TRENDS IN SCIENCES 2026; 23(4): 12148
https://doi.org/10.48048/tis.2026.12148
REVIEW ARTICLE

Effects of Different *Morus alba* L. Parts on Glycemic and Lipid Profiles: A Systematic Review and Meta-Analysis

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Received: 3 October 2025, Revised: 5 November 2025, Accepted: 3 December 2025, Published: 5 January 2026

Abstract

Metabolic syndrome is a growing global health challenge. Given the limitations of conventional therapies, mulberry (*Morus alba* L.) has gained attention as a functional food with potential metabolic benefits. This systematic review and meta-analysis evaluated recent evidence on its efficacy and safety across various plant parts. The review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and was registered with PROSPERO (CRD42024600762). Randomized controlled trials (RCTs) were identified from PubMed, Embase, Scopus, and gray literature sources, up to May 2025. Risk of bias was assessed using the Risk of Bias 2 tool. Meta-analysis applied a random-effects model, with subgroup analyses to explore heterogeneity. Eighteen RCTs were included in this review. The meta-analysis showed that single mulberry intervention significantly lowered postprandial glucose (PPG) levels compared to the control group at 30 min (MD = −10.37 mg/dL; 95% CI: −19.30 to −1.45; $p = 0.02$) and 60 min (MD = −6.01 mg/dL; 95% CI: −11.97 to −0.05; $p = 0.05$). In addition, significant reductions were observed in the PPG area under the curve (AUC), PPG-positive incremental AUC, and the postprandial insulin (PPI) total AUC over 120 min. The leaf subgroup showed notable effects on both PPG and PPI levels. For long-term effects, 4 - 16 weeks of mulberry intervention significantly lowered glycated hemoglobin A1c (HbA1c) (MD = −0.30%; 95% CI: −0.56 to −0.05; $p = 0.02$), with no significant changes in fasting blood glucose (FBG), fasting plasma insulin (FPI), or lipid profiles. Mulberry treatment was well tolerated and considered safe for use. Mulberry, particularly the leaf, demonstrated significant efficacy in improving postprandial glycemic responses and HbA1c levels, with a favorable safety profile. Further research is called for to assess any long-term effects and the potential of other plant parts.

Keywords: *Morus*, Mulberry, Metabolic syndrome, Blood glucose, Insulin, Lipids, Triglycerides, Cholesterol, Diabetes mellitus, Dyslipidemias

Introduction

Metabolic syndrome, defined as a cluster of metabolic abnormalities including obesity, hyperglycemia, dyslipidemia, and hypertension, affects over 30% of the global population and is projected to reach 50% within the next 2 decades [1,2]. Among its components, type 2 diabetes mellitus (T2DM) and dyslipidemia are the most prevalent and clinically significant disorders, driven by insulin resistance, chronic hyperglycemia, and abnormal lipid metabolism. Poor glycemic control accelerates atherogenesis and increases cardiovascular disease (CVD) risk [3,4], whose prevalence continues to rise globally [5]. Dyslipidemia, involving elevated total cholesterol (TC) and triglycerides (TG), further contributes to CVD-related morbidity and mortality [6]. In Thailand, diabetes prevalence increased from 7.5% in 2004 to 10.1% in 2020, while more than half of adults (56.7%) have elevated cholesterol levels (TC ≥ 200 mg/dL) [7,8]. These trends underscore the urgent need for effective

and accessible strategies for glycemic and lipid control through lifestyle modification, pharmacotherapy, and management of other modifiable risk factors [9,10].

Although pharmacotherapy remains the mainstay treatment for T2DM and dyslipidemia, its long-term use is often limited by adverse effects such as gastrointestinal irritation from metformin, hypoglycemia from sulfonylureas, and statin-associated myopathy or renal dysfunction [11-13]. These safety concerns have stimulated increasing interest in functional foods and herbal interventions that may offer metabolic benefits with fewer side effects.

Mulberry (*Morus alba* L.) has emerged as promising natural interventions for modulating blood glucose and lipid profiles [14,15]. Its anti-metabolic effects are derived from abundant phytochemicals, especially cyanidin-3-*O*-glucoside, cyanidin-3-*O*-rutinoside, and 1-deoxynojirimycin (DNJ) [16,17]. However, findings remain inconsistent. For example, while mulberry twig consumption significantly reduced fasting blood glucose (FBG) and glycated hemoglobin A1c (HbA1c) in Chinese T2DM patients [18], another study reported no improvement with mulberry fruit extract in Iranian T2DM patients [19].

Several systematic reviews and meta-analyses have examined the metabolic effects of mulberry [20-23]. However, important gaps remain. Previous reviews primarily focused on long-term glycemic and lipid outcomes and often evaluated only isolated plant parts. Only one meta-analysis [20] included short-term postprandial glucose responses, without insulin-related parameters. Moreover, most existing reviews relied on outdated trials and provided limited assessment of safety. To address these gaps, the present systematic review and meta-analysis provides an updated and comprehensive synthesis of randomized controlled trials involving mulberry leaf, fruit, and twig interventions. Both short-term and long-term outcomes were integrated, with risk of bias assessed using the Cochrane RoB 2 tool and certainty of evidence evaluated by GRADE. This review aims to establish an up-to-date, policy-relevant evidence base supporting the multifaceted functional role of mulberry in metabolic health and its potential application in functional food claim systems.

Materials and methods

Protocol and registration

This systematic review and meta-analysis was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [24]. The review protocol was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO), with the registration number CRD42024600762.

Eligibility criteria

Eligible studies were RCTs that had investigated the effects of mulberry (*Morus alba* L.) consumption on glycemic and lipid profiles. Participants consisted of adults aged 18 years or older, regardless of their health status, including healthy individuals or those diagnosed with metabolic disturbances such as hyperlipidemia, prediabetes, or T2DM. Studies involving participants with advanced confounding diseases, such as cancer or severe cardiovascular complications, were excluded. The intervention was defined as any orally administered, mulberry-derived product, consisting of leaf, fruit, or twig, in various forms such as powders, teas, extracts, or capsules. Studies using multi-herbal formulations were excluded unless the specific effects of mulberry could be isolated. The comparators were placebo or no treatment. Studies comparing mulberry with pharmacological agents, including standard treatments, as well as those lacking a comparator, were excluded. Primary outcomes encompassed glycemic parameters and lipid parameters. Secondary outcomes consisted of reported adverse events. Only full-text articles published in English or Thai were considered, while observational studies, animal or *in vitro* experiments, and non-randomized trials were excluded.

Data sources and search strategy

A systematic and comprehensive literature search was conducted across several electronic databases, (PubMed, Embase, Scopus) to identify relevant studies published from January 2000 to May 2025. Grey literature searches were also conducted, including Thai databases, such as Thai Journals Online (TJO) and the Thai Digital Collection (TDC), as well as Thai university libraries, to ensure the inclusion of local research. The search strategy was developed using a

building-block approach, combining controlled vocabulary (such as Medical Subject Headings (MeSH) and Excerpta Medica Tree (EMTREE)) with free-text keywords related to 3 core concepts: The intervention (mulberry), the population and conditions of interest (diabetes, dyslipidemia), and the study design (RCTs). Initially, no language restrictions were applied during the search process to maximize sensitivity. The search across all sources was completed on 15 May 2025, prior to final data extraction and analysis, to ensure the review reflected the most current evidence available. The full, exemplary search strategy for the PubMed database is provided (**Table S1**).

All records were imported into the EndNote software for initial deduplication, followed by additional deduplication and screening using the Rayyan AI software. Follow-up manual verification ensured the removal of any residual duplicates. Searches were updated prior to the final analysis.

Study selection

In the first stage, 2 reviewers independently screened the titles and abstracts of all articles against the predefined eligibility criteria. In the second stage, the full texts of all potentially relevant articles were retrieved and independently assessed by the 2 reviewers for final inclusion by the same 2 reviewers. Any discrepancies or disagreements between reviewers at either stage were resolved through discussion and consensus. If a consensus could not be reached, a third senior reviewer was consulted for a final decision.

Data extraction

The 2 reviewers independently extracted a comprehensive dataset from each eligible article. This information encompassed general study identifiers and characteristics (first author, year of publication, country, study design, duration), participant demographics (sample size, age, sex, baseline health status), and detailed intervention and comparator information (part of mulberry used, preparation form, dosage, frequency of administration). Furthermore, mean values, standard deviations (SDs), and sample sizes were recorded for all primary and secondary outcome data at baseline and post-intervention time points. The entire extraction process was conducted in duplicate (one each by a reviewer), with any discrepancies verified against the original articles and resolved by consensus. Any missing or unclear data were resolved by contacting the study authors. Extracted data were managed and organized using the Microsoft Excel software.

Risk of bias assessment

The methodological quality and risk of bias for each included RCT were assessed independently by 2 reviewers using the revised RoB 2 tool to evaluate 5 key domains: Bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, and bias in the selection of the reported result. Based on these domains, an overall risk of bias judgment for each study was categorized as 'Low risk of bias,' 'Some concerns,' or 'High risk of bias' [25]. Disagreements between reviewers were resolved through discussion or the involvement of a third reviewer if necessary.

Data synthesis and meta-analysis

A narrative synthesis was performed to describe the characteristics of all the included studies. These characteristics were presented in a tabular format. Quantitative meta-analyses were conducted for outcomes reported by at least 2 comparable studies, using the STATA software. Effect sizes for continuous outcomes were calculated as the mean difference (MD) with 95% confidence intervals (CIs). When only baseline and post-treatment values were reported, changes from the baseline and their SDs were calculated. Standardized formulas were used to convert data in different formats into means and SDs [26]. Where different measurement scales were used across studies, outcome units were standardized to a universal format to facilitate meta-analysis; for example, where necessary, blood glucose was converted from micromoles per liter to milligrams per deciliter. Where there were multiple groups within the same study, relevant groups were combined to create a single pairwise comparison, or the shared group was split and included as 2 or more reasonably independent comparisons [26]. The results of the meta-analyses were presented in forest plots.

A random-effects model was selected *a priori* for all meta-analyses to account for the anticipated clinical and methodological diversity across studies. Statistical

heterogeneity was assessed visually using forest plots and statistically based on Cochran's Q test (with $p < 0.10$ indicating significant heterogeneity) and the I^2 statistic. (^{2} values of 25%, 50% and 75% were interpreted as representing low, moderate, and high levels of heterogeneity, respectively) [27].

Subgroup analyses were conducted to explore potential sources of heterogeneity, stratified by the part of the mulberry plant used (leaf, fruit, twig) or the test meals (boiled rice or rice porridge). Funnel plots were not generated, as fewer than 10 studies were available for each outcome [28].

Certainty of evidence

The overall certainty of the evidence for each primary outcome was rated independently by 2 reviewers using the GRADE approach and the GRADEpro tool. Initially, the evidence was rated as high (as all included studies were RCTs) and then downgraded based on 5 potential limitations: Risk of bias, inconsistency of results, indirectness of evidence, imprecision of the effect estimate, and publication bias. The final certainty for each outcome was graded as high, moderate, low, or very low. Disagreements between reviewers were resolved through discussion or the involvement of a third reviewer if necessary. The assessment was focused exclusively on 7 clinically meaningful outcomes from the long-term trials to ensure clarity and interpretability, in line with the Cochrane recommendations [29].

Results and discussion

Study selection

The literature search and study selection process in this systematic review is presented in **Figure 1**. In total 2,720 records were retrieved from the database searches (PubMed, Embase, Scopus) and 9 records were obtained from the gray literature search. From the 1,661 records retrieved from databases, 1,608 studies were excluded by title and abstract screening. Among the 53 remaining relevant records, 42 full texts were obtained and screened according to the eligibility criteria. For the gray literature, 2 full texts were unable to be retrieved, and 6 studies did not meet eligibility criteria. In conclusion, 18 eligible full texts were included in this systematic review.

