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The impact of Emblica Officinalis (*Amla*) on lipid profile, glucose, and C-reactive protein: A systematic review and meta-analysis of randomized controlled trials

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ABSTRACT

Background and aims: *Emblica Officinalis* (*Amla*) is a plant often utilized in traditional medicine due to its purported anti-inflammatory, antioxidant, hypoglycemic, and hypolipidemic properties. However, current evidence regarding its potential for preventing and treating metabolic abnormalities associated with chronic diseases remains unclear.

Methods: This systematic review and meta-analysis aimed to examine the effects of *Amla* supplementation on lipid profile, glucose, and C-reactive protein (CRP) concentrations in adults. We completed a systematic search (current as of December 2022) of all available randomized controlled trials (RCTs) in the database including ISI Web of Science, PubMed, Scopus, and Embase. Any effect's mean difference (MD) was calculated using a random-effects model. Weighted mean difference (WMD) and 95% confidence intervals (CIs) were calculated also calculated using a random-effects model.

Results: Five RTCs were included in the meta-analysis. Following *Amla* supplementation, pooled results showed a significant reduction in CRP ($p = 0.002$), fasting blood glucose (FBG) ($p < 0.001$), low-density lipoprotein cholesterol (LDL-c) ($p < 0.001$), total cholesterol (TC) ($p < 0.001$), and serum triglyceride (TG) ($p < 0.001$) concentrations as well as an increase in high-density lipoprotein cholesterol (HDL-c) ($p < 0.001$). The baseline concentration of biochemical indicators was used for subgroup analysis.

Conclusion: *Amla* supplementation shows promise for improving metabolic parameters in adults. In general, the populations included in the analysis were generally 40–58 years with an average BMI of 25.5 and a length of intervention ranging from 3 to 12 weeks. Thus additional investigations are warranted to confirm and expand the findings presented herein.

1. Introduction

Morbidity and mortality rates attributed to cardiovascular disease (CVD) are consistently rising [1], persisting as the leading cause of death worldwide. Metabolic abnormalities (i.e., dyslipidemia, hyperglycemia, and inflammation) independently and additively increase the risk of CVD-related mortality attributable to

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sudden cardiac death, acute myocardial infarction, and stroke [2]. Common interventions for managing CVD and metabolic disorders include pharmacotherapy as well as lifestyle modifications such as increasing physical activity, weight loss, and dietary interventions [3–6]. The success of these approaches is limited by the accessibility and cost of pharmacological treatment and/or the feasibility of lifestyle change. As rates continue to rise, without signs of abating, novel sustainable approaches are highly warranted.

Traditional medicinal plants, which contain bioactive phytoconstituents, represent an alternative therapy for improving and managing cardio-metabolic disorders [7–11]. While many phytoconstituents have been included in clinical trials, these plant metabolites are largely tannins and tea extracts with limited beneficial effects on cardiometabolic diseases. However, *Amla* has recently emerged as a plant of interest due to its ethnomedicinal properties [12].

Amla (*Phyllanthus Emblica, Emblica Officinalis*, Indian gooseberry) is a medium-sized tree in the Phyllanthocin family found in all parts of Asia and widely distributed in tropical and subtropical countries [13]. Although there are various pharmacological properties within the entire plant, the *Amla* fruit has been used in traditional medicine [14–18]. The potential anti-inflammatory, antioxidant, anti-hyperglycemic, and antihyperlipidemic effects, of *Amla* are hypothetically due to its rich source of ascorbic acid, phenols, and tannins, such as gallic acid and flavonoids. These collective phytoconstituents may explain its beneficial effect on respiratory illnesses (e.g., asthma, bronchitis, pulmonary tuberculosis), cancer, and diseases (e.g., obesity, type 2 diabetes, cardiovascular diseases) reported in Chinese and Indian medicine [19]. In addition, *Amla* the dietary fiber component decreases the discharge of cholesterol by inhibiting the enterohepatic circulation of cholesterol [20]. Moreover, the hydrophobic properties of *Amla* increased capacity for micelle formation in the intestine, interfering with the absorption of cholesterol [21].

While there is great potential to leverage bioactive components of plants for the discovery and development of modern therapies, the results from randomized controlled trials (RCTs) examining the effect of *Amla* supplementation on the constellation of risk factors for cardiometabolic diseases (total cholesterol large, serum triglyceride [TG], low-density lipoprotein cholesterol [LDL-c], high-density lipoprotein cholesterol [HDL-c], fasting blood glucose [FBG], and C-reactive protein [CRP], the high variability among completed human trials limits conclusive support for supplementation. Therefore, this systematic review and meta-analysis aimed to determine the current state of the evidence and elucidate the effectiveness of *Amla* supplementation for improving lipid profile, glucose, and CRP concentrations in adults.

2. Materials and methods

This systematic review and meta-analysis were conducted in adhering to the PRISMA (Preferred Reporting Items for Systematic review and Meta-Analyses) guidelines [22]. The following criteria were employed population (aged >18 years old), Intervention (*Amla* supplementation), Comparison (matched control group), Outcome (CRP, FBG, and lipid profile) (PICOS) model, and TC, LDL-c, HDL-c, serum TG, FBG and CRP levels collected from randomized controlled trials (RCTs) were included.

