Review

Systematic review of the effect of *Phyllanthus emblica* in glycaemic control

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DOI: https://doi.org/10.4038/jccpsl.v29i4.8476

Received on 14 Dec 2022
Accepted on 21 Oct 2023

Abstract

Introduction: Diabetes mellitus which is characterized by chronic hyperglycaemia accounts for 1.6 million deaths per year globally. In Sri Lanka, 7.4% of adults are with raised fasting blood glucose. *Phyllanthus emblica*, some fruit, which is also called by *Nelli, Amla* or *Indian Gooseberry,* is traditionally believed to facilitate control of hyperglycaemia.

Objectives: To systematically review the glycaemic control effect of *Phyllanthus emblica*

Methods: PubMed, EMBASE, Cochrane Library, CINAHL and AGRICOLA databases were searched to select relevant studies. Studies were selected in two rounds. Three screening questions consisted of; whether study was a human study with *Phyllanthus emblica* included as a fruit or an ingredient, outcomes were related to glycaemic control and outcomes being reported quantitatively. Following the review of titles and abstracts, full articles were reviewed with screening questions such as, study design, participants, intervention, and findings of outcome. Two reviewers independently screened articles with the third intervening in resolving the conflicts. Meta-analysis was not performed following the heterogeneity assessments and narrative review of the findings was done.

Results: Eighteen studies were selected, having respectively excluding 81, 106 and 22 studies with reference to three screening questions. Six studies were done among healthy individuals and 12 were done among patients with diabetes. The studies were conducted among the age group of 18-75 years. Sample sizes of studies ranged from 10 to 150 participants, with 951 participants in total. In three studies, *Phyllanthus emblica* was used as a single entity and in 15, it was one component of a combined product. Fifteen selected studies described the mean fasting blood sugar (FBS) levels and 13 of them showed statistically what *Phyllanthus emblica* or products containing it had on glycaemic control, compared to control group ($p<0.001$). Out of those 13 studies with significant findings on glycaemic control, 10 studies were done among hyperglycaemic patients. In eight studies, a significant reduction in HbA1c results ($p <0.05$) was observed and nine studies showed a significant reduction in post prandial blood sugar (PPBS) levels ($p<0.05$). None of the selected studies showed any negative impact of *Phyllanthus emblica* on blood glucose levels among either healthy or diabetics individuals.

Conclusions & Recommendations: *Phyllanthus emblica* is found to be with favourable effects in facilitating blood sugar control. Further research on the potential application of it as a glycaemic controller, must be encouraged.

Keywords: *Phyllanthus emblica, Emblica officinalis, Amla, glycaemic control*

Introduction

Globally, non-communicable diseases (NCDs) impose a major health burden. These are accountable for 74% of all deaths worldwide. Almost 86% of the NCD deaths in lower-and middle-income countries occur before the age of 70 years as premature deaths (1). The leading NCDs include heart disease, stroke, cancer, diabetes mellitus (DM) and chronic lung disease. The International Diabetes Federation in 2021 has projected that the global prevalence of DM would increase to 643 million by 2030 (2). Meanwhile, the prevalence of DM is increasing all over the world irrespective of gender, social class or income (3).

According to World Bank, the prevalence of DM among people aged 20-79 years in Sri Lanka was 11.3% in 2021 (4). The pre-DM prevalence was 11.5 %, reflecting a significant burden in Sri Lanka. Important risk factors associated with DM include urban residency and familial inheritance. It is associated with many other comorbidities, such as cardiovascular disease, chronic kidney diseases and cerebrovascular diseases (5).

There are several studies conducted by Sri Lankan researchers assessing the effect of herbal products on DM treatment (6). Modern methods such as oral medications, injectable insulin and some surgical procedures as well as traditional medicines are being practised and experimented for the control of DM. Among traditional medicines, *Phyllanthus emblica*, also known as *Amla* or Indian gooseberry, has been used in some settings (7). This plant is cultivated in most parts of the Southeast Asian countries (8) and is highly abundant in vitamin C, amino acids, alkaloids and organic acids (9). *Phyllanthus emblica* has been consumed both as fresh fruit and in dried powder form. Furthermore, it is utilized in various preparations, particularly in formulations like *Triphala* (10). Regular usage of *Phyllanthus emblica* is believed to be associated with many health benefits including the control of high blood sugar levels (11).

Numerous studies, involving both animals and humans, have explored the effects of *Phyllanthus emblica* preparations on glycaemic control. These studies have shown that *it* exhibits a hypoglycaemic effect and can prevent DM-induced cardiac issues, neuropathy, nephrotoxicity as well as mitigate the wasting associated with DM. As *Phyllanthus emblica* possesses free radical scavenging and antioxidant effect, it improves glucose utilization, maintains glucose homeostasis, stimulates pancreatic insulin secretion, restores and regenerates beta-cell architecture (secretagogue effect). Regeneration of secretagogue effect established by prevention of apoptosis of pancreatic beta cells, modulation of adipokines to decrease Advanced Glycation End product (AGE) and inhibition alpha-glucosidase (12). However, there has not been a documented systematic review on the effectiveness of *Phyllanthus emblica* in terms of glycaemic control. In bridging this gap, the current review was done to systematically review the impact of *Phyllanthus emblica* on glycaemic control.