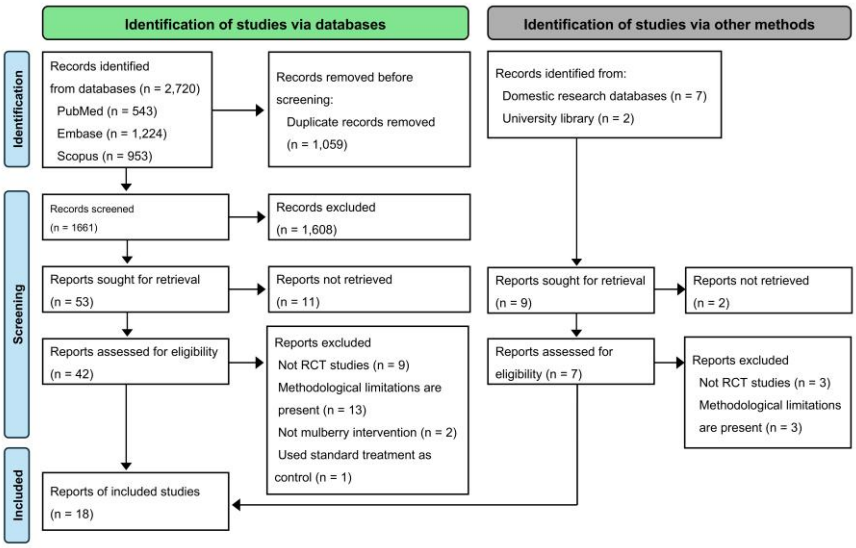

Figure 1 PRISMA flow diagram of literature search and study selection process.

Study characteristics

In total, 18 RCTs were included in this systematic review. These were categorized as 11 short-term studies [30-40], involving a single administration of mulberry intervention, and 4 long-term studies [18,19,41,42], involving multiple administrations, with 3 studies assessing both short-term and long-term interventions [43-45].

The characteristics of the short-term studies are shown in **Table 1**. Most studies applied a crossover design, whereas 2 utilized a parallel design [44,45]. Participants were generally healthy adults, except in 2

studies that included individuals with T2DM or prediabetes [33,45]. The age range of the participants was approximately 20 - 50 years, included both male and female. The interventions consisted of mulberry leaf extract, fruit extract, twig extract, and leaf powder, administered in various dosages and forms. Most studies focused on DNJ as the bioactive compound, with one study investigating oxyresveratrol [37]. Most studies used placebo controls that matched appearance and taste with intervention. The test meals varied in form and composition and were standardized to 50 - 75 g of carbohydrates. The primary outcomes assessed various measures related to postprandial glycemic effect. Most studies collected data on adverse events, such as gastrointestinal symptoms.

The characteristics of the long-term studies are shown in **Table 2**. Most studies utilized a parallel design, except one study with a crossover design [42]. The mulberry administration period was in the range 4 - 16 weeks. Most studies targeted obese individuals with insulin resistance, prediabetic individuals, or T2DM patients, except one study that was conducted on healthy participants [43]. The age range of the participants was approximately 46 - 55 years, with both males and females included. The intervention consisted of leaf extract, leaf powder and twig extract in capsule, tablet or beverage forms. In the control groups, the participants received placebo or diet control. Outcomes included glucose-related measures, lipid profiles, and anthropometric parameters. Data on adverse events were collected in all long-term studies.

Table 1 Characteristics of short-term studies.

Author	Study Design	Participants*	Type and Amount of Mulberry Intervention	Active Compound Content	Comparator	Test Meal	Outcomes	Outcome Measurement Time Points and Washout Period	Adverse Events
Asai *et al.* [43]#	Trial 1 Crossover	N (M/F) = 10 (8/2) Age: 50.0 ± 10.6 Healthy	Leaf extract 1) 1 capsule 2) 2 capsules 3) 3 capsules	DNJ 1) 3 mg 2) 6 mg 3) 9 mg	Placebo	200 g of boiled white rice with 2 g of dry seasoning	PPG and PPI	0, 30, 60, 90, 120 min Washout: 2 weeks	No gastrointestinal symptoms observed
Gheldof *et al.* [36]	Crossover	N (M/F) = 30 (19/11) Age: 31 ± 7 Healthy	Reducose® (Leaf extract) 0.25 g/dose	DNJ 12.5 mg/dose	No treatment	Curry rice and white bread (energy: 510 kcal; glycemic Load 48 g)	PPG	120 min Washout: not reported	Not reported
Kim *et al.* [45]	Parallel	N (M/F) = 38 (15/23) Age: 51.58 ± 7.56 Prediabetic	Leaf extract 5 g	DNJ 18 g	Placebo	High-carbohydrate meal (76 g of white bread and 24 g of strawberry jam)	PPG and PPI	0, 30, 60, 120 min	No adverse events and gastrointestinal symptoms observed
Mela *et al.* [35]@	Crossover	N = 65 Age: 31.2 ± 5.5 Healthy	1) Leaf Extract 1.0 g 2) Fruit Extract 1.5 g	1) Leaf extract DNJ 8 mg 2) Fruit extract DNJ 7.5 mg	No treatment	Rice porridge (50 g carbohydrate) mixed with the intervention	PPG and PPI	−15, 0, 15, 30, 45, 60, 90, 120, 180 min Washout: 1 week	Gastrointestinal symptoms: Vomiting, mild bloating and nausea
Mela *et al.* [34]	Crossover	N = 120 Age: 37 ± 8.5 Healthy	Fruit extract 0.37 g	DNJ 1.85 mg	No treatment	1) Sona masoori rice 64 g 2) Bora saul rice 60 g 3) Gobindobhog rice 62 g 4) Banskati rice 62 g (50 g carbohydrate)	PPG and PPI	15, 30, 45, 60, 90, 120 and 180 min Washout: 7 days	No gastrointestinal symptom observed
Mela *et al.* [32]	Trial 1^ Crossover	N = 78 Age: 33.15 ± 6.8 Healthy	Fruit extract 1) 0.37 g 2) 0.75 g 3) 1.12 g 4) 1.5 g	DNJ 1) 1.85 mg 2) 3.75 mg 3) 5.6 mg 4) 7.5 mg	No treatment	1) Rice porridge 2) Boiled rice (50 g carbohydrate)	PPG and PPI	0 and 120 min Washout: 1 week	Gastrointestinal symptoms: Vomiting Others: Upper respiratory tract infection
	Trial 2# Crossover	N = 77 Age not available Healthy	Fruit extract 1) 0.04 g 2) 0.12 g 3) 0.37 g	DNJ 1) 0.2 mg 2) 0.6 mg 3) 1.85 mg	No treatment	Boiled rice (50 g carbohydrate)	PPG and PPI	0 and 120 min Washout: 1 week	Gastrointestinal symptoms: Vomiting Others: Dizziness, spider bite
Mela *et al.* [33]#	Crossover	N = 24 Age not available	Fruit extract 1) 0.37 g	DNJ 1) 1.85 mg	Placebo	Boiled Sona Masuri rice 64 g (50 g carbohydrate)	PPG and PPI	15, 30, 45, 60, 90, 120, 150, 180,	Gastrointestinal symptoms:

Author	Study Design	Participants*	Type and Amount of Mulberry Intervention	Active Compound Content	Comparator	Test Meal	Outcomes	Outcome Measurement Time Points and Washout Period	Adverse Events
		T2DM	2) 0.75 g	2) 3.75 mg		and 140 mL of water		210, 240 min Washout: 5-7 days	Vomiting, dizziness, nausea, abdominal distension
Park *et al.* (2022)[37]	Trial 1[#] Crossover	N (M/F) = 24 (12/12) Age: 30.5 ± 5 Healthy	Twig extract 1) 0.5 g 2) 1 g 3) 2 g	Oxyresveratol 29.90 - 44.86 mg/g	Placebo	High fat sucrose drink	PPG	0, 15, 30, 60, 120 and 180 min Washout: at least 1 week	Not reported
	Trial 2 Crossover	N = 36 Age not available Healthy	Twig extract 2 g	Oxyresveratol 29.90 - 44.86 mg/g	Placebo	High fat sucrose drink	PPG and PPI	0, 30, 60, 120 and 240 min Washout: At least 1 week	No adverse events observed
Sukriket *et al.* [39]	Crossover	N (M/F) = 14 (7/7) Age: 51.21 ± 9.45 Healthy	Leaf tea powder 2 g	NA	Placebo	75 g of sucrose in 150 mL of warm water	PPG	30, 60, 90, 120, 150 min Washout: 1 week	No adverse events observed
Takahashi *et al.* [40]	Morning Trial Crossover	N (M/F) = 12 (8/4) Age: 29.8 ± 7.62 Healthy	Leaf extract 6 tablets/dose (The total tablet weight was not reported) in the morning.	DNJ 6 mg/dose	Placebo	Mixed meal standardized to 60 kJ/kg BW 70% carbohydrate, 15% fat, 15% protein	PPG, PPI, GIP, GLP-1, TAG, and NEFA	0, 30, 60, 120, 180 min Washout: At least 1 week	Not reported
	Evening Trial Crossover	N (M/F) = 12 (8/4) Age: 29.8 ± 7.62 Healthy	Leaf extract 6 tablets/dose (The total tablet weight was not reported) in the evening.	DNJ 6 mg/dose	Placebo	Mixed meal standardized to 60 kJ/kg BW 70% carbohydrate, 15% fat, 15% protein	PPG, PPI, GIP, GLP-1, TAG, and NEFA	0, 30, 60, 120, 180 min Washout: At least 1 week	Not reported
Thaipitakwong *et al.* [44][#]	Parallel	N (M/F) = 85 (17/68) Age: 23.31 ± 6.94 Healthy	Leaf powder 1) 2.3 g 2) 4.6 g 3) 6.9 g	DNJ 1) 6 mg 2) 12 mg 3) 18 mg	Placebo	Sucrose solution 50 g in 150 mL of water	FBG, PPG	−5, 30, 60, 90, 120, 180 min	Gastrointestinal symptoms: Bloating, flatulence, loose stools, nausea No serious or moderate adverse events reported
Thondre *et al.* [31]	Crossover	N = 36 Age: 31.8 ± 10.6 Healthy	Reducose® (Leaf extract) 250 mg	DNJ 11.25-13.75 mg	Placebo	75 g sucrose solution	PPG and PPI	0, 15, 30, 45, 60, 90, 120 min Washout: at least 2 days	No adverse events observed
Thondre *et al.* [30][#]	Crossover	N (M/F) = 37 (15/22) Age: 30.0 ± 10.4 Healthy	Reducose® (Leaf extract) 1) 200 mg 2) 225 mg 3) 250 mg	DNJ 1) 10 mg 2) 11.25 mg 3) 12.5 mg	Placebo	Egg sandwich carbohydrate 68.7 g, protein 18.7 g, fat 10.2 g and 250 mL water	PPG and PPI	0, 15, 30, 45, 60, 90, 120, 150, 180 min Washout: At least 48 h	No adverse events observed
Wang *et al.* [38][†]	Crossover	N (M/F) = 15(9/6) Age: 23.80 ± 1.47 Healthy	Leaf extract 750 mg	DNJ 7.5 mg	No treatment	Carbohydrate powder (glucose or maltose or sucrose or maltodextrin) with 150 mL of drinking water	PPG	−15, 15, 30, 45, 60, 90, 120 min Washout: 3 days	No adverse events observed

*Participants' information presented as sample size, age (mean ± SD) and health status.

[#]The studies/trials included multiple intervention doses; therefore, the groups were combined into a single pairwise comparison.

[@]Mela *et al.* [35] included different types of intervention (fruit and leaf extracts); therefore, the shared control group was split.

[^]Mela *et al.* [32] consisted of 2 subsets. In subset 1, where the comparator was boiled rice, multiple intervention doses were combined into a single pairwise comparison. In subset 2, where the comparator was rice porridge, it was not combined.

[†]Wang *et al.* [38] included multiple test meals; therefore, the groups were combined into a single pairwise comparison.

N = number, M = male, F = female, DNJ = 1-deoxynojirimycin, mg = milligram, g = gram, PPG = postprandial glucose, PPI = postprandial insulin, min = minute, kcal = kilocalorie, T2DM = type 2 diabetes mellitus, mL = milliliter, kJ = kilojoule, BW = body weight , GIP = glucose-dependent insulinotropic polypeptide, GLP-1 = glucagon-like peptide-1, TAG = triacylglycerol, NEFA = non-esterified fatty acid, FBG = fasting blood glucose.

Table 2 Characteristics of long-term studies.