PubMed, Scopus, Cochrane library, Embase, and ISI Web of Science databases were searched up to December 2022, with no limitation on years since publication or language. Our search strategy consisted of the following medical subject headings (MeSH) and non-MeSH keywords: ((Phyllanthus Emblica [Title/Abstract]) OR (Phyllanthus emblicas [MeSH Terms])) OR (emblica, Phyllanthus [Title/Abstract])) OR (Emblica Officinalis [Title/Abstract])) OR (Emblica Officinalis [Title/Abstract])) OR (officinali, Emblica [Title/Abstract])) OR (Mirobalanus embilica [Title/Abstract])) OR (Mirobalanus embilicas [Title/Abstract])) OR (embilicas, Mirobalanus [Title/Abstract])) OR (*Amla* [Title/Abstract])) OR (*Amlas* [Title/Abstract])) OR (PEPW80-1 polysaccharide, Phyllanthus emblica [Title/Abstract]) OR (Indian gooseberry [Title/Abstract])).

2.1. Search strategy and eligibility criteria

All citations found in our searches were entered into endnote software for screening (EndNote X8, Thomson Reuters, New York). The title and abstract were screened by two independent reviewers and performed a full-text assessment (LS and MR). Disagreements were resolved by consensus. Investigations were included if the following criteria were met: (1) carried out as an RCT; (2) study participants were adults (≥18 years old); (3) investigated the impact of *Amla* supplementation on CRP, glucose, and lipid profile (including blood TG, TC, LDL-c, and HDL-c); (4) contained enough information to establish effect size for our outcome measures; and (5) had a trial duration of more than 1 week. Studies were excluded if: (1) a placebo or control group was not incorporated, (2) semi-experimental, (3) they were non-RCTs or trials without a control/placebo group, (4) literature reviews, (5) cross-sectional, (6) case reports, (7) republished data, (8) animal studies, and (9) grey literature, including congress abstracts, dissertations, and patents; (10) if their information could not be extracted, and (11) if publications did not report outcomes. We also manually checked the reference lists of included and previous review studies. More search strategy details can be found in Supplementary Table 1.

2.2. Data extraction

Two reviewers (LS and MR) abstracted data from eligible studies by using a standardized electronic form (Excel, Microsoft Office): first author, country, year of publication, participant's health status, study design, indication, sample size, body mass index (BMI), age, study duration, dose, and the mean ± standard deviation (SD) of our outcome measures for both the intervention and placebo/control groups (at baseline and follow-up). Values were converted to the most common units of expression whenever possible. Additionally, data in graphical figures were extracted via the GetData Graph Digitizer 2.24 program [23].

2.3. Quality assessment

Two reviewers (MR and LS) assessed the quality of each selected study using the Cochrane risk of bias tool for RCTs [24]. The quality of studies was assessed using the following seven criteria: 1) random sequence generation, 2) allocation concealment, 3) blinding of participants and personnel, 4) blinding of outcome assessment, 5) incomplete outcome data, 6) selective reporting, and 7) other probable sources of biases. Based on The Cochrane Handbook recommendation, studies were categorized as low (L), high risk of bias (H), or unclear (U) regarding each field of bias [24]. Cochrane risk of bias of included studies is outlined in Supplemental Table 2.

2.4. Statistical analysis

The statistical analysis was conducted using STATA MP V.16.0. (StataCorp, College Station, Texas, USA). $P < 0.05$ was considered statistically significant. For RTCs with no reported SD of the mean difference, the following formula was used: SD change $= \sqrt{[(\text{SD baseline})\,2 + (\text{SD final})\,2 - (2 \times 0.9 \times \text{SD baseline}}$

×SD final)] [25]. For RTCs that only reported the Standard Error of the Mean (SEM), SD was calculated using the following formula: $SD = SEM\ x\ \sqrt{n}$, where "n" is the number of participants in each group. Weighted mean differences (WMD) and 95% confidence interval (CI) of our outcome measures from both intervention and placebo/control groups were utilized to produce overall effect sizes as established by the random-effects model approach of DerSimonian and Laird [26]. Subgroup analyses were conducted based on baseline marker concentration, *Amla* dosage (≤1 g/d and >1 g/d), and duration of the intervention (<8 weeks and ≥8 weeks). Heterogeneity was assessed with the I^2 statistic ($p < 0.05$ and $I^2 > 50\%$) after visual inspection of forest plots [27]. A significance level of $I^2 > 40\%$ was considered as clinically important heterogeneity. Sensitivity analysis was conducted by removing each study, one by one, and recalculating the pooled evaluations. The evidence for small-study effects was assessed by the Egger regression asymmetry test. Publication bias was assessed by the funnel plot and Egger's tests [28]. The current investigation is an analysis of published data, which does not require ethics committee approval.

