

Research Article

A comparison of the effects of green tea and cocoa on glycaemic control and insulin sensitivity in patients with type 2 diabetes mellitus: a systematic review and meta-analysis

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Abstract.

BACKGROUND: Type 2 Diabetes Mellitus (T2DM) is among the most frequent chronic diseases in virtually all countries, posing a global health threat. Therefore, Preventive interventions are critical for reducing the enormous burden of diabetes. Flavanols may assist people with metabolic disorders to maintain glucose homeostasis by inhibiting digestive enzymes and glucose transporters. Green Tea (GT) and cocoa have gotten much attention since their flavanols are high.

OBJECTIVES: To investigate the effects of polyphenols from GT and cocoa (>4 weeks) on reducing the incidence of complications and improving glycaemic control and insulin sensitivity in adult patients with T2DM through outcomes Fasting Blood Glucose (FBG), Fasting Blood Insulin (FBI), Haemoglobin A1c (HbA1c) and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR).

METHODOLOGY: An electronic research programme was applied, using different databases (including Web of Science, PubMed/Medline, Scopus, and Cochrane Reviews) to find studies that have evaluated the impact of polyphenols from GT and cocoa on reducing the incidence of complications and improving glycaemic control and insulin sensitivity in adult patients with T2DM. Articles published between 2005 and 2021 in English were selected.

RESULTS: 15 and 7 studies involved 738 participants on GT (348 male/390 female). In contrast, the ones focused on cocoa had 331 participants (83 male/ 248 female) with T2DM aged 18–65 years, and a BMI range of 25–34.9 kg/m² was identified and included in the present review. 43 and 27% of studies were low-risk bias in cocoa and GT, respectively. The results of the meta-analysis showed no significant difference in FBG levels following GT and cocoa consumption compared to the control group (SMD: -0.08; 95% CI: -0.43 to 0.28; *P* = 0.68 and SMD: -0.65; 95% CI, -1.40 to 0.10; *P* = 0.09, respectively). Also, the results showed no significant difference for GT and cocoa intervention (SMD: 0.18; 95% CI: -0.27 to 0.64; *P* = 0.43

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and SMD: -0.80 ; 95% CI: -1.92 to 0.31 ; $P=0.16$, respectively). In addition, the results of the HbA1c analysis showed no significant reduction after GT and cocoa consumption (SMD: -0.41 ; 95% CI: -0.85 to 0.03 ; $P=0.07$ and SMD, -0.37 ; 95% CI, -0.77 to 0.04 ; $P=0.08$, respectively). There was no evidence that GT and cocoa interventions effectively improved HOMA-IR (SMD: 0.02 ; 95% CI: -0.16 to 0.20 ; $P=0.80$ and SMD, -1.65 ; 95% CI, -3.77 to 0.46 ; $P=0.13$, respectively).

CONCLUSION: The evidence shows that the short-term administration of cocoa and GT did not significantly reduce the FBG, FBI, HbA1c, and HOMA-IR levels in adult patients with T2DM.

Keywords: Cocoa, green tea, dark chocolate, catechin, glycaemic control, diabetic patients, meta-analysis

1. Introduction

1.1. Diabetes management strategies and dietary flavonoids

Type 2 diabetes mellitus (T2DM) are among the most frequent chronic diseases in virtually all countries, posing a global health threat [1]. As of 2017, T2DM affected more than 8.4% of individuals globally; by 2045, this percentage is expected to climb to 9.9% [2]. Preventive interventions are critical for reducing the enormous burden of diabetes. Although drugs may help postpone the onset of diabetes complications, long-term use can be expensive and have various adverse effects [3]. Therefore, diabetic patients and doctors contemplate alternative and complementary treatments, such as herbal medications with anti-diabetic effects [4]. Indeed, plants have traditionally been a valuable source of pharmaceuticals, and many currently accessible medications are produced directly or indirectly from plants [5]. The herbal remedies may be promising for controlling diabetes.

Lifestyle changes can slow the evolution of T2DM in prediabetic people with impaired glucose tolerance or fasting glucose [6–10]. For example, Flavanols, a subset of plant-derived phytochemicals known as flavonoids, have recently received increased attention after epidemiological studies found a negative relationship between flavanol consumption and the development of diabetes [11, 12] Flavanols may assist people with metabolic disorders in maintaining glucose homeostasis by inhibiting digestive enzymes and glucose transporters, a strategy that assists people with metabolic disorders in maintaining glucose homeostasis [10;13]. In vitro studies have demonstrated that flavanols help inhibit carbohydrate digestive enzyme activity, enhance insulin sensitivity, inhibit hepatic gluconeogenesis by reducing gluconeogenic genes, and improve oxidative stress [14–17].