Methods

Protocol and registration

The review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) registration (CRD42020180902). Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines were referred to when writing the review.

Eligibility criteria

The criteria for the selection of studies included: being a randomized or nonrandomized clinical study, the intervention group including DM patients or healthy people, and the intervention being delivered either as *Phyllanthus emblica* alone or as a combined product with other ingredients. Articles not written in English language were excluded as it could lead to erroneous interpretations of the findings.

Search strategy

We searched the CINAHL, Cochrane Central Register of Controlled Trials, PubMed, EMBASE and AGRICOLA databases. Study selection was done with three screening questions, namely whether the study was a human study with *Phyllanthus emblica* included as a fruit or an ingredient, whether outcomes were related to glycaemic control or whether reported quantitatively. Two rounds of study selection were done. In the first round, title and abstracts were reviewed. Full articles were reviewed in the second round. Throughout the selection process, two reviewers independently evaluated the articles. Any discrepancies in article selection were resolved through consensus discussions involving a third reviewer.

Data collection and extraction

All relevant data from each study were inserted into a pre-designed template. We extracted data on the methodological quality of studies, study design, description of setting, characteristics of participants, details about the intervention/exposure, description of outcomes, date of the study and location of study. Two reviewers extracted data from each study and the third reviewer cross-checked both sets of data to ensure uniformity. Any discrepancy was dealt with by the involvement of all three reviewers involved in data extraction.