Author	Study Design	Participants*	Type and Amount of Mulberry Intervention	Active Compound Content	Comparator	Study Duration	Outcomes	Adverse Events
Asai *et al.* [43]	Trial 2 Parallel	N (M/F) = 65 (43/22) Intervention (21/12), Placebo (22/10) Age: 53.55 ± 6.64 Healthy	Leaf extract tablet 3 tablets/day before meals	DNJ 18 mg/day	Placebo	Treatment: 12 weeks Follow-up: 4 weeks	FBG, FPI, HbA1c, glycated albumin, 1, 5-anhydroglucitol, TC, TG, HDL, LDL	No gastrointestinal symptoms observed in participants in intervention group
Kim *et al.* [45]	Parallel	N (M/F) = 38 (15/23) Age: 51.58 ± 7.56 Prediabetic	Leaf extract 5 g, 6 tablets/meal total of 18 tablets/day	DNJ 3.6 mg/g	Placebo	Run-in: 2 weeks Treatment: 4 weeks Follow-up: None	PPG 30, 60, 120 min, PPI, C-peptide	No adverse events and gastrointestinal symptoms observed in both intervention and control group
Parklak *et al.* [42]	Crossover	N = 12 Age: 46.57 ± 8.49 Persons with metabolic risk factors	Concentrated mulberry drink from mulberry fruit 100 g/day	Total phenolic 1041.90 mg/100 g Total anthocyanin 35.34 mg/100 g	Placebo	Run-in: none Treatment: 6 weeks Washout: 2 weeks Follow-up: None	FBG, FPI, HOMA-IR, TC, TG, LDL, HDL, blood pressure, CRP	No adverse events and gastrointestinal symptoms observed
Qu *et al.* [18]	Parallel	Sangzhi alkaloids: N = 77 Age: 54.6 ± 8.9 Placebo: N = 74 Age: 55.2 ± 9.0 T2DM	Sangzhi alkaloids Week 1 - 4: 150 mg, 3 tablets (50 mg each) Week 5-16: 300 mg, 6 tablets (50 mg each)	DNJ, FA, DAB	Placebo	Run-in: 2 weeks Treatment: 16 weeks Follow-up: None	HbA1c, FBG, PPG	Gastrointestinal disorders: flatulence, stomach swelling, diarrhea, abdominal discomfort
Riche *et al.* [41]	Parallel	N = 17 Age not available T2DM	Leaf extract 1 g, 3 times/day	NA	Placebo	Run-in: 2 weeks Treatment: 12 weeks Follow-up: None	HbA1c, blood pressure, BW	Gastrointestinal symptoms: stomach upset, bloating Others: influenza, hyperparathyroidism, warfarin toxicity
Taghizadeh *et al.* [19]	Parallel	N (M/F) = 57 (18/39) Age: 49.34 ± 15.35 T2DM	Leaf extract 300 mg, 2 times/day	NA	Placebo	Run-in: none Treatment: 12 weeks Follow-up: None	FBG, FPI, HOMA-IR, HbA1c, QUICKI, TG, VLDL, cholesterol, LDL, HDL	Liver function test: No significant abnormalities in both intervention and control group
Thaipitakwong *et al.* [44]	Parallel	N (M/F) = 54 (15/39) Age: 52.59 ± 6.89 Obese persons with prediabetes and patients with early stage T2DM	Leaf powder a sachet of leaf powder with 120 mL warm water 3 times/day before meal	DNJ 36 mg/day	Diet control	Run-in 2 weeks Treatment: 12 weeks Follow-up: None	FBG, PPG, HbA1c, FPI, TC, LDL, HDL, TG, AST, ALT, Cr, HOMA-IR Anthropometric data: weight, height, BMI, waist circumference, SBP, DBP, HR	Gastrointestinal symptoms reported (bloating, flatulence, abdominal pain, loose stools, and constipation)

*Participants' information presented as sample size, age (mean ± SD) and health status.

N = number, M = male, F = female, DNJ = 1-deoxynojirimycin, FBG = fasting plasma glucose, FPI = fasting plasma insulin, HbA1c = hemoglobin A1c, TC = total cholesterol, TG = triglyceride, HDL = high density lipoprotein, LDL = low density lipoprotein, g = gram, mg = milligram, PPG = postprandial glucose, PPI = postprandial insulin, HOMA-IR = homeostasis model assessment of insulin resistance, CRP = C reactive protein, T2DM = type 2 diabetes mellitus, FA = fagomine, DAB = 1,4-dideoxy-1,4-imino-d-arabinitol, NA = not applicable, BW = body weight, QUICKI = quantitative insulin sensitivity check index, VLDL = very low density lipoprotein, mL = milliliter, AST = aspartate transaminase, ALT = alanine transaminase, Cr = creatinine, BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, HR = heart rate.

Risk of bias

The risk of bias assessment for crossover and parallel studies is presented in **Figure 2**. Of the 13 crossover studies, 3 (23.1%) were judged to have some concerns or high risk of bias. Gheldof *et al.* [36] lacked clear information on washout period and applied an open-label design without blinding. Furthermore, the analysis approach was not explicitly described as intention-to-treat, while the details on handling protocol deviations were limited. Thondre *et al.* [31] did not report a washout period, raising concerns about potential carryover effects. Sukriket *et al.* [39] did not report allocation concealment, provided unclear participant numbers, and omitted some baseline data and outcome results. All the parallel studies (100%) [18,19,41,43-45] were assessed as having low risk of bias across all domains (**Figures S1** and **S2**).

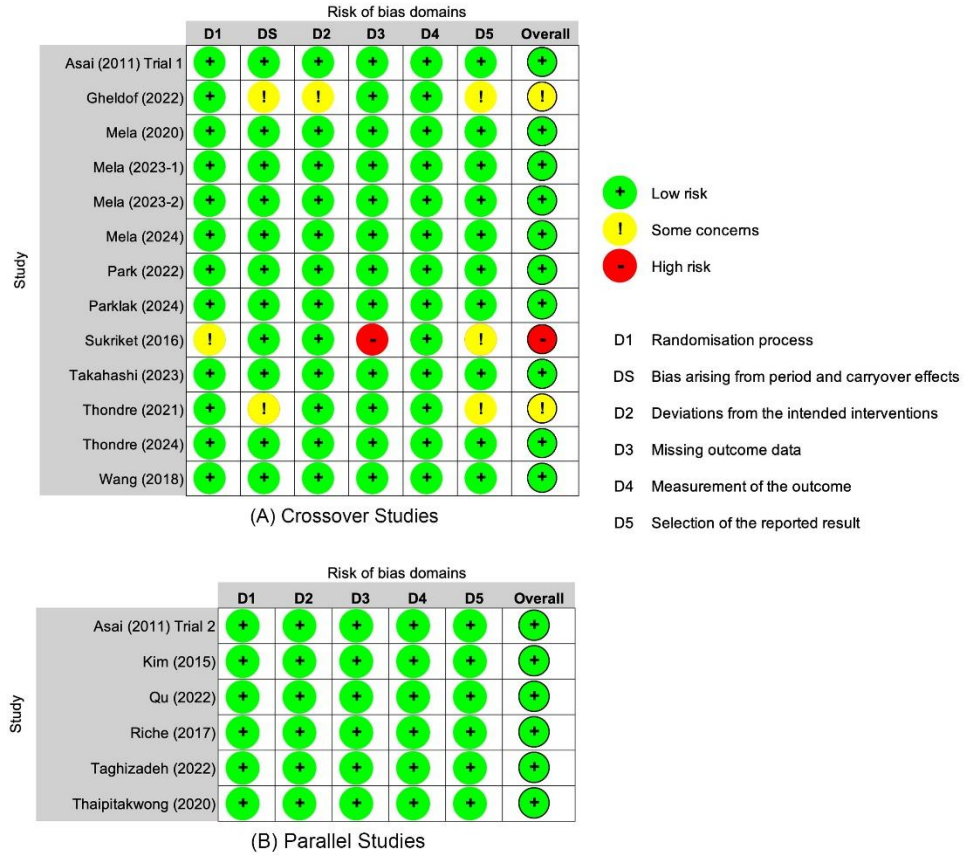

Figure 2 Risk-of-bias diagram of (A) crossover studies and (B) parallel studies.

Short-term study results

The outcomes in the meta-analysis of short-term studies were postprandial glucose (PPG) levels, PPG area under the curve (AUC), PPG positive incremental AUC (piAUC), postprandial insulin (PPI) levels, and PPI total AUC (tAUC).

Effect on postprandial glucose (PPG)

The pooled effects of a single mulberry dose on the PPG levels were analyzed at 3 different time points (30, 60 and 90 min), as shown in **Figure 3**. There were statistically significant reductions in the PPG levels in the mulberry group compared to the control group at 30 min (MD = −10.37 mg/dL; 95% CI: −19.30 to −1.45; p = 0.02) and 60 min (MD = −6.01 mg/dL; 95% CI: −11.97 to −0.05; p = 0.05). There was no significant difference at 90 min (MD = −1.17 mg/dL; 95% CI: −6.64 to 4.31; p = 0.68). Although considerable heterogeneity was observed among the studies at 30 and 60 min, it was reduced after the subgroup analysis based on the part of the mulberry (**Figures S3** and **S4**). Based on these results, the mulberry leaf subgroup significantly lowered PPG levels compared to the control group at both 30 min (MD = −14.85 mg/dL; 95% CI: −24.20 to −5.50; $p < 0.01$) and 60 min (MD = −10.25 mg/dL; 95% CI: −15.19 to −5.31; $p < 0.01$). However, there is no significant effect with the twig subgroup at either 30 or 60 min.

A statistically significant reduction in PPG AUC (MD = −925.17 mg·min/dL; 95% CI: −1256.71 to −593.63; $p < 0.01$) and PPG piAUC (MD = −445.14 mg·min/dL; 95% CI: −609.95 to −280.34; $p < 0.01$) was observed over 120 min in the mulberry group compared to the control group (**Figure 4**). Heterogeneity across the studies was low to moderate. In the subgroup analysis of PPG piAUC over 120 min based on the test meals, heterogeneity was reduced in both the boiled rice and rice porridge subgroups (**Figure S5**).

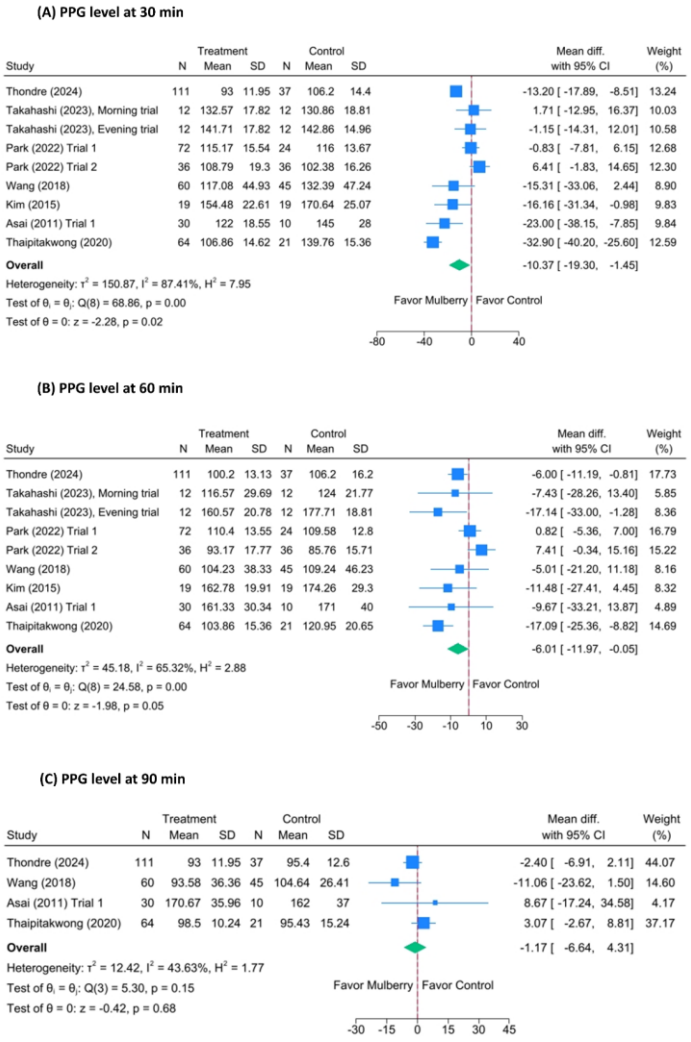

Figure 3 Forest plot of the effect of mulberry on PPG levels at (A) 30, (B) 60, and (C) 90 min.