3. Results

3.1. Study selection

Out of the 2936 relevant publications identified in the primary search, 936 duplicates were excluded. The 2020 remaining records were consequently screened, and 1619 were excluded based on title and abstract (n = 1212) as well as other reasons such as lack of relevance (n = 300), cell line (n = 20), and animal (n = 14), review articles (26) and study design (n = 21). A total of 26 publications were selected for further evaluation of the full text. An additional 17 records were excluded from these due to a lack of relevance, not incorporating a placebo/control group and duplicate data (n = 4), or not reporting adequate data of outcomes (n = 7). Finally, a total of 5 eligible RCTs were incorporated for meta-analysis in the current investigation. The PRISMA flow diagram of the study selection process is depicted in Fig. 1.

3.2. Study characteristics

Five studies were included in the current meta-analysis. The general characteristics of the five eligible RCTs allocated into 11 arms are shown in Table 1. In total, 327 participants were included across the studies. Sample sizes varied from 8 to 97 participants, with ages ranging from 40 to 58 years, and mean baseline BMI ranged from 24 to 27 kg/m^2 across studies. All trials included both sexes, except for one [29], which was only performed in men. Two studies were conducted on individuals with type 2 diabetes [30,31], two on individuals with dyslipidemia [32,33], and one included smokers [29]. There was a difference in the extract from *Amla*, such that four studies used Emblica Officinalis [29,30,32,33], and one used Phyllanthus Emblica [31]. The duration of intervention ranged from three [30] to 12 31, 33 weeks. The studies were published between 2011 [30] to 2019 [33] and were conducted in Oman [30] and India [29,31–33].

3.3. Results from quality assessments

All RCTs had a low risk of bias in the randomization process [29,31,32,34,35] and low deviation from the intended intervention, except one study [32]. All studies showed a low outcome measurement and low selection of the reported result [29,31,32,34,35]. All except one study [32] had low missing outcome data and low overall bias [29–31,35]. Details of the risk of bias assessment are described in Table 2. Based on the Cochrane tool, four studies were deemed high-quality [29–31,33], whereas one had medium-quality [32] due to deviation from the intended interventions and missing outcome data. Two trials had randomized designs [34,36], and three were double-blind randomized.

3.4. Meta-analysis results

3.4.1. The effect of Amla supplementation on serum TG

Four studies, including 220 participants, reported the effect of *Amla* supplementation on TG concentration in the serum [29,30,33,37]. The collective data supported *Amla* supplementation as a contributor to reduced serum TG (WMD: 51.92 mg/dL, 95% CI: 76.70, −27.14; $p < 0.001$) (Fig. 2A) with considerable heterogeneity between studies ($p < 0.001$, $I^2 = 79.8\%$). Regarding the finding of the source of heterogeneity, we conducted a subgroup analysis based on baseline concentration, the dosage of intervention (≤1 g/d and >1 g/d), and duration of the intervention (<8 weeks and ≥8 weeks), which considerably removed the heterogeneity. The results of subgroups revealed that A*mla* supplementation had a protective effect on blood TG concentration in all of the subgroups except those who had TG > 150 mg/dL in their baseline (Table 3).

3.4.2. The effect of Amla supplementation on TC

The impact of *Amla* supplementation on TC was examined in four studies [29,30,33,37], including a total of 322 participants, and the outcome reported TC as an outcome measure reduced after the intervention period (WMD: 39.39 mg/dL, 95% CI: 54.80, −23.98; $p < 0.001$) with considerable between-study heterogeneity ($I^2 = 87.7\%$, $p < 0.001$) (Fig. 2B). We performed all of the subgroups mentioned above. It was observed that *Amla* supplementation was associated with a decrease of TC in all categories (Table 3).

3.4.3. The effect of Amla supplementation on LDL-c

Overall, 11 arms of RCTs were included (four studies, including 322 participants) [29,30,33,37], and the effect of *Amla* supplementation was evaluated on LDL-c. The pooled effect size indicated a substantially decreased LDL-c concentration (WMD: 34.30 mg/dL, 95% CI: 48.65, −19.94; $p < 0.001$) with a high source of heterogeneity ($I^2 = 84.7\%$, $p < 0.001$) (Fig. 2C). The result of the subgroup analysis showed that *Amla* supplementation significantly reduced LDL-c concentration in all groups (Table 3).

3.4.4. The effect of Amla supplementation on HDL-c

Eleven arms of RCTs (Four studies, including 322 participants) [29,30,33,37] reported HDL-c as an outcome measure. The effect size of these studies was combined and showed a significant increase in HDL-c (WMD: 9.22 mg/dL, 95% CI: 3.74, 14.70; $p < 0.001$) with high heterogeneity ($I^2 = 91.3\%$, $p < 0.001$) (Fig. 2D). To minimize the possible source of heterogeneity, subgroup analysis was performed. These analyses showed that HDL-c concentration increased in all subgroups with supplementation < g/d of *Amla* (Table 3).

3.4.5. The effect of Amla supplementation on FBG

Two included studies, including 62 participants, evaluated the effects of *Amla* on the FBG concentration [29,30]. The test of overall effects indicates that *Amla* supplementation significantly reduced FBG (WMD: 12.69 mg/dL, 95% CI: 24.10, −1.27; $p = 0.030$) with high heterogeneity ($I^2 = 79.5\%$, $p < 0.001$) (Fig. 2E). The increase was observed in all of the subgroups with supplementation >1 g/d and continuing ≥8 weeks among participants with a FBG≥100 (Table 3).