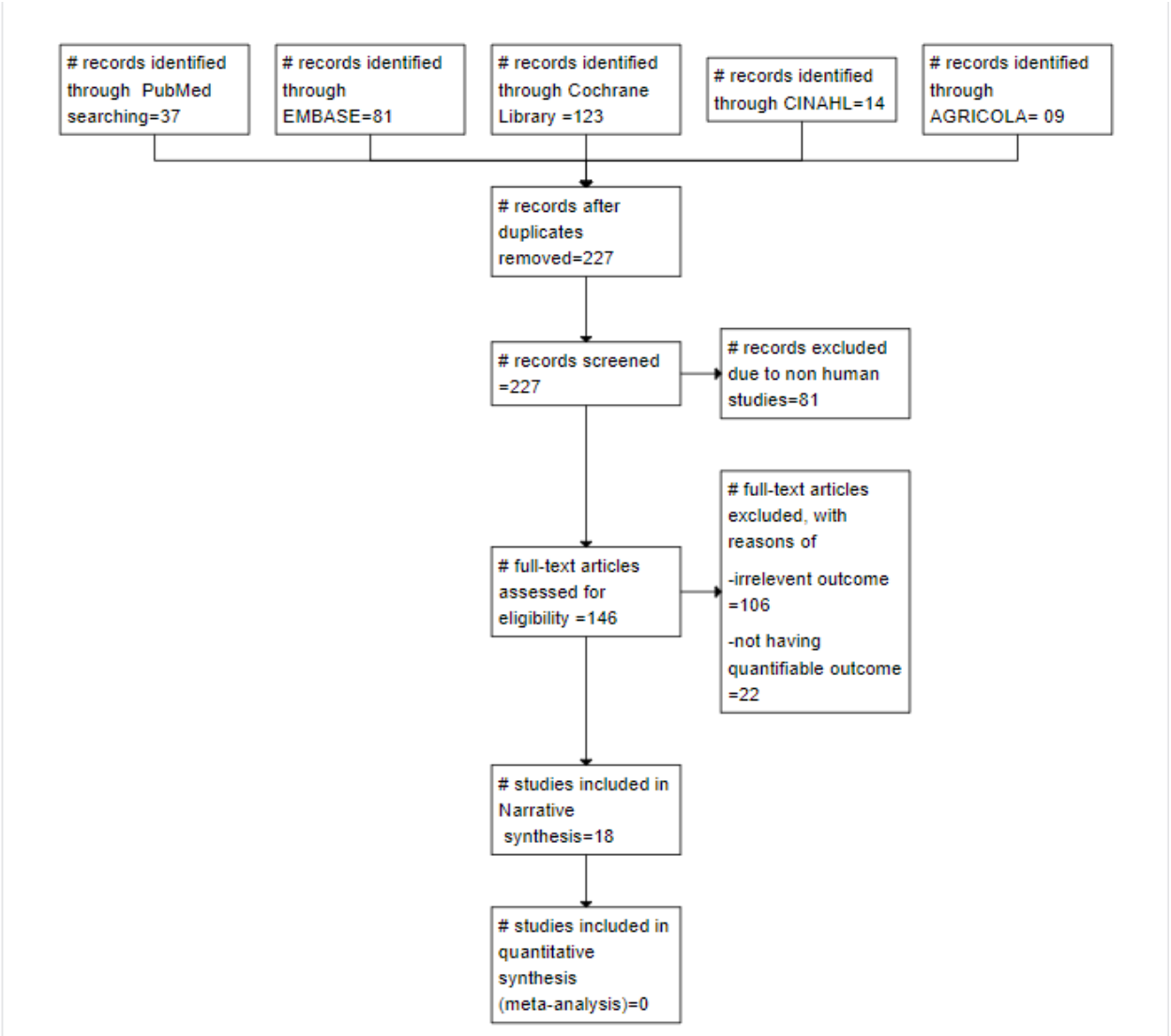

Figure 1. Study selection flow diagram

Estimation of bias

The risk of bias table was composed based on the recommendations for randomized clinical trials and non-randomized clinical trials. Based on the methodological issues related to random number generation, allocation concealment, performance bias, detection bias, attrition bias, reporting bias, and any other bias the bias assessment was performed using GRADE criteria for randomized controlled trials. ROBINS-I tool was utilized for non-randomized trials. Determination of the level of bias was done by two reviewers independently and was contributed by a third reviewer in case of a disparity of decisions.

Synthesis of findings

After the clinical and methodological heterogeneity assessments, it was decided that the homogeneity was not found to proceed with meta-analyses. Hence, narrative review of the findings was done.

Results

Selection of studies

The study selection flow diagram is shown in Figure 1. Altogether, 227 experimental and observational studies were selected after removing duplicates. Of these, 81 studies were excluded due to non-human studies. Out of the remaining 146 studies, 106 were excluded due to irrelevant outcomes, and 22 were due to not having quantifiable outcomes, and therefore the number of articles included in the systemic review was 18.

Among the selected articles (Table 1), three were on pure *Phyllanthus emblica* (13-15), while the remaining 15 were on *Phyllanthus emblica* combined with other herbal preparations. Five of the studies were conducted among healthy individuals (13, 16-19) while 11 were carried out among patients with DM (14, 20-29) and remaining 2 studies were conducted among both the healthy individuals and DM patients (15, 30). All the studies were conducted in the age group of 18-75 years. Sample sizes ranged from 10 to 150 participants, with 951 participants in total.

All three of the studies that were based only on *Phyllanthus emblica* were randomized control trials. In two of these studies, it was given as a fruit or in powder form, and in the other as a capsule. One study recruited eligible healthy adult subjects (n=15) and were given either *Phyllanthus emblica* in capsular form or a placebo (500 mg per day) after each meal during an 18-week study (13). Another study included 80 eligible patients who were randomized to receive either one capsule of *Phyllanthus emblica* 250 mg twice daily, one capsule of *Phyllanthus emblica* 500 mg twice daily, atorvastatin 10 mg at bedtime or a matching placebo in the morning daily, or placebo twice daily for 12 weeks as per the prior randomization schedule (14). In the other study, *Phyllanthus emblica* was given as a fruit (15). This study was conducted to evaluate the anti-hyperglycaemic properties of *Phyllanthus Emblica* in normal and diabetic human volunteers. A total of 32 volunteers (16 diabetic patients and 16 age- and gender-matched normal subjects) participated in this study. Both normal and diabetic subjects received 1, 2 or 3g of *Phyllanthus emblica* powder per day as compared with their baseline values. All these three studies were with low risk with regards to attrition and reporting bias (Figure 2), while two were with low risk in performance bias and detection bias and the other categorized as with unclear bias. All studies were categorized as high risk for selection bias due to the lack of allocation concealment and only one study had clear evidence on showing low risk with a random sequence generation.