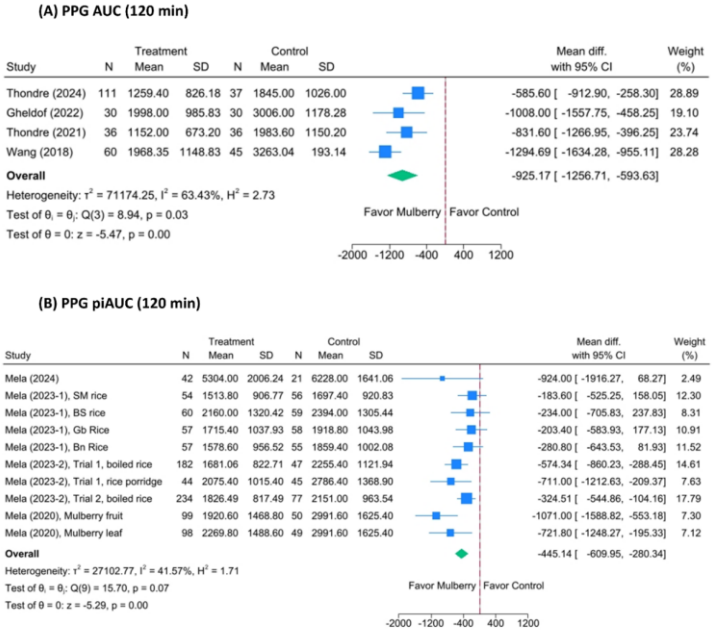

Figure 4 Forest plot of the effect of mulberry on (A) PPG AUC and (B) PPG piAUC at 120 min.

Effect of mulberry on postprandial insulin (PPI)

The pooled effects of a single mulberry dose on the PPI levels and PPI tAUC over 120 min were analyzed (**Figure 5**). There was no significant reduction in the PPI levels in the mulberry group compared to the control group (MD = −0.23 μIU/mL; 95% CI: −7.77 to 7.32; $p = 0.95$), with substantial heterogeneity across the studies. In the subgroup analysis based on the mulberry part, there was a significant reduction in PPI in the leaf subgroup compared to the control (MD = −4.64 μIU/mL; 95% CI: −8.92 to −0.37; $p = 0.03$) with no heterogeneity observed (**Figure S6**).

Furthermore, there was a statistically significant reduction in the PPI tAUC in the mulberry group compared to the control group (MD = −1,035.80 μU min/mL; 95% CI: −1,560.62 to −510.98; $p < 0.01$), again with substantial heterogeneity observed. The subgroup analysis based on the test meals reduced heterogeneity in both the boiled rice and rice porridge subgroups (**Figure S7**).

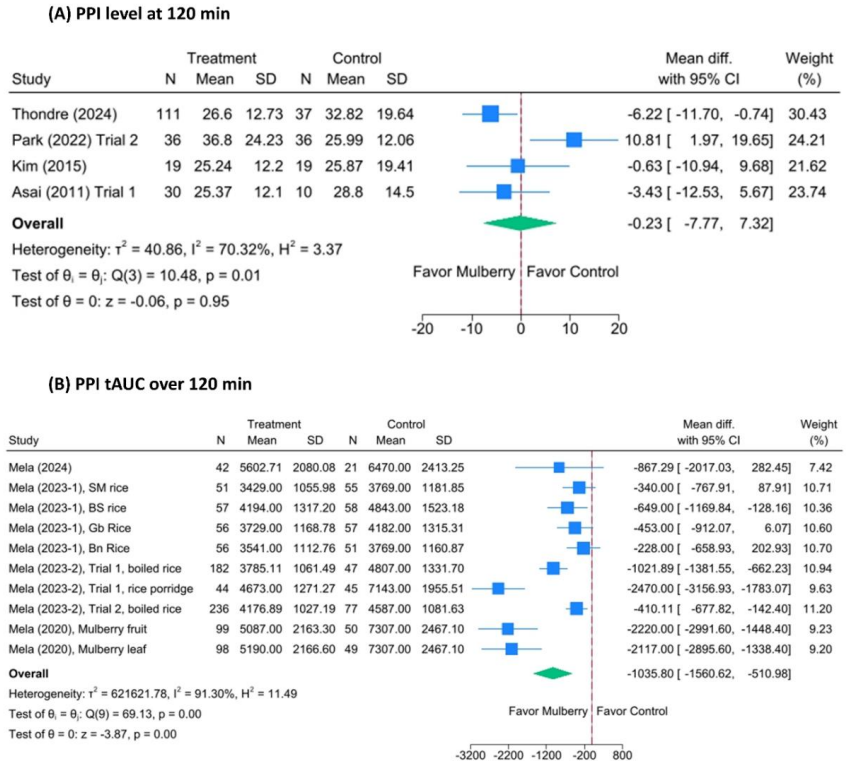

Figure 5 Forest plot of the effect of mulberry on (A) PPI level and (B) PPI tAUC at 120 min.

Long-term study results

The glycemic outcomes included in the meta-analysis of long-term studies were based on FBG, HbA1c, and fasting plasma insulin (FPI), as shown in **Figure 6**. There was no significant effect of mulberry on FBG following long-term treatment compared to the placebo (MD = −5.71 mg/dL; 95% CI: −14.46 to 3.03; $p = 0.20$), with considerable heterogeneity among studies. Subgroup analysis by mulberry part reduced heterogeneity (**Figure S8**). Neither the leaf nor the fruit subgroups had a significant improvement in FBG compared to the control group. In contrast, there was a significant reduction in the twig subgroup (MD = −18.00 mg/dL; 95% CI: −28.28 to −7.72; $p < 0.01$).

Based on the pooled analysis of mulberry's effect on HbA1c, there was a significant reduction in the treatment group compared to the control group (MD = −0.30%; 95% CI = −0.56 to −0.05; $p = 0.02$), with considerable heterogeneity observed. Subgroup analysis by mulberry part resulted in reduced heterogeneity (**Figure S9**). Both the leaf (MD = −0.16%; 95% CI = −0.29 to −0.03; $p = 0.01$) and twig (MD = −0.71%; 95% CI = −0.97 to −0.45; $p < 0.01$) subgroups had significant improvements in HbA1c compared to the control group.

The pooled analysis of mulberry's effect on FPI indicated no effect in the treatment group compared to the control group (MD = −0.82 μIU/mL; 95% CI = −2.68 to 1.04; $p = 0.39$), with low heterogeneity.

The lipid outcomes included in the meta-analysis of long-term studies were based on TC, TG, LDL, and HDL (**Figure 7**). Mulberry had no significant effect on TC (MD = −4.13 mg/dL; 95% CI = −13.42 to 5.17; $p = 0.38$), TG (MD = −16.08 mg/dL; 95% CI = −34.91 to 2.75; $p = 0.09$), LDL (MD = −2.22 mg/dL; 95% CI = −10.87 to 6.43; $p = 0.61$), and HDL (MD = 1.13 mg/dL; 95% CI = −3.73 to 5.98; $p = 0.65$). The heterogeneity across studies evaluated for all lipid outcomes was low to moderate.

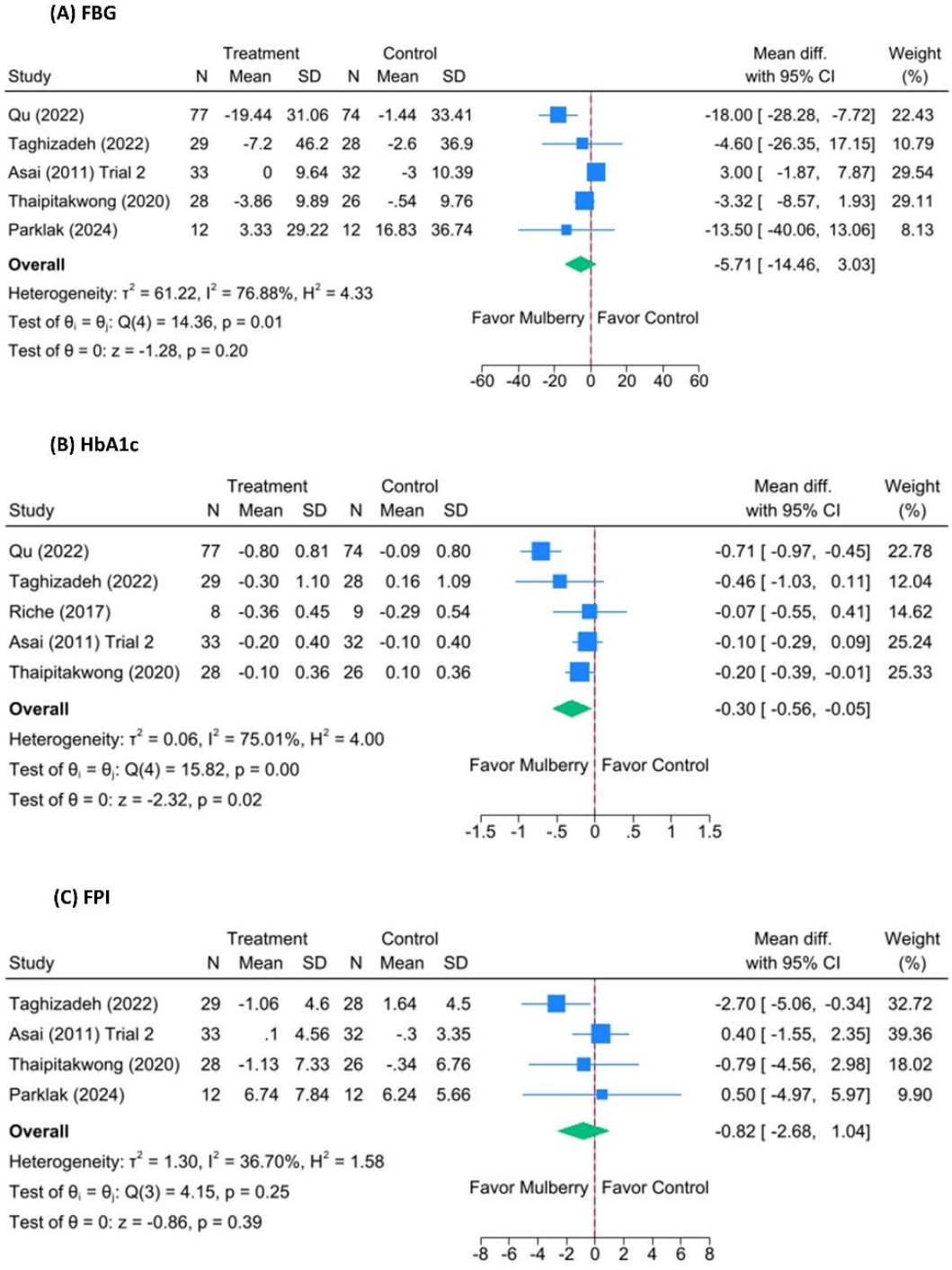

Figure 6 Forest plot of the effect of mulberry on (A) FBG, (B) HbA1c, and (C) FPI.