GT and cocoa have gotten much attention since they're high in flavanols. Cocoa, GT, grapes, and apples are among the highest sources of flavanols [18]. After the consumption of flavanol-rich food, including cocoa, and tea, various polyphenol-derived phenolic acids, for example, m-hydroxyphenyl acetic acid, m hydrox-yphenylpropionic acid, m-hydroxybenzoic acid, and phenyl-g-valerolactones are generated [19–21]. Furthermore, cocoa may have a favourable effect on insulin signalling, possibly by increasing the incretin response or reducing oxidative stress and inflammation in the insulin-signalling pathways [22]. According to systematic reviews and meta-analyses, chocolate/cocoa improves FBI and insulin resistance in healthy adults [23–29]. The analysis of RCTs included in the review by [10] shows that cocoa consumption lowered FBG.

Catechins, flavonoid-like polyphenols, are primarily responsible for GT's beneficial effects on human health [3]. These catechins include epigallocatechin-3-gallate (EGCG), as well as quercetin, theaflavins, theanine, caffeine, chlorogenic acid, and gallic acid [30–32]. Epicatechin (EC), epigallocatechin (EGC), epicatechin gallate (ECG), and epigallocatechingallate are the four primary catechins present in green tea extract (GTE) [33;34]. Moreover, epidemiological studies in humans have suggested that long-term use of GT is related to a lower risk of diabetes [35, 36]. Several randomised controlled studies (RCTs) have found that consuming GTE regularly can improve oral glucose tolerance in healthy persons and lower FBG and HbA1c levels in people at risk of diabetes [37–40].

However, systematic studies and meta-analyses on the link between GT intake, insulin resistance, and glycaemic control have produced conflicting results. For example, GT has been shown to enhance glycaemic control in some trials [41], whereas others have found no link between GT consumption and glycaemic management [42, 43]. According to a meta-analysis of seven RCTs by [44], the consump-

tion of GT does not decrease FBG, FBI, HbA1c or HOMA-IR levels in populations at risk of T2DM. Another meta-analysis of 22 RCTs showed that the administration of GT with or without caffeine significantly reduced FBG. Still, the results did not support a positive effect on FBI, HbA1c or HOMA-IR in adults with [45]. In 27 RCTs, short-term GT supplementation significantly reduced FBG but did not significantly affect FBI or HbA1c in T2DM patients [3]. In the results of six RCTs, no evidence supports the suggestion that consuming GT/GTE could reduce HbA1c, HOMA-IR, FBG or FBI levels in adults with prediabetes and T2DM [31]. However, this survey study concluded that the benefits of GT ingestion were due to caffeine and not catechins [46]. The meta-analysis indicated that the supplementary intake of GT had no significant effect on FPG, FBI, HbA1c or HOMA-IR in patients with T2DM [47].

1.2. Rationale for the review

Even among researchers that advocate polyphenol consumption, GT and/or cocoa consumption for T2DM is debatable. For example, according to [48, p. 303], “Indeed, tea, red wine and cocoa are good sources of flavanols (a class of polyphenol), but it is not completely established whether these food-stuffs exert a beneficial effect against diabetes.” In addition, [3, p. 2], ‘findings from randomized controlled trials (RCTs) on GT supplementation and glycaemic control or insulin sensitivity in individuals with preclinical diabetes or T2DM are debatable’. The focus was on consuming green tea and cocoa compared to other types reported to contain more abundant flavonoids because tea and cocoa consume more than other foods. For example, Cocoa and its product, chocolate, is a primarily consumed food worldwide [49]. Furthermore, according to the 2013 World Tea Market Report, tea is the most consumed beverage in the world [50]. Cocoa and GT are rich sources of various polyphenol compounds [3, 51]. We want to investigate what the most beneficial for diabetics, which are considered well available. Therefore, this research systematically reviews all existing studies that have evaluated the outcomes of GT and cocoa supplementation in adults with T2DM to assess the effectiveness of polyphenol supplementation in improving glycaemic control and insulin sensitivity. According to [52], FBG measurements do not adequately indicate glycaemic management because they do not reflect what happens after meals and during the

day in free-living situations. Therefore, this systematic review and meta-analysis aimed to investigate the effects of polyphenol supplementation (GT and cocoa) on improving glycaemic control and insulin sensitivity in adult patients with T2DM through outcomes FBG, FBI, HbA1c and HOMA-IR.

2. Methodology

Existing studies that have assessed the long-term positive effect of GT and cocoa on glycaemic control and insulin sensitivity in patients with T2DM were reviewed after assessing their quality.