Table 1: Summary of study characteristics and outcome

Study	Study design	Population	Intervention	Outcome (1-FBS, 2- HbA1C, 3- PPBS, 4- RBC)
1. Chen, 2010 (30)	Interventional study	Uremic patients with DM and healthy volunteers	I (n=13)- Oral administration of 1:1 mixture of epigallocatechin gallate (EGCG), a major component of green tea extract and Amla extract (AE) from *Emblica officinalis* for 3 months. C (n=15)- Data for the healthy volunteers served as normal ranges Duration- 3 months	Oral administration of 1:1 EGCG=AE for 3 months significantly improved diabetes in Uremic patient with DM Normal (n=15), 100.93-13.77 mg/dL; Uremic-DM (n=13)- M0, 171.92-13.77 mg/dL; and Uremic-DM (n=13)- M3, 134.62-25.43 mg/dL. The values for Uremic-DM-M0 and Uremic-DM-M3 were significantly different ($p<0.05$). HbA1C- healthy volunteers, 4.5-0.2%; Uremic-DM-M0, 7.54-0.79%; and Uremic-DM- M3, 7.5-0.96%. The values for Uremic-DMM0 and Uremic-DM-M3 were not significantly different
2. Chepulis, 2016 (16)	Randomized, single-blinded control study	Healthy individuals aged 18-45 years with FBG ≤5.7 mmol/L and HbA1c ≤38.8 mmol/L	I (n=10)- Extracts of Amla berry containing capsules consumed one per session (each >48 hours apart) matched for total antioxidant content 10 minutes prior to ingestion of 50 g of available carbohydrate from either a glucose load (study 1) or white bread with ham (study 2) after an overnight fast C- The control PPBS responses were measured by calculating the incremental area under the blood glucose response curve (IAUC) of 50 g of available carbohydrate from glucose (study 1) or 50 g of actual carbohydrate from a simple meal (study 2) Duration- 4 weeks	**FBS-** Baseline: 4.55 (SD=0.4) mmol/L **HbA1c-** Baseline: 31.2 (SD=2.4) mmol/L **Mean IAUC of the glucose control:** 258.2 (SD=31.8) mmol/min/L. The antioxidant-rich food extracts significantly reduced the IAUC compared to the glucose-only control with green-tea, alma berry, grape seed and rooibos tea-extracts showing a greater than 30% reduction in the postprandial glucose response (all $p<0.005$). There were no significant differences observed between the food extract groups.

3. Agte, 2018 (17)	Randomized double-blinded control trial	Healthy volunteers aged 18-35 years	I1 (F1) (n=16)- F1 comprised six different sources of antioxidants i.e., raw gooseberry juice (Emblica officinalis), Jamun juice (Syzygium cumini) and water extracts of powders of bael fruit, bael leaf (Aegle marmelos), Holy basil leaf (Ocimum sanctum) and Indian pennywort leaf (Bacopa monnieri) I2 (F2) (n=16)- F2 comprised juice blend of black grapes (Vitis vinifera) as main ingredient, pomegranate (Punica granatum), grapefruit (Citrus paradise), guava (Psidium guajava) and kokum (Garcinia indica) F1 or F2 were served as fruit juices (100 g as a drink using whole fruit purees) C (Placebo) (n=16)- 100 gm drink with artificial fruit flavours and colours Duration- 4 weeks	• No significant differences in baseline FBG between the three groups (p=0.2) • No significant changes in plasma glucose in the placebo group (p>0.1) • Significant changes in plasma glucose in F2 group (p<0.05) • A significant decrease (p<0.05) in FBG and 2hr-PPBS on Day 21 in both normal and diabetic subjects with 2 or 3 gm amla (E. officinalis) powder per day
4. Singh, 2016 (29)	Before- after study	Patients of type II DM aged 30-70 years, with 8-hr FBS of 126-250 mg/dl and 2-hr PPBS of 200-350 mg/dl	IA (n=36)- Chanaka Yoga (10 g once a day) IB (n=20)- Glimepiride (1 mg) twice daily Duration- 90 days (every 15-day interval estimations of 8-h FBG and 2-h PPBG)	**FBS-** Significant decrease of 45.18 (p<0.05) in Group A and 22.5 ((p<0.05)) in Group B **HbA1c-** Slight decline of 69.73 (P<0.001) in Group A and 54.65 (p<0.05) in group B **PPBS-** Decrease of 69.73 (p<0.001) in Group A and 54.65 (p<0.001) in Group B
5. Banerji, 2016 (28)	Prospective, single arm, open label	Non-insulin dependent type 2 DM patients aged 30-60 years on metformin	I (n=50)- One capsule each morning and evening before meals along with their prescribed medication on Day 0, 21, 42 & 63	**FBS-** A significant reduction in the average FBS from 8.8 mmol/l to 6.95 mmol/l; p<0.001 **PPBS-** A significant reduction in the average PPBS 14.6 mmol/l to 10.4 mmol/l; p<0.001