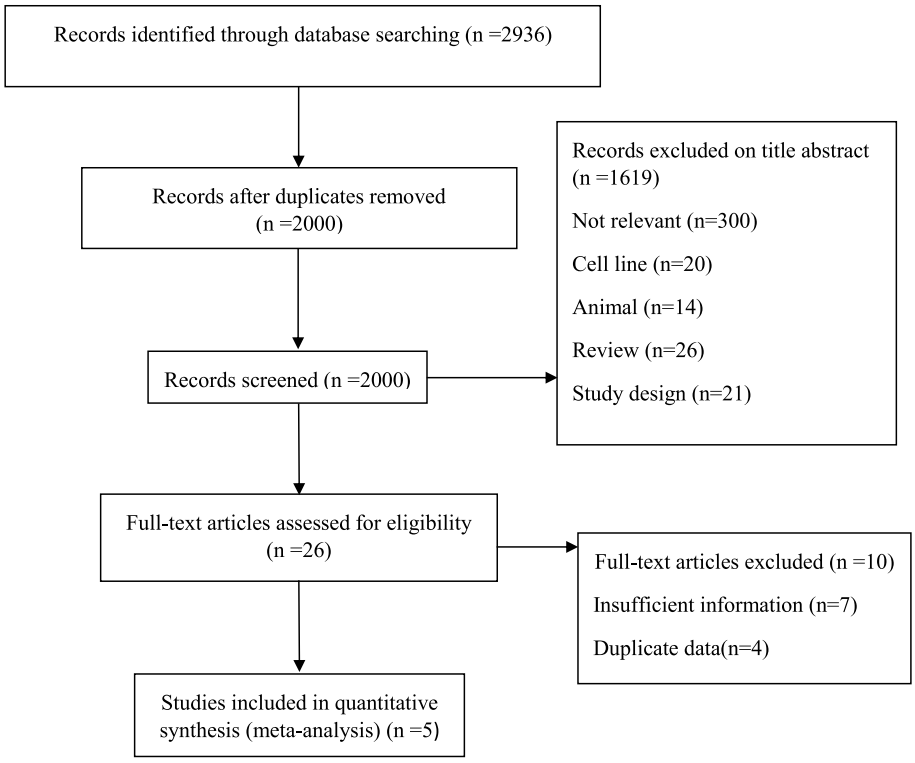

Fig. 1. PRISMA flow diagram of the study selection process.

3.4.6. The effect of Amla supplementation on CRP

Two studies, including 90 participants, were analyzed to evaluate effects on CRP [29,37]. In the three arms, *Amla* supplementation significantly reduced CRP concentration (WMD: 1.30 mg/dL, 95% CI: 2.14, −0.46; $p = 0.002$) (Fig. 2F), with evidence of high heterogeneity ($I^2 = 87.8\%$, $p < 0.001$). We did not perform subgroup analyses given the small number of available studies.

3.5. Sensitivity analysis

To identify the influence of each trial on the total effect size, we excluded each study and repeated the analysis of the effect sizes for the influence of *Amla* supplementation on lipid profile, glucose, and CRP concentrations.

3.6. Publication bias

Begg's test and Egger's linear regression were implemented to assess publication bias in studies evaluating the effects of *Amla* supplementation on lipid profile, FBG, and CRP concentrations. These tests did not show publication bias for CRP (Egger's linear regression $p = 0.624$, Begg's test $p = 1.000$), FBG (Egger's linear regression $p = 0.705$, Begg's test $p = 0.548$), HDL-c (Egger's linear regression $p = 0.168$, Begg's test $p = 0.640$), LDL-c (Egger's linear regression $p = 0.257$, Begg's test p = 0.640), TC (Egger's linear regression $p = 0.812$, Begg's test $p = 0.755$), and serum TG (Egger's linear regression $p = 0.322$, Begg's test $p = 0.474$) (Fig. 3).

4. Discussion

The current meta-analytic is the first that evaluated the effects of *Amla* supplementation on lipid profile, FBG, and CRP concentrations in adults. Outcomes support *Amla* supplementation as a consistently contributor to improvements in lipid profile as evidenced by reduced TC, LDL-c, and TG levels and increased HDL-c. Moreover, lower FBG and reduced CRP were observed relatively consistent throughout the studies. According to subgroup analysis, *Amla* supplementation at tested doses raning 3−12 weeksappears to afford beneficial effects on lipid profile. However, the HDL-c was increased in that studies used *Amla* at a dosage of <1 g/d.