2.1. Types of studies

This study included every pertinent experimental study (including randomized controlled trials with either a parallel or crossover design), regardless of whether a double-blind method was used. Furthermore, reviews, papers and meeting abstracts were examined to obtain more evidence. The inclusion and exclusion criteria were applied as described below.

2.1.1. The inclusion criteria

Previous studies among adult patients aged 18 years or older with T2DM, regardless of gender or ethnicity or the number of participants, with interventions that are relevant to GT (beverage or capsule) and/or cocoa (beverage or capsule or solid chocolate) and published in the English language from 2005 onwards (this date span was common to all sampled databases) were included in this review. The outcome of the studies was at least one of the following: (1) fasting glucose, (2) fasting insulin, (3) HbA1c and (4) HOMA-IR. Therefore, studies with paediatric participants were excluded from this review. The main objective of this systematic review was to compare the effect of GT and cocoa on glycaemic control and insulin sensitivity in patients with T2DM; therefore, only words related to this objective were used when searching the databases.

2.1.2. The exclusion criteria

Studies that had the following criteria were excluded from this review –

(1) studies that included adult patients without T2DM, (2) studies that used an unclear number/rate of any intervention was relevant to GT and/or cocoa, (3) a review or a meeting abstract, (4) ongoing stud-

ies, (5) studies that lacked detailed information on baseline results or follow-up, (6) studies that lacked information on the study design, (7) nonhuman-based studies, (8) studies with limited access to the full text, (9) studies were ongoing when this review was conducted, (10) studies that lacked an appropriate control group in the research design, (11) studies on GT and/or cocoa but not type 2 diabetes or that did not focus on examining fasting glucose, fasting insulin, HbA1c and/or HOMA-IR, (12) studies on T2DM but did not include interventions assessing the effect of GT or cocoa, (13) studies not on T2DM or GT or cocoa or fasting glucose or fasting insulin or HbA1c or HOMA-IR, (14) studies that did not meet the outcome variables, (15) studies that used combination intervention, (16) studies that assessed type 1 diabetes or insulin-dependent diabetes, (17) studies not published in the English language and (18) repeated studies.

2.2. Participants

Adult patients with T2DM were included in this study regardless of ethnicity.

2.3. Intervention/Exposure types

The included studies conducted interventions that were relevant to the effect of GT and/or cocoa on T2DM, and some had information regarding the intensity and/or duration of their studies. The sources of this information were included where available.

2.4. Types of outcome measures

In this review, the effectiveness of GT and/or cocoa on glycaemic control and insulin sensitivity in patients with T2DM was assessed using the following: (1) fasting glucose, (2) fasting insulin, (3) HbA1c and/or (4) HOMA-IR.

2.5. Search strategy

To identify original research articles, Web of Science, PubMed/MEDLINE, Scopus, and Cochrane were used. Retrieved references and reviews were also examined to select relevant articles. First, the keywords/terms used for green tea were ‘tea’ OR ‘green tea’ OR ‘green tea extract’ OR ‘tea polyphenols’ OR ‘green tea catechins’ OR ‘catechin’ OR ‘epigallocatechin’ OR ‘epicatechin’ OR

‘tea component(s)’ OR ‘epigallocatechin gallate’ AND ‘glycated protein’ OR ‘insulin sensitivity’ OR ‘hyperglycemia’ OR ‘insulin resistance’ OR ‘diabetes’ OR ‘glucose’ OR ‘glycaemic control’ OR ‘HbA1c’ OR ‘fructosamine’ OR ‘insulin’ OR ‘type 2 diabetes’. Second, the keywords/terms used for cocoa were ‘Cocoa’ OR ‘Cacao’ OR ‘Chocolate’ OR ‘dark chocolate’ OR ‘Cocoa powder’ OR ‘dark chocolate’ OR ‘cocoa flavanols’ OR ‘cocoa polyphenols’ AND ‘glycated protein’ OR ‘insulin sensitivity’ OR ‘hyperglycemia’ OR ‘insulin resistance’ OR ‘diabetes’ OR ‘glucose’ OR ‘glycaemic control’ OR ‘Hb A1c’ OR ‘fructosamine’ OR ‘insulin’ OR ‘type 2 diabetes’.

2.6. Identification of relevant studies

Studies were selected for close examination based on the abstracts of the articles in the studies that were examined to ensure their eligibility for inclusion. Subsequently, these studies were evaluated and verified for inclusion or exclusion based on a thorough review of the full texts. The last search for data was performed on January 3, 2022.