	before-after study	and sulphonyl urea for ≥ 3 months with no improvement in diabetic control	Duration- 84 days	**HbA1c-** A significant reduction from baseline 8.76 mmol/l to 7.5 mmol/l, p<0.001
6. Akhtar, 2011 (15)	Randomized control study	Type 2 DM patients aged 30- 60 years and age- and gender-matched normal healthy volunteers	C (n=16)- Normal persons randomly divided into A, B, C, D groups with 4 volunteers each. Carboxymethyl cellulose fibre given to group A (control), while groups B, C and D were given 1, 2 or 3 g powdered E. officinalis fruit orally with 30 ml water once daily in the morning after breakfast. I (n=16)- DM patients randomly divided into E, F, G, H groups with 4 volunteers each. E (control): received Glibenclamide 5 mg twice daily; F, G, H: 1, 2 or 3 g powdered E officinalis fruit orally with 30 ml water once daily in the morning after breakfast Duration- 21 days	**FBS-** A significant decrease on Day 21 as compared with baseline on Day 0 (p<0.05) in both normal and diabetic volunteers in all groups **PPBS-** A significant decrease on Days 8, 15 and 21 in normal volunteers given either 2 or 3 g powdered Amla fruit as compared with baseline (p<0.05)-
7. Mahajan, 2015 (27)	Before-after study	Non-insulin dependent DM patients aged 30-65 years with body mass index of 18.5-40 kg/m^2	32 patients attending a weekend diabetes clinic run by the School of Studies in Biochemistry, Jiwaji University, India Duration- 6 months	A significant decrease in FBS (23.5%) and PPBS (26.7%) (p<0.001)
8. Santhi, 2014 (26)	Non-randomized control study	Uncomplicated type 2 DM patients of 1-10 years over 40 years of age	I (n=30)- Taught pranayama for one hour every day by yoga expert and prescribed medicines and diet	I group significantly changed in **FBS-** Initial 178.2 ±34.51; after 6 months 154.0 ±31.77 **PPBS-** Initial 269.8 ±44.97; after 6 months 246.13 ±46.93

			C (n=30)- Only prescribed medicines and diet Duration- 6 months	**HbA1C-** Initial 8.19 ±0.73; after 6 months 7.94 ±0.68 C group- No significant changes
9. Iyer, 2010 (25)	Non-randomized controlled study	Type 2 DM patients with an average FBS of 150 mg/dl	IA (n=15)- Fresh panchratna juice IB (n=20)- Processed panchratna juice C (n=20)- No intervention Duration- At baseline, 45 days and 90 days	IA- A transient fall in FBS (7%) and HbA1C (3%) levels IB- FBS of 9.56% on Day 45 and 15.8% on Day 90 ($p>0.05$) HbA1C of 3.22% on Day 45 and 5.87% on Day 90 ($p>0.05$) C-FBS and HbA1C levels remained unaltered throughout the study period
10. Kapoor, 2020 (13)	Randomized, placebo-controlled, double-blinded crossover study	Healthy volunteers aged 36-67 years	I (n=8)- Amla C (n=7)- Placebo (500 mg per day) Duration- 18 weeks	**FBS-** Significantly changed after four weeks ($p=0.03$) and after withdrawal ($p=0.06$) of Amla intake **HbA1C-** No significant difference
11. Haldar, 2019 (18)	Randomized controlled crossover trial	Healthy men aged 21-40 years having BMI of 18.5-27.5 kg/m^2	I (n=20)- Test meals matched for calories, macronutrients and total vegetables comprising either Dose 0 Control (D0C- meal comprising 180 g of low polyphenol mixed vegetables) or Dose 1 Curry (D1C- meal comprising an Indian curry dish prepared with 6 g of mixed spices and 90 g of curry-based vegetables) or Dose 2 Curry (D2C- meal comprising 12 g of mixed spices and 180 g of curry- based vegetables) served with white rice	Significant linear dose–response reductions in the 3-h postprandial incremental Area under the curve for continuous glucose monitoring of 19% and 32% during D1C and D2C meals respectively ($p<0.05$) Significant dose-dependent increases in postprandial triglyceride with increasing curry doses ($p<0.01$)

			The mixed spice preparations for both D1C and D2C were identical, consisting of a blend of seven spices including amla-	
12. Gupta,2014 (24)	Before and after intervention study	T2DM patients aged 25-75 years with FBS level ≥120 mg/dl and/or 2-h PPBS level ≥200 mg/dl	I- Advised to follow dietary interventions and lifestyle modifications	Significant improvement in clinical signs and symptoms along with FBG (maximum difference of 108.29 (SD=55.88) ($p<0.001$) and 2-hour PPBS (maximum difference of 77.02) ($p<0.001$)
13. Kurian, 2014 (23)	Randomized clinical trial	Type 2 DM patients aged 35-60 years with FBS >140 mg/dl	Patients were treated with a polyherbal combination drug namely G-400 (1000 mg/d) for 8 weeks and asked to continue their usual treatment regimen for T2DM along with G-400 and follow-up of 2 weeks interval	• Mean FBG significantly ($p<0.001$) decreased from 184.84 to 127 mg/dL and 277.53 to 176.92 mg/dL, respectively with normal medication, with diabetic control, with treatment with G-400, with 100 mg G-400 and with glibenclamide treatment • Significant reduction of HbA1c with G-400- before-8.58; after-7.98 ($p<0.05$) • Significant improvement in PPBS with G-400 (amla combination)- before-277.53; after-176.92 ($p<0.05$)
14. Faizal, 2009 (22)	Intervention study	DM patients aged 35-75 years Normal healthy adults aged 35-75 years	I (n=43)- C (n=15) normal healthy individuals) Participants divided into 6 group based on their age and FBS Group I: Normal controls (n=10) Group II: 35-45 years (n=15) Group III: 46-55 years (n=13) Group IV: > 55 years (n=15) Group V: FBS < 145.9 mg/dl (n=21) Group VI: FBS > 145.9 mg/dl (n=22) Duration- 3 months	Significant decrease of FBS and HbA1c in all the diabetic patients (group II-VI) ($p>0.05$)