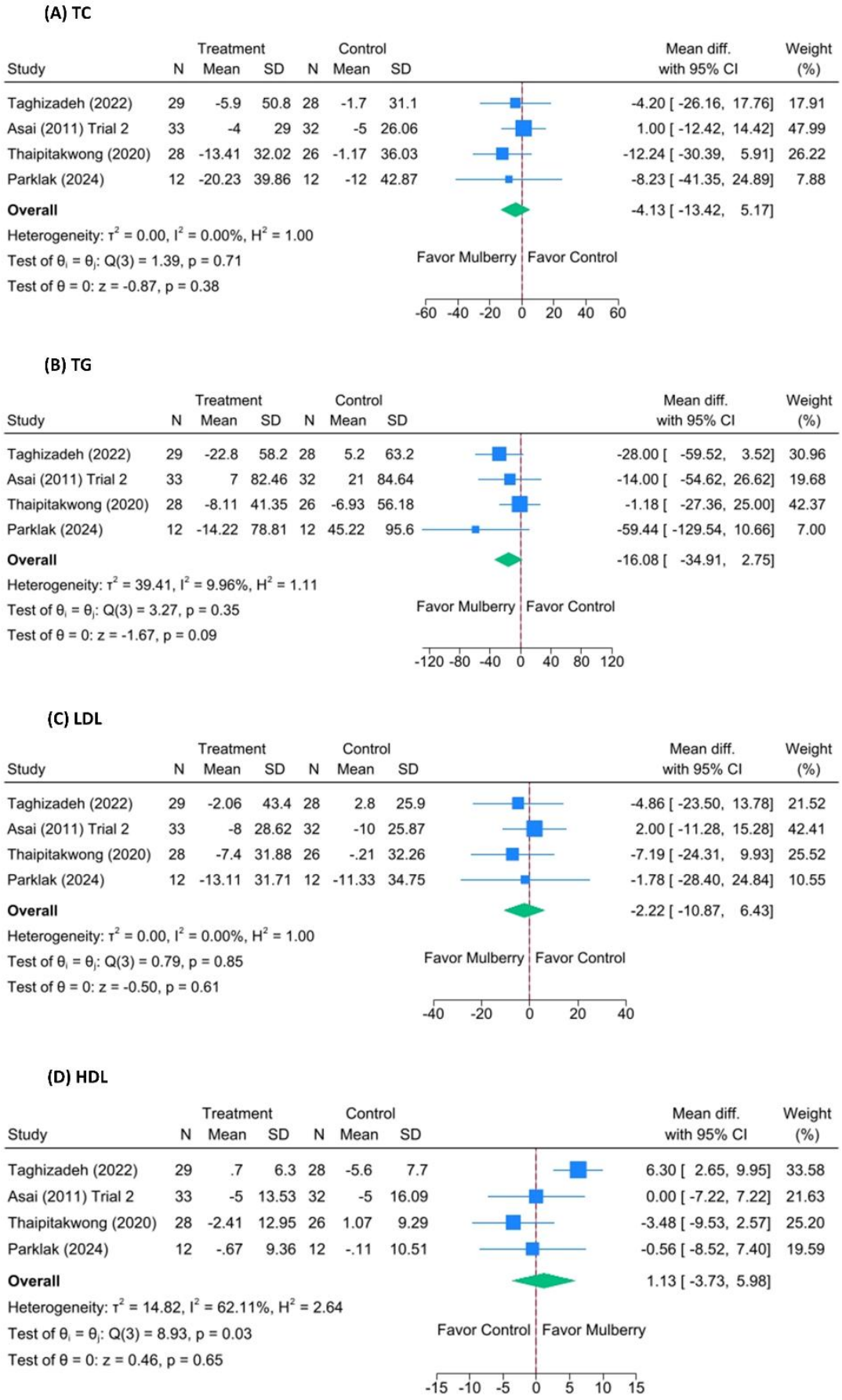

Figure 7 Forest plot of the effect of mulberry on (A) TC, (B) TG, (C) LDL, and (D)

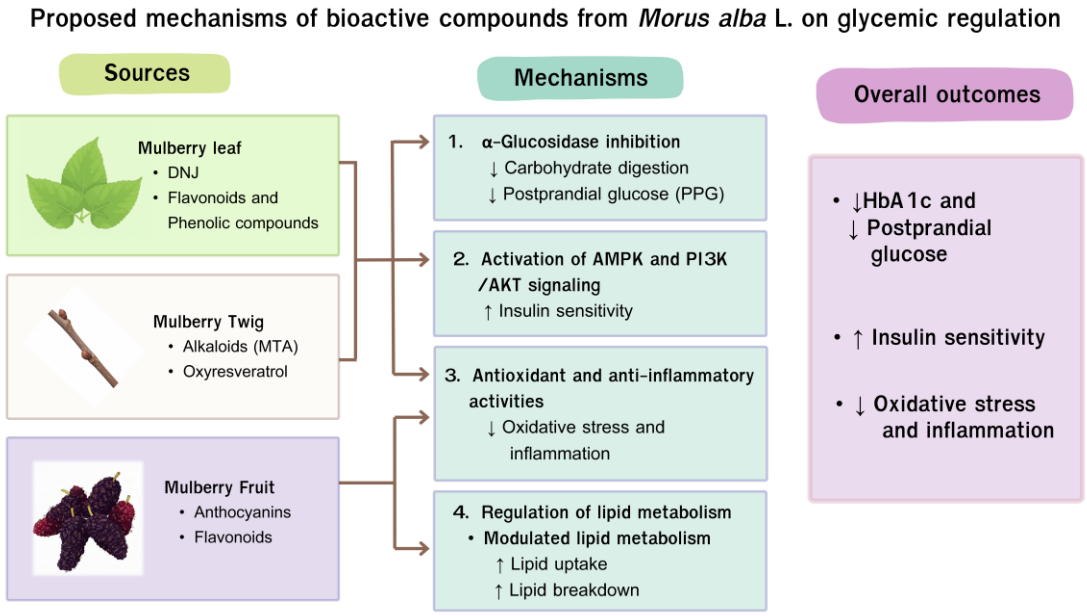

Figure 8 Bioactive compounds from *Morus alba*, including leaf, twig, and fruit, contribute to glycemic regulation through α-glucosidase inhibition, antioxidant and anti-inflammatory effects, and AMPK/PI3K-AKT activation, leading to improved glucose control and insulin sensitivity.

Adverse events

Reporting of adverse events was inconsistent across the included trials. Several studies clearly stated the absence of adverse events, while others did not specify whether safety outcomes were assessed. Among studies that reported safety data, mild gastrointestinal symptoms such as bloating, nausea, and loose stool were the most frequently observed, and no serious adverse events were reported. Overall, mulberry interventions appeared to be well tolerated, although incomplete and variable reporting suggests a potential for reporting bias. Standardized safety monitoring in future trials is recommended to improve the reliability of safety evidence.

Certainty of evidence

The certainty of the evidence for the key long-term outcomes was evaluated using the GRADE approach (**Table S2**). No serious risks of bias were identified across the evaluated outcomes. The certainty of evidence for HbA1c and FPI was rated as moderate, while FBG was rated as low. For lipid outcomes (TC, TG, HDL, and LDL), the certainty of evidence was also rated as moderate. **Table S2** presents the GRADE assessment for certainty of evidence of the long-term study outcomes.

Discussion

The aim of this systematic review and meta-analysis was to evaluate the short- and long-term effects of various mulberry parts (leaf, twig and fruit) on glycemic and lipid parameters, with a focus on their potential use as functional food. Based on the findings, mulberry exerted a potent acute effect in attenuating PPG levels and PPG AUC. In addition, mulberry demonstrated potential in reducing PPG piAUC, and PPI tAUC, with most studies focusing on mulberry fruit [32-35]. Notably, a significant reduction in PPG and PPI levels was observed specifically in the leaf subgroup. With long-term administration, mulberries produced a significant reduction in HbA1c. However, there were no significant effects on FBG, FPI, or lipid parameters. The minimally clinically important difference (MCID) for HbA1c reduction in diabetes management is at least 0.5%. In this review, although the overall HbA1c reduction (0.3%) was smaller than the established MCID, the confidence interval (−0.56 to −0.05) still crossed the threshold. This finding suggests a modest yet potentially clinically relevant improvement in long-term glycemic control, particularly when mulberries are used as a supplement or functional food rather than pharmacotherapy. Gastrointestinal symptoms were the most common adverse effect reported in both the short-

term and long-term studies, consistent with another review [46]. Overall, the treatment was generally well tolerated and considered safe for use.

PPG is an established risk factor for CVD, which can lead to morbidity and mortality [47-50]. PPG has been shown to be more strongly linked to complications than fasting hyperglycemia in T2DM patients and in subjects with a prior history of diabetes, highlighting the importance of its control [51,52]. Based on the current analysis, mulberry exerted its most pronounced effect in rapidly reducing PPG levels at 30 and 60 min. This was consistent with the findings from another review, which reported a significant reduction at 30 min, indicating that mulberry's glucose-lowering effect was evident within the 30 - 60 min timeframe [53]. Furthermore, our findings showed that mulberry significantly lowered PPG AUC and PPI piAUC, consistent with other findings on PPG iAUC [46,53].

Evidence regarding mulberry twig interventions remains limited but informative. The mulberry twig preparations produced no significant effects on PPG or PPI levels after a single administration. Our analysis was restricted to one study by Park *et al.* [37], which reported significant reductions in PPG and PPI at 240 min in the treatment group compared with the placebo, suggesting that effects may emerge at later time points. Oxyresveratrol (29.90 - 44.86 mg/g) was identified as the main active compound in that study; however, mulberry twigs also contain other phenolic constituents, including maclurin, rutin, isoquercitrin, resveratrol, and morin. These compounds have demonstrated antioxidant and antityrosinase activities in vitro, indicating the need for further investigation in human studies [58]. In the pooled long-term analysis, fasting parameters such as FBG and FPI showed no significant changes, consistent with previous reviews [23,46]. However, markers reflecting longer-term glucose regulation demonstrated significant improvement in HbA1c [23]. This effect was also evident in the mulberry leaf subgroup (DNJ 18 - 36 mg/day), corresponding with short-term improvements in PPG. As reductions in PPG contribute to lower HbA1c, these results support the potential of mulberry leaves for glycemic control [47]. Notably, the twig subgroup demonstrated significant reductions in both FBG and HbA1c [18]. Given that these findings were derived from a single trial, they should be interpreted with caution and regarded as exploratory rather than confirmatory evidence.

In addition to differences among plant parts, variability in postprandial outcomes may also depend on the characteristics of the test meal. Subgroup analyses were conducted based on the type of test meal (rice porridge or boiled rice) for PPG piAUC and PPI tAUC, which reduced heterogeneity in both meal outcomes, indicating that the method of test meal preparation may influence postprandial responses. Significant reductions were observed across test meal types, suggesting that mulberry provided beneficial effects across various rice meal forms. The variation in the magnitude of postprandial responses may be explained by differences in the starch structure and digestion characteristics associated with the different rice processing methods [59]. Further studies are warranted directly comparing different meal matrices to clarify the mechanisms underlying these effects.

The improvements in postprandial glucose and insulin-related outcomes observed across the included trials are likely mediated by diverse bioactive constituents of *Morus alba* L. A primary mechanism explaining the significant reduction in PPG involves intestinal α-glucosidase inhibition. 1-DNJ, an alkaloid abundant in mulberry leaves and twigs, delays carbohydrate digestion and absorption, thereby attenuating postprandial glycemic responses [17,54-56]. Reported DNJ concentrations in the included studies ranged from 0.2 - 18 mg in leaves and 1.85 - 7.5 mg in fruits, consistent with levels shown to exert α-glucosidase inhibitory activity. Beyond enzymatic inhibition, flavonoids and other phenolic compounds present in mulberry exhibit potent antioxidant and anti-inflammatory properties, which may counteract oxidative stress and low-grade inflammation associated with metabolic dysregulation [57]. Furthermore, evidence suggests that mulberry extracts enhance insulin sensitivity and regulate lipid metabolism, possibly through activation of cellular signaling pathways such as AMPK and PI3K/AKT [23]. Anthocyanins, mainly found in mulberry fruits, also contribute antioxidant effects and may improve lipid profiles and vascular function [33,42]. Although long-term effects on fasting blood glucose (FBG) and lipid parameters were less pronounced in this analysis, these integrated biological mechanisms highlight the potential

of *Morus alba* L. to modulate glycemic control and related metabolic pathways. The proposed regulatory mechanisms are summarized in **Figure 8**.

For lipid-related outcomes, mulberry interventions did not produce significant improvements. The certainty of evidence for all lipid markers was rated as moderate, supporting confidence in these null findings. These results align with another review focusing on mulberry leaf interventions [20]. Both the present and previous reviews included trials of relatively short duration (up to 12 - 16 weeks), which may be insufficient to influence lipid metabolism given the slower physiological turnover of lipoproteins compared with glucose markers. In contrast, a meta-analysis of berberine, a functional food that inhibits carbohydrate-digesting enzymes, reported significant reductions in TC, LDL, and TG after 2 - 24 months of intervention. These findings suggest that longer intervention durations may be necessary to observe lipid-modifying effects of mulberry interventions [60].