2.7. Data extraction

Related findings were derived from the selected studies, and the data extracted from the studies include the name of the author (including the year of publication), country where the study was conducted, study design, study period, population number (total enrolled/completers) and participants’ characteristics, exclusion criteria, intervention type, dose, and duration (intervention/control group), main/other outcomes and *p*-value.

2.8. Risk of Bias assessment

The Risk of Bias 2 (RoB 2) tool is an update to the original risk of bias tool launched in 2008 [53]. RoB 2 tool was used to appraise the risk of bias in the randomized controlled trials included in this review. Bias is assessed as a high, low or some concerns judgment. The following criteria were considered in the evaluation: (1) Randomisation process, (2) Deviations from the intended interventions, (3) Missing outcome data, (4) Measurement of the outcome, and (5) Selection of the reported result. In addition, we used RoB 2 to create a funnel chart to analyse the bias of the studies in this systematic review.

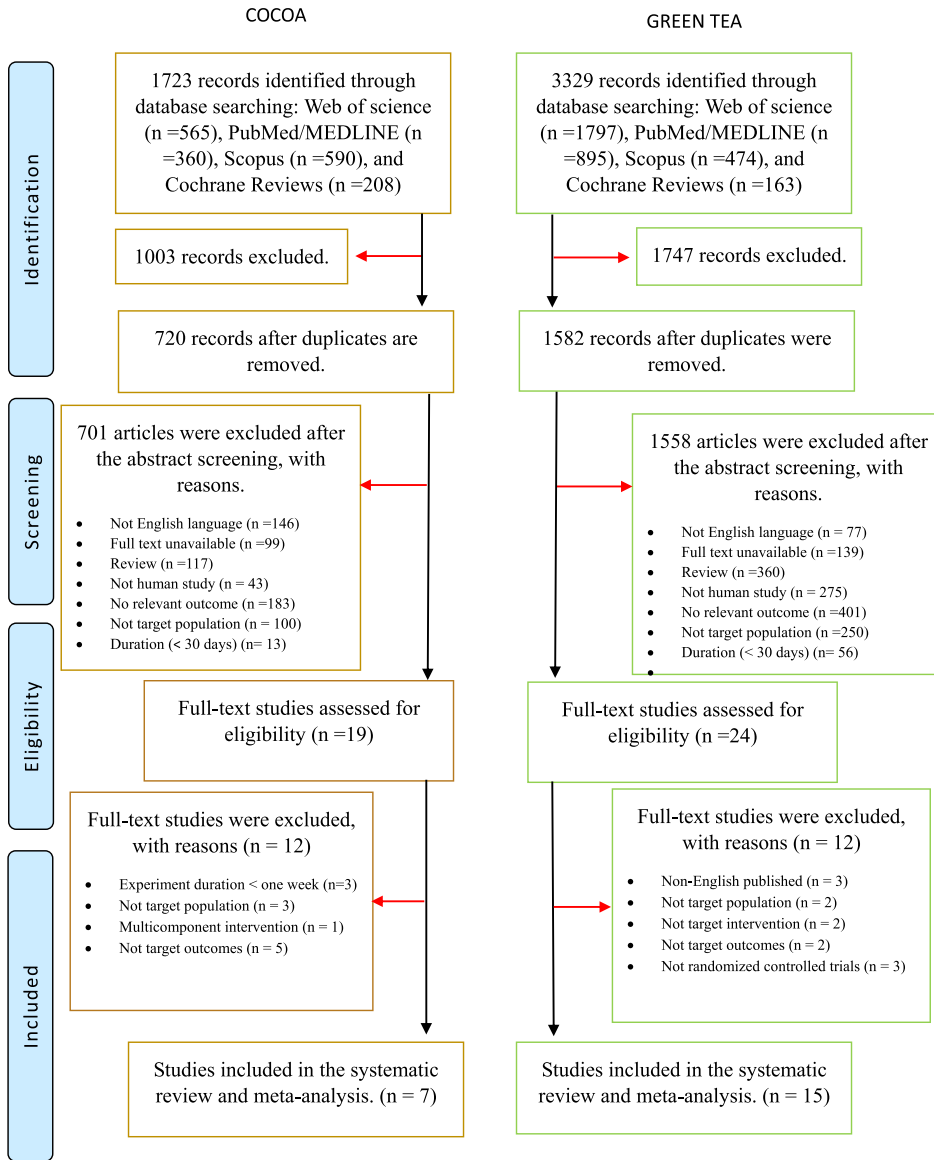


Fig. 1. Flowchart of study selection and exclusion in detail.