15. Rajan 2008 (21)	Non-randomized control study	NIDDM patients	I (n=30)- Supplementation of 5 g of Triphala (Terminalia bellirica, Terminalia chebula, Embilica officinalis) C (n=30)- Not mentioned Duration- 45 days	Control group: No significant difference in mean FBS and PPBS before and after the treatment Intervention group: Significant lowering effect of FBS level with 44.26g/dl difference ($p<0.05$) Significant reduction of PPBS level with 32.8 g/dl difference ($p<0.005$) before and after the study
16. Gurupadayya, 2017 (20)	Randomized open-label, clinical trial	Type 2 DM patients aged 35-65 years	Group A (n=39)- Glibenclamide 2.5 mg/day for 6 months Group B (n=36)- 500 mg poly-herbal 2 tablets thrice a day (one tablet containing 20 mg Phyllanthus emblica) Group A subdivided as: A1 (n=20)- Glibenclamide 2.5 mg/day A2- Glibenclamide 2.5 mg/day together with 500 mg polyherbal 2 tablets thrice a day Duration- 90 days	Significantly decreased in FBS ($p<0.01$), PPBS ($p<0.04$) and HbA1c ($p<0.03$) compared to baseline demographic and clinical values in Group A1 compared to Group A2
17. Manjunatha, 2001 (19)	Randomized blind control trial	Normal healthy adult male volunteers aged 20-32 years	I (n=5)- 5 g Chyawanprash powder per day C (n=5)- Received 500 mg/day vitamin C as dietary supplement for the first 8 week of the study. During the next 8 weeks, neither group received any supplement. Duration- 16 weeks	At 8^{th} week, a significant reduction ($p<0.05$) compared to baseline in FBG (16mg/dl reduction), 0.5·h glucose level, 1 h glucose level and area under 2-h plasma glucose curve (AUC) when compared to '0' week value. After discontinuation of Chyawanprash at 8^{th} week, the follow-up showed that the values returned close to baseline (0 week) values by 16 weeks. The supplementation with vitamin 0 for a week did not lead to any significant change in glucose tolerance at 4 or a week.

18. Usharani, 2013 (14)	Prospective, randomized, double-blind, placebo-controlled study	Adults aged 30-68 years with FBS of 110-126 mg/dL, HbA_{1c} of 7-9% and on metformin 1500-3000 mg	I 1 (n=20)- *P. emblica* 250 mg twice daily I 2 (n=20)- *P. emblica* 500 mg twice daily C 1 (n=20) atorvastatin 10 mg in the evening twice daily C 2 (n=20)- Placebo in the morning, or placebo twice daily Duration- 12 weeks	**HbA1c-** Significant difference ($p<0.01$) between I1 and I2, significant difference ($p<0.05$) between I2 and placebo and non-significant when compared between placebo group and I1 and placebo

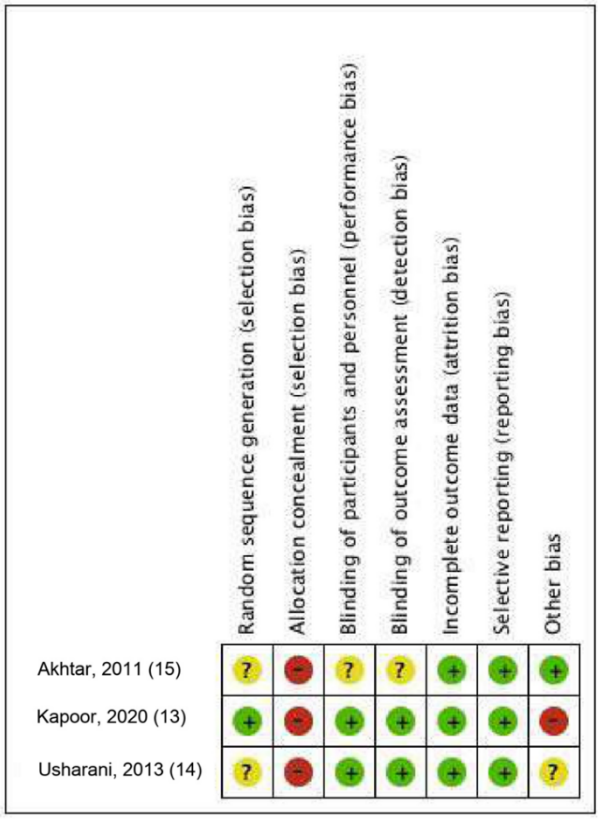

Figure 2: Risk of bias of the three randomised control trials based only on Phyllanthus emblica

Among the randomized controlled trials examining the effects of *Phyllanthus emblica* in combination with other ingredients (Figure 3), five studies were reasoned to have a low risk of detection bias, indicating that the outcome measurements were conducted impartially (16-17, 19-20, 29). However, two studies were identified as having a high risk of detection bias (18, 23). Additionally, one study had unclear data indicating a need for further clarification or more transparent reporting of results (24).