Hyperlipidemia and hyperglycemia known as significant risk factors for the increasing rate of CVD, cerebrovascular disease, and peripheral vessel involvement disease morbidity and mortality [Goodarzi, 2021 #101][7]. According to several preclinical and clinical studies, the *anti*-hyperlipidemic activity of *Amla* extract is related to antioxidant and hypolipidemic effects [2−6]. Although the precise mechanism by which *Amla* exerts this beneficial effect on lipid profile is presently not clear, inhibition of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kB) activity, superior ethoxide scavenging, as well as immunomodulatory and cytoprotective mechanisms, have been proposed related to work in animal models [38]. Notwithstanding the favorable modifications in the lipid profile via several mechanisms, including interference with the cholesterol absorption [8], inhibition of β-hydroxy β-methylglutaryl-*CoA* (HMG-CoA) reductase activity, and an increase in lecithin cholesterol acyltransferase activity, are potential pathways that may explain in humans [9]. This meta-analysis, supports *Amla* supplementation as a potential strategy to reduce serum concentrations of TC and LDL-c, in agreement with previous studies that reported similar effects in dyslipidemic, diabetics, and smokers [3, 4, 10]. Recently, Upadya et al. showed that *Amla* supplementation for 12 weeks significantly lowered TC, LDL-c, and very-low-density lipoprotein (VLDL) in patients with dyslipidemia [4]. In another clinical study, *Amla* supplementation for 60 days improved TC, LDL-c, and HDL-c in chronic smokers [10]. Akhtar et al. also reported significant decreases in TC and TG in serum and increases in HDL-c in both healthy volunteers and diabetic patients receiving 2−3 g/d of *Amla* powder [3]. The analysis herein also found a

Table 1
Characteristic of included studies in meta-analysis.

Author	Publication Year	Country	Study Design	Participant	Sex	Trial Duration (Week)	Means Age		Means BMI	Intervention			Sample Size		Result
							IG	CG		Treatment group	Emblica Officinalis (Amla) dose (gr)	Control group	IG	CG	
Akhtar et al. [30]	2011	Oman	Randomized	healthy	F/M	3	NR	NR	NR	Emblica officinalis	1	cellulose	4	4	TC↓, TG↓, HDL-c ↔, LDL-c↓, FBG↓
Akhtar et al. [30]	2011	Oman	Randomized	healthy	F/M	3	NR	NR	NR	Emblica officinalis	2	Cellulose	4	4	TC↓, TG↓, HDL-c ↑, LDL-c↓ FBG↓
Akhtar et al. [30]	2011	Oman	Randomized	healthy	F/M	3	NR	NR	NR	Emblica officinalis	3	Cellulose	4	4	TC↓, TG↓, HDL-c ↑, LDL-c↓ FBG↓
Akhtar et al. [30]	2011	Oman	Randomized	Type 2 diabetics	F/M	3	NR	NR	NR	Emblica officinalis	1	glibenclamide	4	4	TC↓, TG↓, HDL-c ↔, LDL-c↓, FBG↓
Akhtar et al. [30]	2011	Oman	Randomized	Type 2 diabetics	F/M	3	NR	NR	NR	Emblica officinalis	2	glibenclamide	4	4	TC↓, TG↓, HDL-c ↑, LDL-c↓ FBG↓
Akhtar et al. [30]	2011	Oman	Randomized	Type 2 diabetics	F/M	3	NR	NR	NR	Emblica officinalis	3	glibenclamide	4	4	TC↓, TG↓, HDL-c ↑, LDL-c↓ FBG↓
Usharani et al. [31]	2013	India	Prospective, randomized, DB, PC	Type 2 diabetics	F/M	12	57.6	56.9	24.88	Phyllanthus emblica	0.5	cellulose lactose	20	20	TC↓, TG↓, HDL-c ↑, LDL-c↓ CRP↓
Usharani et al. [31]	2013	India	Prospective, randomized, DB, PC	Type 2 diabetics	F/M	12	57.75	56.9	25.22	Phyllanthus emblica	1	cellulose lactose	20	20	TC↓, TG↓, HDL-c ↑, LDL-c↓ CRP↓
Biwas et al. [29]	2014	India	Randomize, DB, PC	Smoker	M	9	NR	NR	NR	Emblica Officinalis	0.5	cellulose lactose	20	10	TC↓, TG↓, HDL-c ↑, LDL-c↓ CRP↓, FBG↓
Kavita et al. [32]	2016	India	Open randomized	Dyslipidemia	F/M	8	NR	NR	NR	Emblica Officinalis Garten	12	minimal dietary manipulations	52	20	TC↓, HDL-c ↑, LDL-c↓
Upadya et al. [33]	2019	India	Randomize, DB, PC, multicenter	Dyslipidemia	F/M	12	40.7	42.2	26.9	Emblica Officinalis	1	roasted rice powder	49	48	TC↓, TG↓, HDL-c↓, LDL-c↓

Abbreviations: IG, intervention group; CG, control group; DB, double-blinded; PC, placebo-controlled; CO, controlled; R, randomized; NR, not reported; F, Female; M, Male.

Table 2
Risk of bias assessment.