2.9. Statistical analysis

To supplement the systematic review, a meta-analysis was performed. We used Review Manager 5.4 software to assess the heterogeneity of indicators between the GT group and the control group, as well as the cocoa group and control group. The mean difference (MD) between the baseline and final measurements of fasting glucose, fasting insulin, HbA1c and HOMA-IR was calculated, and the indexes between the GT, cocoa, and control groups were compared. In this review, heterogeneity was evaluated

by the index of inconsistency (I^2), and the statistical value of I^2 reflected the level of heterogeneity. The result was considered heterogeneous if I^2 was more than 50%. A random-effects model was employed; otherwise, a fixed-effects model was used. In this review, a P -value<0.05 was considered statistically significant. Some studies did not mention the standard deviation of change. In this case, previous systematic reviews were checked, and the data was obtained. The study [38] from [44] as well as [54] A, [55] and [56] from [31]. [54, 57–62] by calculating S.D. [63]:

Unique ID	Study ID	D1	D2	D3	D4	D5	Overall	
Fukino	2005	!	!	+	+	+	!	+
Ryu	2006	+	-	-	!	+	-	!
Fukino (A)	2008	!	-	+	+	+	-	-
Fukino (B)	2008	!	-	+	+	+	-	
Nagao	2009	!	+	+	+	+	!	D1 Randomisation process
Hsu	2011	+	+	+	+	+	+	D2 Deviations from the intended interventions
Mousavi (A)	2013	!	!	+	+	+	!	D3 Missing outcome data
Mousavi (B)	2013	!	!	+	+	+	!	D4 Measurement of the outcome
Lasaite	2014	!	+	-	+	+	-	D5 Selection of the reported result
Liu	2014	+	+	+	+	+	+	
Mirzaei	2015	!	!	+	+	+	!	
Borges	2016	+	+	+	+	+	+	
Hosseini (A)	2018	+	+	+	!	+	!	
Hosseini (B)	2018	+	+	+	!	+	!	
Quezada-Fern	2019	+	+	+	+	+	+	

Percent of Total Studies in Green Tea

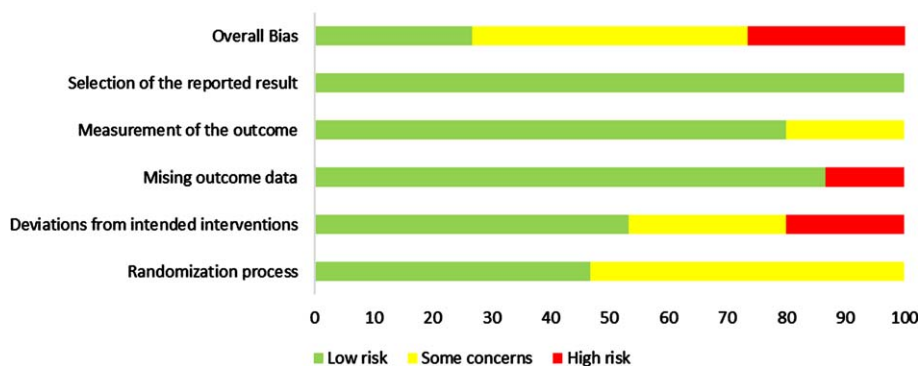


Fig. 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study in green tea.

$$t = \frac{(\bar{X} - \bar{Y}) * \sqrt{n}}{S.D.(\bar{X} - \bar{Y})}$$

68–70], which were published between 2005 and 2021, met the inclusion criteria.

3. Results

3.1. Study selection

A total of 3329 and 1723 studies that evaluated the effect of GT and cocoa, respectively, on glycaemic control and insulin sensitivity in patients with T2DM were identified by searching the literature, as shown in Fig. 2. A total of fifteen articles on GT [38, 40, 46, 54–56, 61, 62, 64–67] and seven on cocoa [57–60,

3.2. Study characteristics

3.2.1. Study design and country

All the studies were parallel randomized controlled trials (studies on GT – [40, 46, 54–56, 61, 62, 65–67, and studies on cocoa – 57, 59, 60, 68–70], except for three that were cross-over randomized controlled trials – two on GT [38, 64] and one on cocoa [58].

The majority of the included studies that focused on GT were conducted in Asia: three in Iran [54, 56, 67], three in Japan [38, 46, 61], two in Taiwan [40,

65], one in Lithuania [55], and one in South Korea [64], except for two, which were conducted in Mexico [62] and Brazil [66]. While for cocoa, three of the studies were conducted in Asia [60, 69, 70], two in the United Kingdom [58, 68], one in the United States [57] and one in Germany [59]. Table 1 shows the basic study characteristics of each study included in this review.