In relation to non-randomized control trials (Table 2), the risk of bias related to missing data was considered to be low in three studies (22, 27-28) as the researchers adequately addressed and reported the handling of missing information. On the contrary, there was insufficient information provided in the remaining studies (21, 25-26, 30) to confidently assess the risk of bias due to missing .

In one randomized controlled study in which *Phyllanthus emblica* fruit was given in powder form showed a significant decrease ($p<0.05$) in FBG and 2-hour PPBS on the 21st day in both normal and diabetic subjects receiving 1, 2, or 3 g of *Phyllanthus emblica* powder per day as compared with their baseline values (15). Another study showed FBG levels significantly changed after four weeks ($p<0.03$) and the significance level has changed after the withdrawal of *Phyllanthus emblica* intake ($p<0.06$) (13).

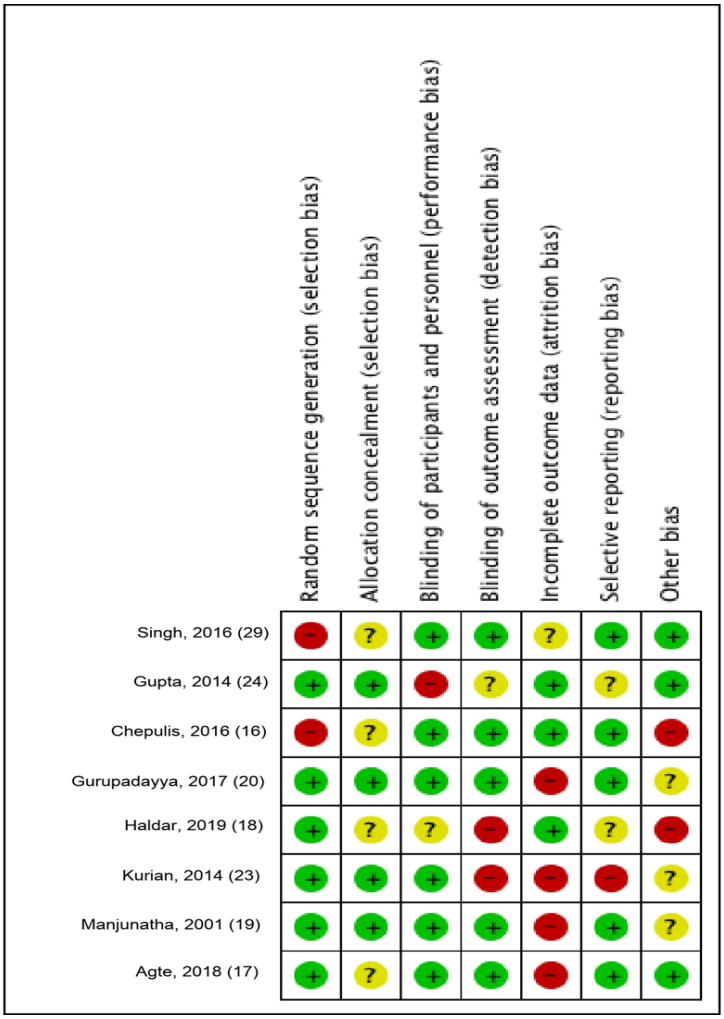

Figure 3: Risk of bias of the randomised control trials based on Phyllanthus emblica in combination with other ingredients

A study in which *Phyllanthus emblica* 250 mg and *Phyllanthus emblica* 500 mg was given, a significant reduction in HbA1c levels was reported compared with the baseline and placebo (14). Another study on both health and diabetic volunteers showed a significant decrease in blood glucose levels (15). A randomized control study of 56 males and females showed a significant decrease in FBS, HbA1c and PPBS levels. Only one study that included RBS level did not show a significant decrease (24).

Discussion

The current study investigating the impact of *Phyllanthus emblica* on glycaemic control represents the first review conducted in this context. This fruit is widely used in tropical and subtropical countries, with some people recognizing its importance while others remain unaware of its significance. Diabetic mellitus has reached a level of a pandemic, with a drastic increase in the incidence of patients. Given the severity of the condition, many complementary approaches other than medication, are being attempted due to the need of a prolonged or even lifelong treatment (31). Out of these approaches, the potential use of *Phyllanthus emblica* has been emphasized, given the easy availability of the fruit and the ability to consume it fresh (32).