This review had several strengths. First, it applied a comprehensive search strategy that followed PRISMA 2020 guidelines and was prospectively registered in PROSPERO. In addition, it included the most recent RCTs available up to May 2025 and evaluated both efficacy and safety outcomes. Furthermore, a rigorous risk-of-bias assessment was conducted using the RoB 2 tool, with most included RCTs rated as having low risk of bias. Another notable strength was the inclusion of various parts of the mulberry plant, which enabled subgroup analyses by plant part and provided a broader perspective on its potential effects.

Despite these strengths, several limitations should be acknowledged. Variations in DNJ dosage, intervention duration, mulberry part used, and participant characteristics may have contributed to the heterogeneity observed across outcomes. While subgroup analyses addressed part of this variability, the limited number of RCTs per outcome prevented meta-regression and reliable funnel plot generation, leaving the possibility of publication bias [61]. The small evidence base also restricted the strength of subgroup conclusions. Evidence for mulberry twig relied on one short-term and one long-term study, and research on mulberry fruit remains scarce despite its frequent use in beverages. Moreover, no trial exceeded 16 weeks, limiting assessment of long-term efficacy. Although no language restrictions were applied, only English and Thai RCTs were included because some potentially relevant Chinese or Japanese studies lacked accessible full texts, which may have introduced language bias. Collectively, these limitations highlight the need for well-designed, longer-term, and more diverse clinical trials to strengthen the evidence base for the health effects of *Morus alba*.

While these limitations exist, the findings remain informative for policy and regulatory considerations. Within Thailand's context, the evidence supports the transition toward science-based regulation of functional foods and herbal products. As *Morus alba L.* is locally available and culturally accepted, these findings may inform its inclusion under the current Other Function Claim framework and advance national efforts to promote evidence-based innovation using indigenous ingredients. Internationally, the results align with global frameworks such as the Codex Alimentarius, Japan's FOSHU, and EFSA, which emphasize human-based scientific substantiation for functional-claim approval. This review provides an updated foundation to guide policy dialogue, product development, and regulatory evaluation of mulberry-based functional foods, while supporting the ongoing establishment of the Food with Function Claims (FFC Thailand) system harmonized with international standards. Continued research and standardization of key bioactives will further facilitate the translation of these findings into regulatory and industrial applications.

Conclusions

The findings from this systematic review and meta-analysis indicated that mulberry, particularly the leaf, showed beneficial effects on postprandial glycemic responses and modest improvement in HbA1c, while no significant effects were observed for FBG, FPI, or lipid outcomes. The intervention appeared safe and well tolerated, suggesting its potential as a functional food for glycemic control. Further well-designed studies with longer intervention periods, as well as investigations of mulberry twig and fruit, are warranted to clarify their long-term efficacy and broader metabolic effects.

Acknowledgements

Funding was provided by the Office of National Higher Education Science Research and Innovation

Policy Council through the Program Management Unit for Competitiveness (PMUC). The funding provider had no part in designing the study, collecting or analyzing data, interpreting findings, or drafting the manuscript.

Declaration of generative AI in scientific writing

Generative AI tools (e.g., ChatGPT by OpenAI, Copilot) were used solely to enhance readability and language during manuscript preparation. No scientific content or data interpretation was generated by AI. The authors take full responsibility for the content.

CRediT author statement

Dalad Siriwan: Conceptualization; Methodology; Supervision; Funding acquisition; Writing - Original draft and Writing - Reviewing and Editing. **Piyapat Trisonthi**: Investigation; Data curation; Validation and Writing - Original draft preparation. **Piya Temviriyanukul**: Investigation; Formal analysis and Writing - Original Draft. **Phenphop Phansuea**: Investigation; Formal analysis and Writing - Original Draft. **Yuraporn Sahasakul**: Investigation; Validation, and Writing - Original Draft. **Woorawee Inthachat**: Investigation and Data curation.

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Supplementary materials

Table S1 Search strategy for PubMed database.

Key Concept	Search Syntax
#1 Participants	((((((((((((((((((((hyperglyc*[Text Word]) OR (dyslipidaem*[Text Word])) OR (dyslipedem*[Text Word])) OR ("diabetes mellitus"[Text Word])) OR ("Healthy"[Text Word])) OR ("Metabolic syndrome"[Text Word])) OR ("Dyslipidemia"[Text Word])) OR ("Diabetes"[Text Word])) OR (adult*[Text Word])) OR (human*[Text Word])) OR ("obesity"[Text Word])) OR (obes*[TextWord])) OR ("insulin resistance"[Text Word])) OR (IR[Text Word])) OR (Hyperglycemia[MeSH Terms])) OR (Adult[MeSH Terms])) OR (Healthy Volunteers[MeSH Terms])) OR (Metabolic syndrome[MeSH Terms])) OR (Metabolic diseases[MeSH Terms])) OR (Diabetes Mellitus[MeSH Terms])) OR (Dyslipidemias[MeSH Terms])) OR ("insulin resistance"[MeSH Terms])
#2 Intervention	((((((mulberr*[Text Word]) OR (morus*[Text Word])) OR ("Moraceae"[Text Word])) OR ("Morus"[Text Word])) OR ("Mulberry"[Text Word])) OR ("Mulberry extract"[Text Word])) OR (Morus[MeSH Terms])
#3 Outcomes	((((((((((((((((((((((((((((("glycaemic"[Text Word]) OR ("glycated haemoglobin"[Text Word])) OR ("plasma glucose"[Text Word])) OR ("blood sugar"[Text Word])) OR ("blood glucose"[Text Word])) OR ("glycemic"[Text Word])) OR ("postprandial glucose"[Text Word])) OR ("glycated hemoglobin"[Text Word])) OR ("HbA1c"[Text Word])) OR ("insulin"[Text Word])) OR (glycemic*[Text Word])) OR (GI[Text Word])) OR ("low density lipoprotein"[Text Word])) OR ("high density lipoprotein"[Text Word])) OR (HDL[Text Word])) OR (LDL[Text Word])) OR (TG[Text Word])) OR (TC[TextWord])) OR ("total cholesterol"[Text Word])) OR ("low-density lipoprotein"[Text Word])) OR ("high-density lipoprotein"[Text Word])) OR (glycaemic*[Text Word])) OR (triglyceride*[Text Word])) OR ("blood lipid"[Text Word])) OR ("lipid profile"[Text Word])) OR (Blood glucose[MeSH Terms])) OR (Glycemic Control[MeSH Terms])) OR (Glycated Hemoglobin[MeSH Terms])) OR (Insulin[MeSH Terms])) OR (Cholesterol[MeSH Terms])) OR (Triglycerides[MeSH Terms])) OR (Lipoprotein[MeSH Terms])
Final search: #1 AND #2 AND #3	((((((((((((((((((((hyperglyc*[Text Word]) OR (dyslipidaem*[Text Word])) OR (dyslipedem*[Text Word])) OR ("diabetes mellitus"[Text Word])) OR ("Healthy"[Text Word])) OR ("Metabolic syndrome"[Text Word])) OR ("Dyslipidemia"[Text Word])) OR ("Diabetes"[Text Word])) OR (adult*[Text Word])) OR (human*[Text Word])) OR ("obesity"[Text Word])) OR (obes*[TextWord])) OR ("insulin resistance"[Text Word])) OR (IR[Text Word])) OR (Hyperglycemia[MeSH Terms])) OR (Adult[MeSH Terms])) OR (Healthy Volunteers[MeSH Terms])) OR (Metabolic syndrome[MeSH Terms])) OR (Metabolic diseases[MeSH Terms])) OR (Diabetes Mellitus[MeSH Terms])) OR (Dyslipidemias[MeSH Terms])) OR ("insulin resistance"[MeSH Terms])) AND ((((((mulberr*[Text Word]) OR (morus*[Text Word])) OR ("Moraceae"[Text Word])) OR ("Morus"[Text Word])) OR ("Mulberry"[Text Word])) OR ("Mulberry extract"[Text Word])) OR (Morus[MeSH Terms]))) AND ((((((((((((((((((((((((((((("glycaemic"[Text Word]) OR ("glycated haemoglobin"[Text Word])) OR ("plasma glucose"[Text Word])) OR ("blood sugar"[Text Word])) OR ("blood glucose"[Text Word])) OR ("glycemic"[Text Word])) OR ("postprandial glucose"[Text Word])) OR ("glycated hemoglobin"[Text

Key Concept	Search Syntax
	Word])) OR ("HbA1c"[Text Word])) OR ("insulin"[Text Word])) OR (glycemic*[Text Word])) OR (GI[Text Word])) OR ("low density lipoprotein"[Text Word])) OR ("high density lipoprotein"[Text Word])) OR (HDL[Text Word])) OR (LDL[Text Word])) OR (TG[Text Word])) OR (TC[TextWord])) OR ("total cholesterol"[Text Word])) OR ("low-density lipoprotein"[Text Word])) OR ("high-density lipoprotein"[Text Word])) OR (glycaemic*[Text Word])) OR (triglyceride*[Text Word])) OR ("blood lipid"[Text Word])) OR ("lipid profile"[Text Word])) OR (Blood glucose[MeSH Terms])) OR (Glycemic Control[MeSH Terms])) OR (Glycated Hemoglobin[MeSH Terms])) OR (Insulin[MeSH Terms])) OR (Cholesterol[MeSH Terms])) OR (Triglycerides[MeSH Terms])) OR (Lipoprotein[MeSH Terms]))

* Final search was conducted on 15 May 2025

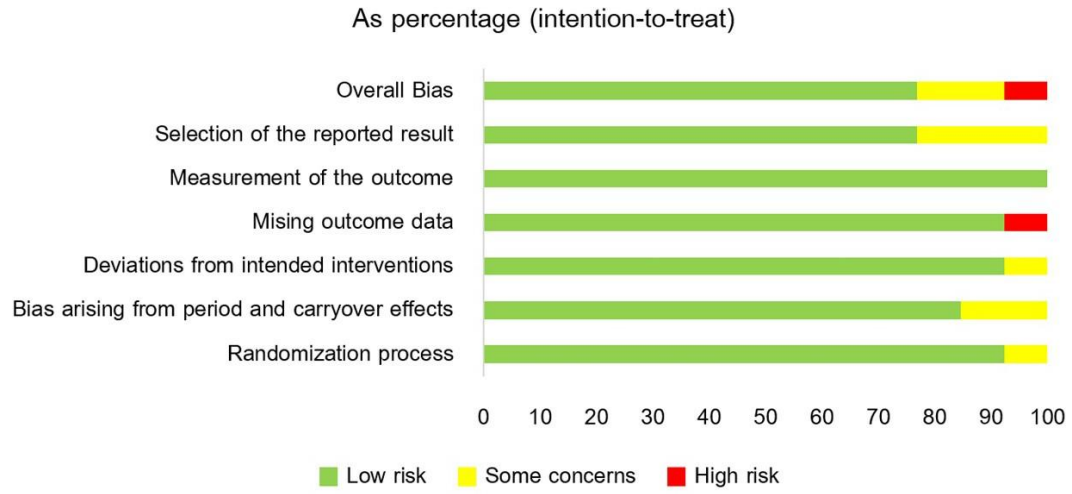

Figure S1 Risk of bias distribution in crossover studies.