3.2.2. Duration of study and follow-up

The follow-up period for most of the studies was less than three months, except for three studies (which focused on GT) [40, 55, 65] and one study (which focused on cocoa) [68]. [55] follow-up period was 18 months (study period: none-mention), [38] four months (study period: late February and early March 2003), [65] four months (study period: December 2007 to November 2008), [40] four months (study period: April 2011 to March 2012), [46] three months (study period: May 2004 to November 2004), [66] three months (study period: November 2013 to December 2014), [62] (study period: January to December 2016), [68] three months (study period: none-mentioned) and [59] three months (study period: September 2016 to April 2017). Four studies that focused on GT ([61] [study period: late February to early March 2003]; [54] [study period: none-mentioned]; [56] [study period: January to June 2008]; [67] [study period: August 2017 to March 2018]) and four studies focused on cocoa ([58] [study period: January 2008 to October 2008]; [69] [study period: March 2011 to February 2012]; [70] [study period: none-mention]; [60] [study period: none-mentioned]) were carried out with a follow-up period of two months. One study on GT ([64] [study period: none-mention]) and one study on cocoa ([57] [study period: none-mentioned]) were carried out with a follow-up period of one month.

3.3. Participants' characteristics

The studies that focused on GT had 738 participants (348 male/390 female), while the ones that focused on cocoa had 331 participants (83 male/248 female) with T2DM, aged 18–65 years. All the participants were overweight/obese (BMI: 25–34.9 kg/m²), except for the participants in [64] study (which focused on GT) and [68 and 70] studies (which focused on cocoa) (BMI < 25 kg/m²).

Most of the included studies did not report the duration of the diagnosis of T2DM, except for six studies

on GT [55, 56, 62, 65–67] and five studies on cocoa [58, 59, 68, 69, 70]. The duration of the diagnosis of diabetes reported by these studies was less than eight years, except for one study on GT that reported a duration > 12 years [66].

3.4. Quality assessment and publication bias

Based on the assessment tool, only four studies on GT were of low risk [40, 62, 65, 66]. In contrast, just two studies among studies on cocoa were of low risk [59, 69]. Five studies on GT [46, 54, 56, 61, 67] and only two studies on cocoa [57, 70] had some concerns. Only three studies on GT [38, 55, 64] and three studies on cocoa [58, 60, 68] had high risk, as shown in Figs. 2 and 3.

3.4.1. Risk of bias

The risk of bias assessment was carried out with RoB2 tool, as shown in Figs. 2 and 3. The studies by [40, 62, 64–67] on GT and the studies of [57–59, 68–70] on cocoa provided comprehensive explanations of the randomisation process. Seven studies on GT [40, 46, 55, 62, 65–67] and six studies on cocoa [57–59, 68–70] had a low risk of bias regarding deviations from the intended interventions. Ten articles on GT [38, 40, 46, 54, 56, 61, 62, 65–67] and six studies on cocoa [57, 59, 60, 68–70] had a low risk of bias regarding missing outcome data. Ten studies on GT [38, 40, 46, 54–56, 61, 62, 65, 66] and only four studies on cocoa [58–60, 69] had a low risk of bias regarding the measurement of the outcome. The majority of the studies on GT [38, 40, 46, 54–56, 61, 62, 64–67] and five studies on cocoa [57, 59, 60, 69, 70] had a low risk of bias concerning the selection of the reported result.

3.5. Meta-analysis and data synthesis

In total, data from fifteen studies [38, 40, 46, 54–56, 61, 62, 64–67] that compared GT with placebos were included in these meta-analyses. On the other hand, seven studies [57–60, 68–70] that compared cocoa supplements with placebos were included in these meta-analyses. Forest plots depicting the results of the meta-analysis for each assessed outcome are shown in Figs. 4, 5.

Table 1
 Characteristics of the included trials of the effects of green tea intake in T2D patients