Table 2: Risk of bias of the non-randomised control trials based on Phyllanthus emblica

Study	Bias due to confounding	Selection bias	Bias in measurement classification of interventions	Bias due to deviation from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
Banerji, 2016 (28)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Iyer, 2010 (25)	Low risk	Low risk	Low risk	Low risk	No information	Low risk	Low risk
Santhi, 2014 (26)	Low risk	Low risk	Low risk	Low risk	No information	Low risk	Low risk
Mahajan, 2015 (27)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Faizal, 2009 (22)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Rajan, 2008 (21)	No information	Low risk	No information	Low risk	No information	Low risk	Low risk
Chen, 2011 (30)	No information	No information	Low risk	Low risk	No information	Low risk	Low risk

Out of 15 studies of *Phyllanthus emblica* combined with other ingredients, 10 studies showed a significant reduction in fasting blood sugar, and 13 studies showed a significant reduction in PPBS. Also, eight studies showed a significant reduction in HbA1c levels. None of the studies have reported any side effects of *Phyllanthus emblica*.

One of the main limitations faced was the 10 studies that use *Phyllanthus emblica* combined with other ingredients to show a significant reduction in fasting blood sugar may be due to the confounding effect of the combined ingredient.

Some studies have demonstrated that blood glucose levels can be modulated by food-based antioxidants (16). Food-based antioxidants are expected to lower the postprandial glucose response in both healthy and patients with DM (15). It has been confirmed that *Phyllanthus emblica* contains antioxidant properties which might play an important role in its beneficial effect in controlling hyperglycaemia. The systematic review encompassed various studies that showed the enhancement of glucose response and reduction in postprandial glucose levels, wherein it became evident that multiple mechanisms were potentially responsible for these improvements (17, 28-29).

Public Health Implications

- This systematic review elicited the favourable effects of *Phyllanthus emblica* on the control of high blood sugar level without any impact on the safety of the recipients. Thus, the present review sheds light on the potential utility of *Phyllanthus emblica* as a supplementary strategy to control hyperglycaemia among those who are on medication for diabetes mellitus which is a rising burden worldwide.
- Since it is commonly available, once proven further with more robust future research, *Phyllanthus emblica* can be used as a cost-effective supplementary strategy for treating diabetes.

Limitations of this study are that some studies were single arm without a control group or have had other ingredients combined with *Phyllanthus emblica*. Hence, the pure effect of glycaemic control is not reflected in those studies. Various forms of *Phyllanthus emblica* such as whole fruit, juice and capsules were utilized in different studies. However, further research is required to determine which form of *Phyllanthus emblica* is more effective. The amount of *Phyllanthus emblica* that can be taken by diabetic patients and normal healthy adults also should be further specified with clinical trials as some believe precautions should be taken when it is used in people with dry scalp or dry skin. Eating too much *Phyllanthus emblica* can also drastically drop blood sugar levels or is not proven scientifically. Given the high heterogenicity among the studies, the inability to conduct a meta-analysis for the outcome is also a limitation of this review. Yet, the quantitative data synthesized from each study accumulate to the improvement of glycaemic control, which is the main focus of the review.

Conclusions & Recommendations

The systematic review provides compelling evidence on the features of *Phyllanthus emblica* in glycaemic control. The significant reductions in FBG levels, HbA1c levels and PPBS levels, coupled with its apparent safety profile, make *Phyllanthus emblica* a promising supplementary natural nutritional treatment for those on treatment for DM. The studies were conducted with different formulations and dosage forms of *Phyllanthus emblica*, yet consistently showed positive effects on the glycaemic control. This indicates the resourcefulness of this herbal fruit and its potential to be incorporated into various treatment regimens.

While the findings are promising, the combination of *Phyllanthus emblica* with other herbal ingredients in some studies makes it challenging to isolate the pure effects of this fruit. To address this limitation, more rigorous randomized controlled trials with larger samples and standardized methodologies are needed to optimize the use of *Phyllanthus emblica* as a complementary therapy in diabetes management.

Author Declarations

Competing interests: The authors declare that they have no competing interests.

Ethics approval and consent to participate: Ethical approval was not applicable as this review was done on already published articles, hence primary data collection component was not included

Funding: Self-funded

Acknowledgements: We sincerely thank each author of the original research in the chosen publications for this systematic review.

Author contributions: All authors were involved in planning and conducting the review. UK, SW, ST & BM conducted the literature search. UK, SW & ST extracted the data from the articles and assessed the risk of bias in the studies. MA, RF & WG contributed technical guidance throughout the study. UK, SW & ST drafted the initial manuscript. JA guided manuscript drafting. All authors proofread and went through the final manuscript.

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