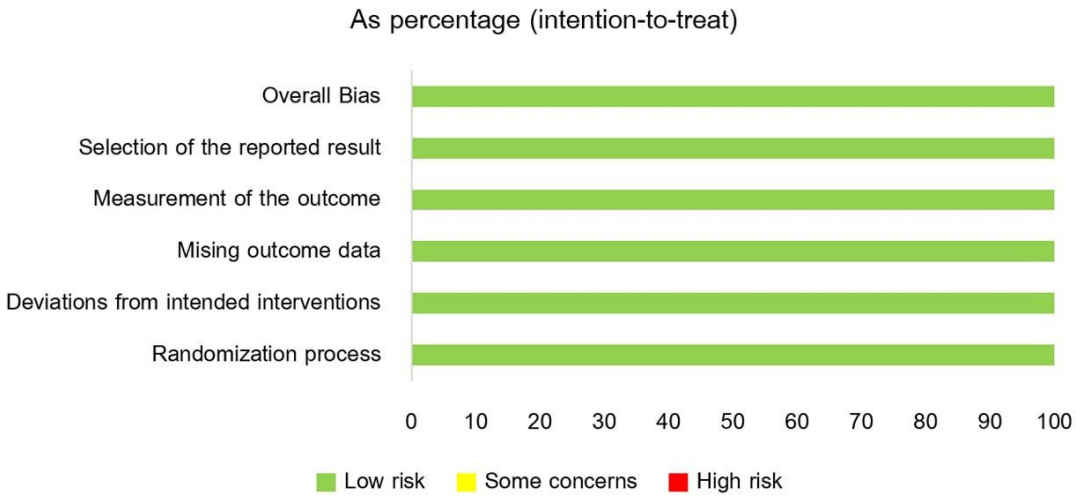

Figure S2 Risk of bias distribution in parallel studies

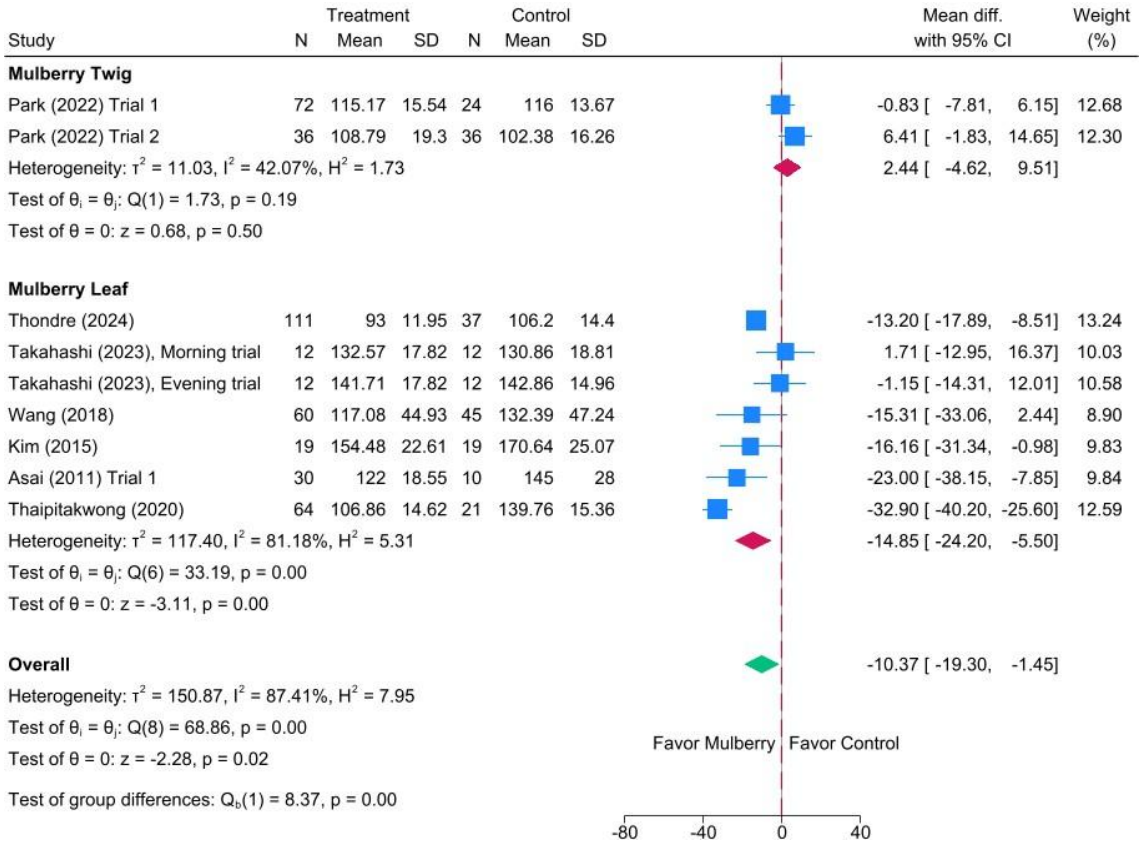

Figure S3 Forest plot of subgroup analysis by mulberry part on PPG at 30 min.

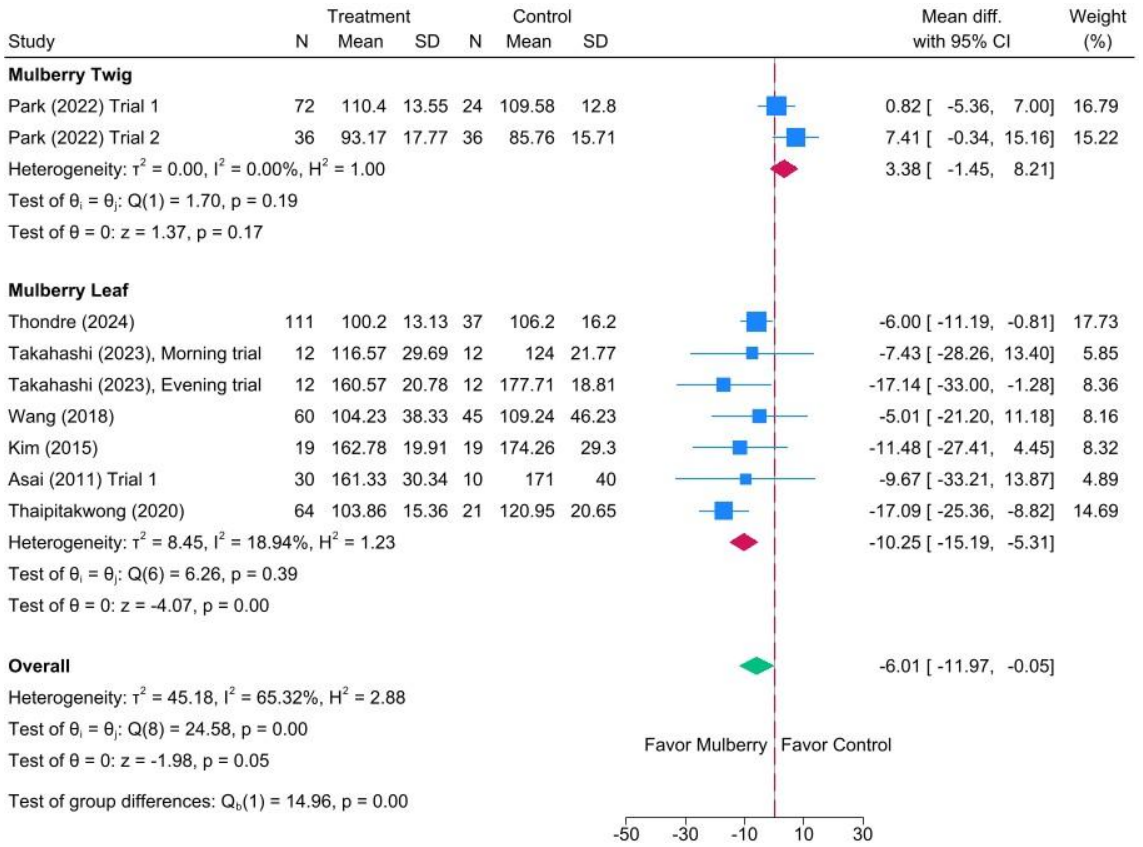

Figure S4 Forest plot of subgroup analysis by mulberry part on PPG at 60 min.

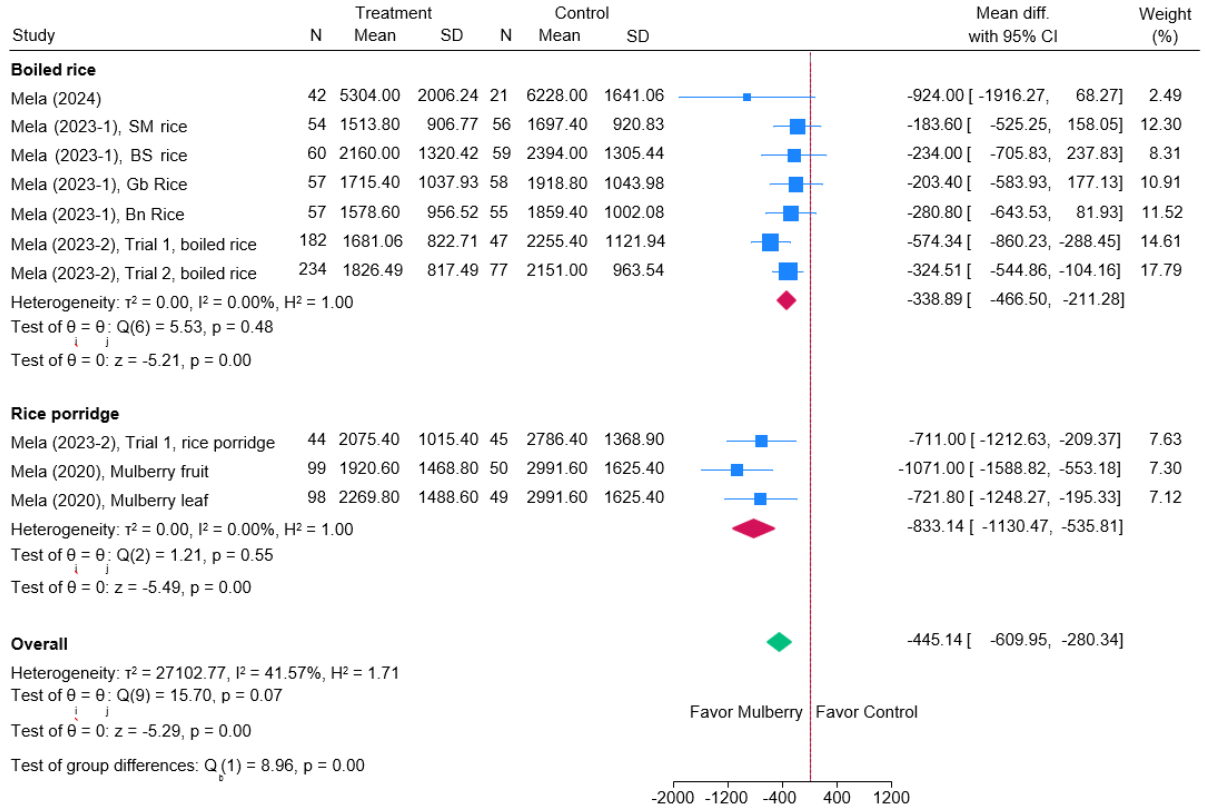

Figure S5 Forest plot of subgroup analysis by test meal on PPG piAUC over 120 min.

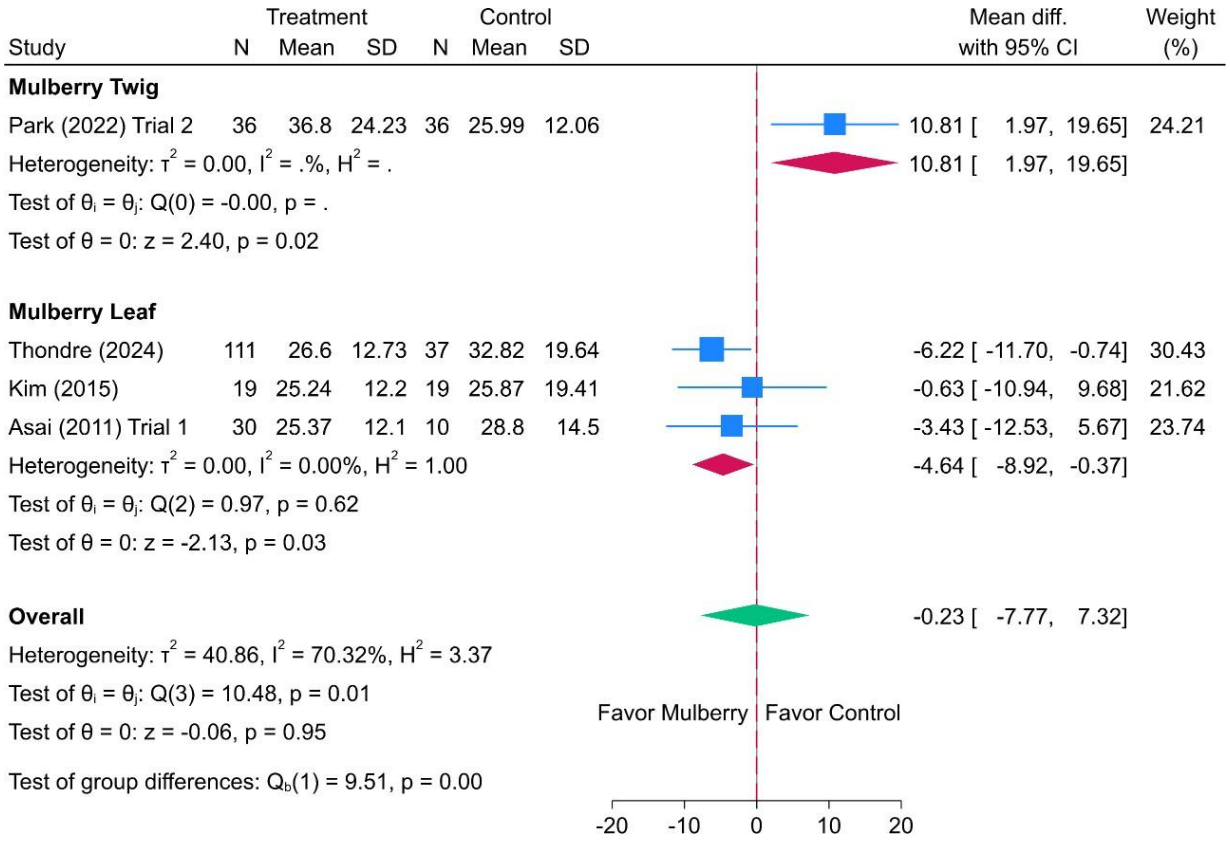

Figure S6 Forest plot of subgroup analysis by mulberry part on PPI over 120 min.