Study	Random Sequence Generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective outcome reporting	Other sources of bias
Akhtar et al., 2011 [30]	L	L	H	U	L	U	U
Usharani et al., 2013 [31]	L	L	U	U	L	L	L
Biwas et al., 2014 [29]	L	L	H	U	L	U	L
Kavita et al., 2016 [32]	L	L	U	U	U	L	U
Upadya et al., 2019 [33]	L	L	U	U	L	L	L

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

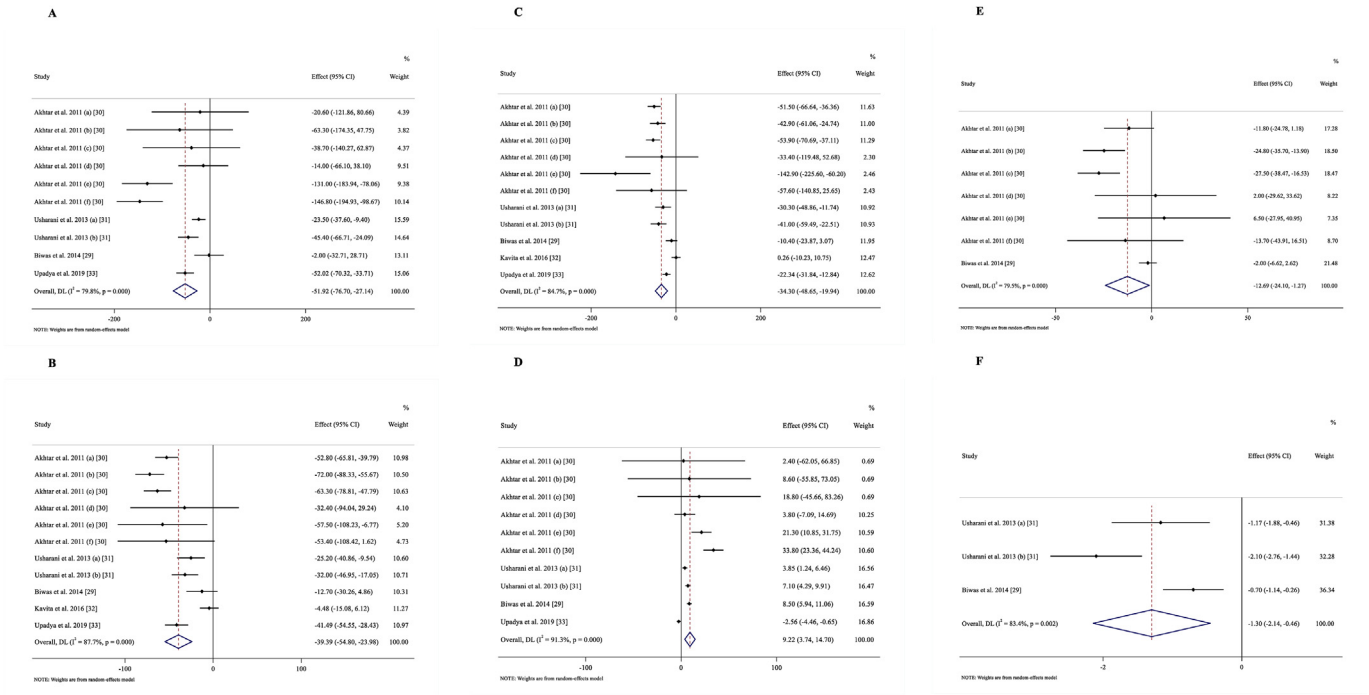

Fig. 2. Forest plots showing the mean difference (MD) and 95% confidence intervals for the effect of *Amla* supplementation on A) serum TG (mg/dL), B) TC (mg/dL) C) LDL-c (mg/dL), D) HDL-c (mg/dL), E) FBG (mg/dL), and F) CRP (mg/dL).

significant decrease in TG concentration following *Amla* supplementation in all subgroups except those who had TG < 150 mg/dL before the intervention, as shown in Biswas et al.'s study [10]. Therefore, it seems that blood TG concentration might be a determinant of response to the *Amla* supplementation. Amla's effect on TG is more likely to be observed in individuals with hypertriglyceridemia or poor TG control.

Amla supplementation also increased HDL-c concentrations in both short-term and long-term supplementation, but not in patients who were supplemented by *Amla* lower than 1 g/d. Therefore, *Amla* supplementation can have a dose dependent effects on HDL-c concentration. Moreover, Upadya et al. showed a trend for decreasing ApoB/ApoA1 ratios after *Amla* supplementation in patients with dyslipidemia [33]. ApoB represents the atherogenic lipoprotein particles such as VLDL, intermediate-density lipoproteins (IDL), and small dense LDL-c [4]. In contrast, Apo A1 represents the main apo-lipoprotein for HDLc- and acts as a mediator in transferring cholesterol from cells to HDLc-particles [39]. Plausibly, enhanced ApoA1 may be in the causal path toward increasing HDL-c with*Amla* supplementation.

Subgroup analysis showed that *Amla* supplementation of >1 g/d and durations of less than 8 weeks in patients with FBG> 100 mg/dl significantly decreased FBG concentration. Previous research has demonstrated the anti-diabetic potential of *Amla* extract in several preclinical as well as clinical studies [11–13]. In line with these results, other investigations have shown the anti-diabetic and *anti*-hyperlipidemic activity of *Amla* [2–4]. The ellagic acid present in *Amla* exerts anti-diabetic activity through its action on β-cells of the pancreas, decreasing blood glucose and an increase in β-cell size and number, antioxidant status, serum insulin, and β-cell morphology and morphometry [14].