Author	Study design	Duration	No. of participants (M/F)	Intervention		Outcome
				GT group (flavanols)	Placebo group (flavanols)	
Fukino et al. (2005)	Parallel RCT	2 mo.	66 (53/13)	544 mg of GT (456 mg of catechins)	NR	=FBG,=FBI,=HbA1c,=HOMA-IR
Ryu et al. (2006)	Cross-over RCT	4 wk.	55 (31/24)	900 ml of GT (1200 mg)	water	=FBG,=FBI,=HOMA-IR
Fukino et al. (2008) (A)	Cross-over RCT	2 mo.	29 (25/4)	GTE (456 mg of catechins)	No intervention	=FBG,=FBI, ↓HbA1c,=HOMA-IR
Fukino et al. (2008) (B)	Cross-over RCT	2 mo.	31 (26/5)	GTE (456 mg of catechins)	No intervention	=FBG,=FBI, ↓HbA1c,=HOMA-IR
Nagao et al. (2009)	Parallel RCT	12 wk.	50 (19/31)	340 ml of GT (582.8 mg of catechins)	(96 mg catechins)	↓FBG,=FBI, ↓HbA1c
Hsu et al. (2011)	Parallel RCT	16 wk.	68 (24/44)	GTE (856 mg of EGCG)	cellulose	↓HbA1c, ↓HOMA-IR
Mousavi et al. (2013) (A)	Parallel RCT	8 wk.	39 (16/23)	4 x2.5 g of GT (1000 mg)	No intervention	=FBG
Mousavi et al. (2013) (B)	Parallel RCT	8 wk.	38 (17/21)	2 x2.5 g of GT (500)	No intervention	=FBG
Lasaite et al. (2014)	Parallel RCT	18 mo.	56 (21/35)	200 mg of GTE (140 mg)	cellulose	=HbA1c
Liu et al. (2014)	Parallel RCT	16 wk.	77 (32/45)	1500 mg of GTE (856 mg of EGCG)	cellulose	=FBG,=HbA1c, ↓HOMA-IR
Mirzaei et al. (2015)	Parallel RCT	8 wk.	82 (16/66)	500 mg of GTE (80 mg)	cellulose	↓FBG, ↓FBI, ↓HbA1c
Borges et al. (2016)	Parallel RCT	12 wk.	47 (27/20)	GT (800 mg of EGCG)	NR	=HbA1c
Hosseini et al. (2018) (A)	Parallel RCT	8 wk.	40 (15/25)	GT (300 mg of EGCG) TT genotype	NR	=FBG,=HOMA-IR
Hosseini et al. (2018) (B)	Parallel RCT	8 wk.	40 (16/24)	GT (300 mg of EGCG) AA+AT genotype	NR	=FBG,=HOMA-IR
Quezada-Fernández et al. (2019)	Parallel RCT	12 wk.	20 (10/10)	400 mg of GTE (≥360 mg)	NR	=FBG,=HbA1c

The arrow indicates a decrease (↓) in the levels or activity of the different parameters analysed. (=) symbol designates unchanged parameters. **RCT**, randomized controlled trial; **FBG**, fasting blood glucose; **FBI**, fasting blood insulin; **HbA1c**, glycated haemoglobin; **HOMA-IR**, homeostatic model assessment of insulin resistance; **GT**, green tea; **GTE**, green tea extract; **EGCG**, epigallocatechin gallate; **wk.**, week; **mo.**, month; **M**, male; **F**, female; **NR**; no report.

Table 2
Characteristics of the included trials of the effects of cocoa intake in T2D patients

Author	Study design	Duration	No. of participants (M/F)	Intervention		Outcome
				Cocoa group (flavanols)	Placebo group (flavanols)	
Balzer et al. (2008)	Parallel RCT	30 days	51 (20/31)	cocoa drink (963 mg)	cocoa drink (75 mg)	=FBG,=HbA1c
Mellor et al. (2010)	Cross-over RCT	8 wk.	12 (7/5)	45 g of CP (16.6 mg)	45 g of CP (<2 mg)	=FBG,=FBI,=HbA1c
Curtis et al. (2012)	Parallel RCT	12 mo.	93 (0/93)	27 g of DC (850 mg)	NR	=HbA1c, ↓HOMA-IR, ↓FBI
Rostami et al. (2015)	Parallel RCT	8 wk.	60 (24/36)	25 g of DC (450 mg)	25 g of WC (0)	↓FBG, ↓FBI, ↓HbA1c
Dicks et al. (2018)	Parallel RCT	12 wk.	35 (18/17)	2.5 g of Cocoa capsules (207.5 mg)	cocoa-free capsules	↓FBG, ↓FBI,=HbA1c, ↓HOMA-IR
Jafarirad et al. (2018)	Parallel RCT	8 wk.	44 (14/30)	30 g of DC (540 mg)	NR	↓FBG,=FBI, ↓HbA1c
Fakhari et al. (2021)	Parallel RCT	8 wk.	36 (0/36)	3x25 g / per week of DC (450 mg)	25 g of WC (0)	=FBG

The arrow indicates a decrease (↓) in the levels or activity of the different parameters analysed. (=) symbol designates unchanged parameters. **RCT**, randomized controlled trial; **FBG**, fasting blood glucose; **FBI**, fasting blood insulin; **HbA1c**, glycated haemoglobin; **HOMA-IR**, homeostatic model assessment of insulin resistance; **DC**, dark chocolate; **WC**, white chocolate; **CP**, Cocoa powder; **h**, hour; **wk.**, week; **mo.**, month; **M**, male; **F**, female; **NR**; no report.