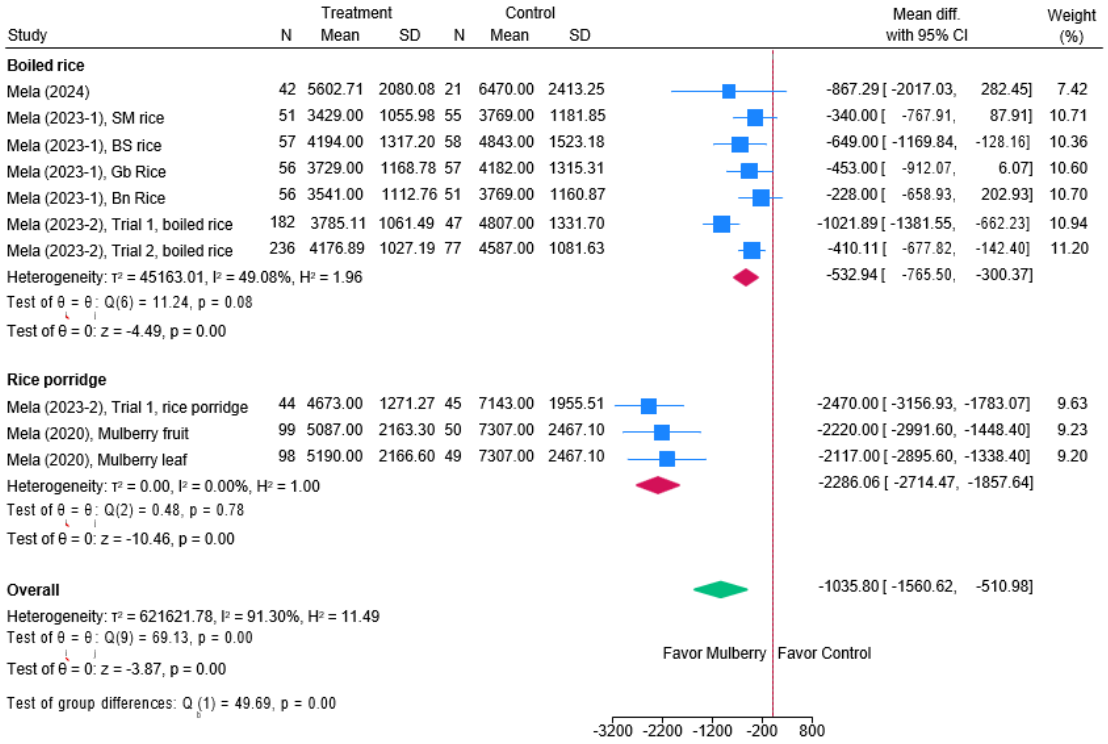

Figure S7 Forest plot of subgroup analysis by test meal on PPI tAUC over 120 min.

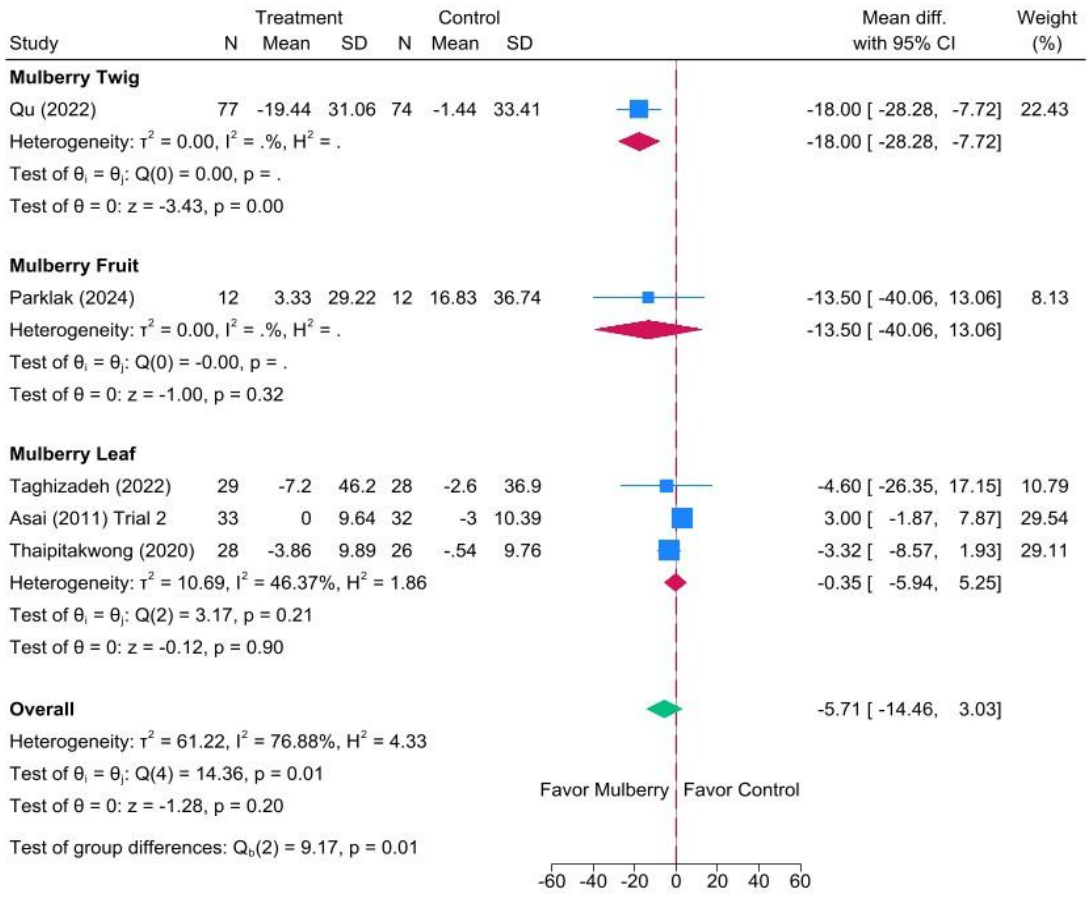

Figure S8 Forest plot of subgroup analysis by mulberry part on FBG.

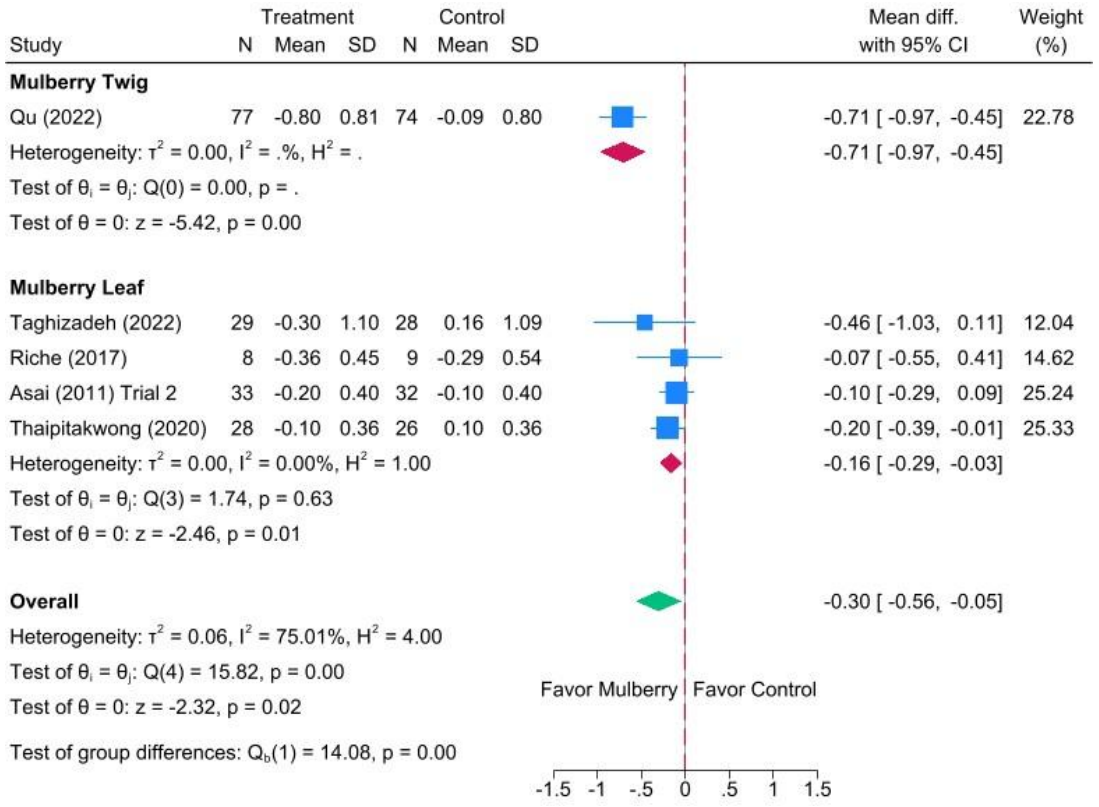

Figure S9 Forest plot of subgroup analysis by mulberry part on HbA1c.

Table S2 Certainty of evidence (GRADE) for long-term outcomes.

Outcome measures	Certainty assessment						
	No. of studies	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Certaintyof Evidence
Hemoglobin A1c (HbA1c)	344 (5 RCTs)	Not serious	Not serious	Not serious	Serious[a]	None	⊕⊕⊕◯ Moderate[a]
Fasting plasma glucose (FBG)	351 (5 RCTs)	Not serious	Not serious	Serious[b]	Serious[a]	None	⊕⊕◯◯ Low[a,b]
Fasting plasma insulin (FPI)	200 (4 RCTs)	Not serious	Not serious	Not serious	Serious[a]	None	⊕⊕⊕◯ Moderate[a]
Total cholesterol (TC)	241 (4 RCTs)	Not serious	Not serious	Not serious	Serious[c]	None	Moderate[c] ⊕⊕⊕◯
Total triglyceride (TG)	241 (4 RCTs)	Not serious	Not serious	Not serious	Serious[c]	None	Moderate[c] ⊕⊕⊕◯
High density lipoprotein (HDL)	241 (4 RCTs)	Not serious	Not serious	Not serious	Serious[c]	None	Moderate[c] ⊕⊕⊕◯
Low density lipoprotein (LDL)	241 (4 RCTs)	Not serious	Not serious	Not serious	Serious[c]	None	Moderate[c] ⊕⊕⊕◯

[a]Confidence interval of the pooled estimate crossed the threshold (Minimal Important Difference (MID) / Minimally Clinically Important Difference (MCID); thus, the certainty was downgraded for imprecision.

[b]Variation in intervention type (leaf, twig, fruit) with differing bioactive profiles introduced indirectness; thus, the certainty of evidence was downgraded.

[c]Overall sample size is small; thus, the certainty was downgraded for imprecision