CRP, an inflammatory parameter, has also been previously used as a biomarker for the atherosclerosis [40]. Diversity in circulating CRP concentration, even within the normal range, is related to the

Table 3
Subgroup analysis to assess the effect of *Amla* supplementation on lipid profile, FBG and CRP.

	NO	WMD (95% CI)	P value	heterogeneity		
	Number of effect sizes	WMD (95%CI)		P heterogeneity	I [2]	P between sub-groups
Subgroup analyses of *Amla* supplementation on serum TG						
Overall effect	10	−51.92 (−76.70, −27.14)	<0.001	<0.001	85.1%	
Baseline TG (mg/dL)						
<150	2	−4.78 (−33.10, 23.53)	0.741	0.646	0.0%	0.010
≥150	8	−63.10 (−91.90, −34.30)	<0.001	<0.001	86.9%	
Trial duration (week)						
<8	6	−72.28 (−126.15, −18.41)	0.009	<0.001	82.3%	<0.001
≥8	4	−32.57 (−51.61, −13.53)	0.001	0.009	74.0%	
Intervention dose (g/d)						
≤1	6	−30.48 (−46.60, −14.37)	<0.001	0.031	59.4%	<0.001
>1	4	−105.19 (−152.72, −57.66)	<0.001	0.039	64.2%	
Subgroup analyses of *Amla* supplementation on TC						
Overall effect	11	−39.39 (−54.80, −23.98)	<0.001	<0.001	90.1%	
Baseline TC (mg/dL)						
<200	6	−43.35 (−60.00, −26.69)	<0.001	<0.001	90.5%	<0.001
≥200	4	−43.39 (−54.95, −31.82)	<0.001	0.801	0.0%	
Trial duration (week)						
<8	6	−60.09 (−68.44, −51.74)	<0.001	0.262	22.9%	<0.001
≥8	5	−23.27 (−36.98, −9.56)	0.001	<0.001	82.7%	
Intervention dose (g/d)						
≤1	6	−33.72 (−46.20, −21.24)	<0.001	<0.001	77.6%	0.426
>1	5	−49.51 (83.15, −15.87)	0.004	<0.001	94.8%	
Subgroup analyses of *Amla* supplementation on LDL-c						
Overall effect	11	−34.30 (−48.65, −19.94)	<0.001	<0.001	89.0%	
Baseline LDL-c (mg/dL)						
<100	2	−48.96 (−59.68, −38.24)	<0.001	0.275	16.0%	<0.001
≥100	8	−38.26 (−53.73, −22.79)	<0.001	<0.001	83.4%	
Trial duration (week)						
<8	6	−53.66 (−67.11, −40.21)	<0.001	0.050	54.8%	<0.001
≥8	5	−20.37 (−34.34, −6.40)	0.004	<0.001	85.1%	
Intervention dose (g/d)						
≤1	6	−31.26 (−44.99, −17.52)	<0.001	<0.001	82.0%	0.490
>1	5	−51.08 (−84.31, −17.84)	0.003	<0.001	93.6%	
Subgroup analyses of *Amla* supplementation on HDL-c						
Overall effect	11	9.22 (3.74, 14.70)	<0.001	<0.001	92.6%	
Baseline HDL-c (mg/dL)						
<40	6	6.15 (2.54, 9.77)	0.001	0.096	49.2%	0.024
≥40	5	12.14 (2.62, 21.66)	0.012	<0.001	96.7%	
Trial duration (week)						
<8	6	17.64 (3.78, 31.51)	0.013	<0.001	80.5%	<0.001
≥8	5	4.47 (0.24, 8.70)	0.038	<0.001	93.8%	
Intervention dose (g/d)						
≤1	6	4.11 (−0.45, 8.67)	0.077	<0.001	92.0%	<0.001
>1	5	18.91 (3.26, 34.57)	0.018	<0.001	91.6%	
Subgroup analyses of *Amla* supplementation on FBG mg/dL.						
Overall effect	7	−12.69 (−24.10, −1.27)	0.030	<0.001	86.1%	
Baseline FBG (mg/dL)						
<100	4	−16.36 (−30.30, −2.41)	0.021	<0.001	92.6%	0.274
≥100	3	−3.07 (−17.49, 11.34)	0.676	0.488	0.0%	
Trial duration (week)						
<8	6	−16.39 (−25.59, −7.19)	<0.001	0.021	62.5%	<0.001
≥8	1	−2.00 (−6.61, 2.61)	0.396	–	–	
Intervention dose (g/d)						
≤1	3	−4.43 (−11.23, 2.35)	0.201	0.240	29.9%	<0.001
>1	4	−21.55 (−30.89, −12.20)	<0.001	0.112	49.9%	
Subgroup analyses *Amla* supplementation on CRP mg/dL.						
Overall effect	3	−1.30 (−2.14, −0.46)	0.002	<0.001	87.8%	

Abbreviations: CI, confidence interval; WMD, weighted mean differences, HDL-c, high-density lipoprotein; LDL-c, low-density lipoprotein; TC, total cholesterol, serum TG, triglyceride; FBG, fasting blood glucose; CRP, C reactive protein.

potential of atherosclerosis. This is similar to other well-known risk factors such as age, smoking, obesity, high blood pressure, and dyslipidemia, which are demonstrated to develop and progress this condition [41]. The significant CRP-lowering effect observed in the current meta-analysis study is comparable to earlier studies on *Amla* supplementation [5, 16, 17], suggesting a potential effect via reducing systemic inflammation and acting as free radical scavengers.

