenic genes.[40] There were previous reports regarding the reduction LDL-c, TC and TG levels related decreased risk in cardiovascular complications.[41,42] A meta-analysis demonstrated that the reduction in LDL-C of low-risk subjects with HMG-CoA reductase inhibitors and this LDL-C reduction associated cardiovascular mortality.[43]

Our systematic review showed that triphala treatment significantly decreased FBS and HbA1c in diabetic patients. As most studies on triphala had been performed on normoglycemic participants, no effects were observed on FBS and HbA1c.[4,16,19] Possible mechanisms of the glucose-lowering activity of triphala could be decrease in insulin resistance and increase in glucose uptake by enhancing peroxisome proliferator activated receptor (PPAR)α, PPARγ,[44,45] and incretin/cyclic adenosine monophosphate (cAMP) signaling as well as by modulating the proliferation of islet β cells.[46] In normoglycemic participants, FBS and HbA1c were not decreased significantly by triphala formula. This may result from the recruited trials in this systematic review conducted in participants with normal blood glucose level or pre-diabetes. The FBS levels may not be high enough to detect the difference between triphala and control group. However, it should be cautious that

with too short duration of study (≤3 months), the HbA1c monitor the previous review suggested that should be provided an average measurement over 3 months.[47]

The RCT studies reported that triphala supplementation reduced BW, BMI, and WC; however, the mechanism is still unclear. An animal study[48] on the effects of triphala on mice fed high fat diet for 10 weeks showed that triphala decreased body weight, body fat, and energy intake. The proposed mechanisms underlying these observed effects were that triphala regulates expression of CCAAT/enhancer-binding proteins (C/EBP) and *PPARγ* and blocks adipogenesis by stimulating Wnt/β-catenin signaling.[49] The current evidence hypothesized obesity increased adipose tissue and reduced adiponectin levels. The adipocyte dysregulation is a factor which associates with the imbalance of body homeostasis and pro-and anti-inflammatory mechanisms. As a results obesity induces metabolic complication and increases cardiovascular risk.[50,51] Although, triphala supplement reduced BW, BMI, and WC significantly, the durations of treatment in the recruited studies were short, with the longest of 3 months. That means our results illustrate short-term anthropometric outcomes. Therefore, a long terms study of triphala on anthropometric parameters reduction should be further investigated.

This systematic review found that triphala had no effect on liver and renal function tests. In addition, only 1 study[28] reported a small number of participants who experienced adverse effects including loose stools, obstipation, change in sense of taste, nausea, dermatological side effects, and tiredness. However, gastrointestinal and dermatological complaints were also found in the placebo group. This indicated that both side effects may be influenced by other diet-or lifestyle-related factors.

The primary strength of our study is the use of a systematic approach. Indeed, this is the first comprehensive systematic review on the efficacy and safety of triphala in hyperlipidemia, hyperglycemia, and obesity. We also used Jadad's scale and A Cochrane Risk of Bias Assessment Tool (ACROBAT) to assess the quality of studies included in the systematic review. Overall, the studies had low risk of bias with high quality although 4 studies were not double-blind trials. These trials were conducted without adequate concealment or blinding. One of the major limitations of this systematic review is the possible existence of bias due to the presentation of small study effect of most of the included studies. Most studies did not indicate whether triphala was used as an extract or a capsule containing powder; hence, all included studies demonstrated a wide range of triphala formulations. Moreover, the number of RCTs should be highlight because only 12 studies were included.

Our results indicated that triphala was safe when used for a duration of 25 days-1 year. There were limited data on the long-term safety of triphala in all studies included in our systematic review; hence, long-term safety of triphala should be studied. Well-designed, large, multicenter, randomized, placebo-controlled trials investigating long-term effects such as risk of cardiovascular disease, mortality or survival rate of triphala are needed to support current evidence. To improve the quality of clinical study of herbal interventions, item 4 is required for reporting RCTs according to CONSORT (Consolidated Standards of Reporting Trials) checklist.[52] For instance, content of herbal product components and standardized products with the quantity of active/marker constituents have to be described and controlled to ensure that the outcomes of the studies are consistency with low batch to batch variability.

Conclusion

Based on our current systematic review, the triphala formula was effective on the reduction of lipid profile and blood glucose level. In addition, body weight and BMI of patients receiving triphala were also significantly decreased with no serious adverse events reported. In order to support the triphala formula as an alternative medicine, more RCT with well-designed and long term intervention should be performed to confirm the efficacy of triphala on lipid profile, blood glucose and anthropometric parameters.

Authors' Note

WP and BS were responsible for design and conception of the study, collected, interpreted data, drafted and revised manuscripts. HI interpreted data, drafted and revised manuscripts. All authors read and approved the manuscript. This research did not involve human subject nor animal. Therefore, research ethics and patient consent were not required. This research did not involve human subject nor animal. Therefore, research ethics and patient consent were not required.

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Declaration of Conflicting Interests

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