Our findings should be interpreted taking into consideration some limitations. Since all trials lasted 12 weeks or less, our analysis

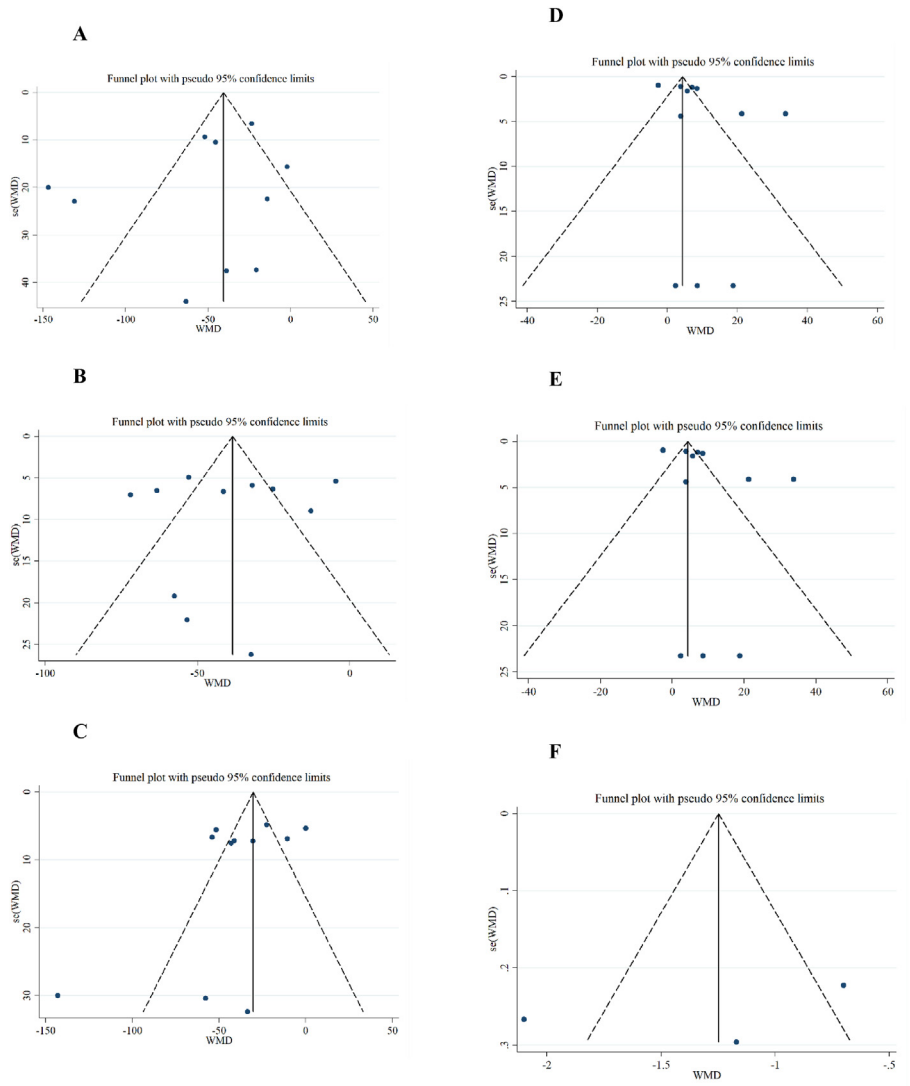

Fig. 3. Funnel plots with pseudo 95% confidence limits for the effect of *Amla* supplementation on A) serum TG (mg/dL), B) TC (mg/dL) C) LDL-c (mg/dL), D) HDL-c (mg/dL), E) FBG (mg/dL), and F) CRP (mg/dL).

is unable to show the long-term effects of *Amla* supplementation on lipid profile, FBG, and CRP concentrations. Moreover, there was significant heterogeneity among the included studies. Another limitation is that the included RCTs were performed in Asia and the Middle East. Therefore, our findings might not fully translate to populations in different geographical areas. Further research in different ethnic cohorts is warranted.

5. Conclusion

The systematic review and meta-analysis of six studies suggested that *Amla* supplementation exerts a beneficial effect on lipid profile as well as glucose and CRP concentrations in adults. Moreover, the *Amla* supplement was more effective in doses of >1 g/d. Additional long-term and well-designed RCTs are necessary to further examine and confirm these findings.

Author contributions

LS contributed to the study concept and design; LS, NR, and NH designed the search strategy; performed statistical analysis; LS, OA, MR, and NH wrote the first draft of the manuscript; RB, KC, RB, and AW. KM and KS was supervisor of the article; all authors read and approved the final manuscript.

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Declaration of competing interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2023.102729.

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