Unique ID	Study ID	D1	D2	D3	D4	D5	Overall	
Balzer	2008	+	+	+	!	+	!	+
Mellor	2010	+	+	-	+	-	-	!
Curtis	2012	+	+	+	!	-	-	-
Rostami	2015	+	+	+	+	+	+	
Dicks	2018	+	+	+	+	+	+	D1 Randomisation process
Jafarirad	2018	+	+	+	+	+	+	D2 Deviations from the intended interventions
Fakhari	2021	!	-	+	+	+	-	D3 Missing outcome data
								D4 Measurement of the outcome
								D5 Selection of the reported result

Percent of Total Studies in Cocoa

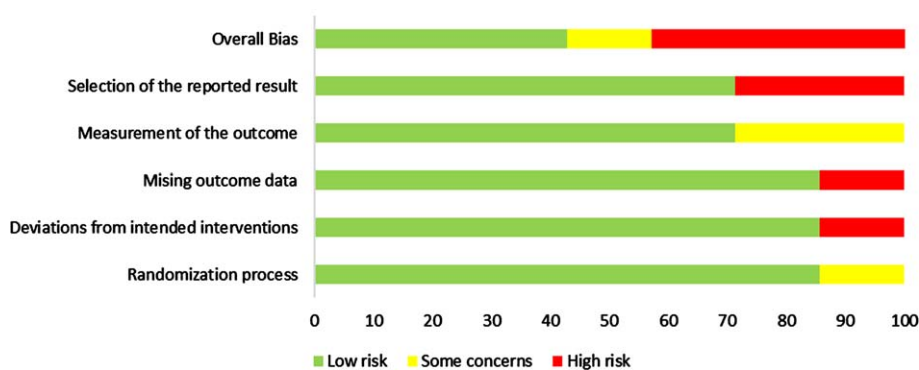


Fig. 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study in cocoa.

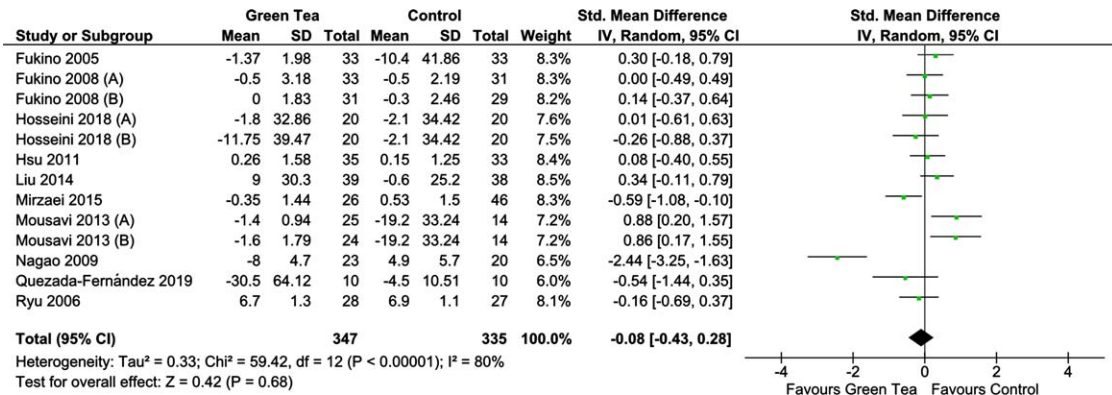
3.5.1. Dietary polyphenols (cocoa vs. green tea) and association with incidence glycaemic control and insulin sensitivity in patients with type 2 diabetes mellitus

3.5.1.1. Fasting glucose. Amongst the included studies, twelve RCTs assessed the effect of GT on FBG levels [38, 40, 46, 54, 61, 62, 64, 65, 67], while seven RCTs assessed the effect of cocoa on FBG levels [57–60, 68–70]. The GT and cocoa studies that involved 635 (300 males/335 females) and 331 (82 males/248 females) participants, respectively, were included in the FBG analysis. The results of the meta-analysis showed no significant difference in FBG levels following GT and cocoa consumption compared to the control group (SMD: -0.08 ; 95% CI: -0.43 to 0.28 ; $P=0.68$ and SMD: -0.65 ; 95% CI, -1.40 to 0.10 ; $P=0.09$, respectively). The forest plot of the meta-analysis for the FBG level is shown in Figs. 4, 5.

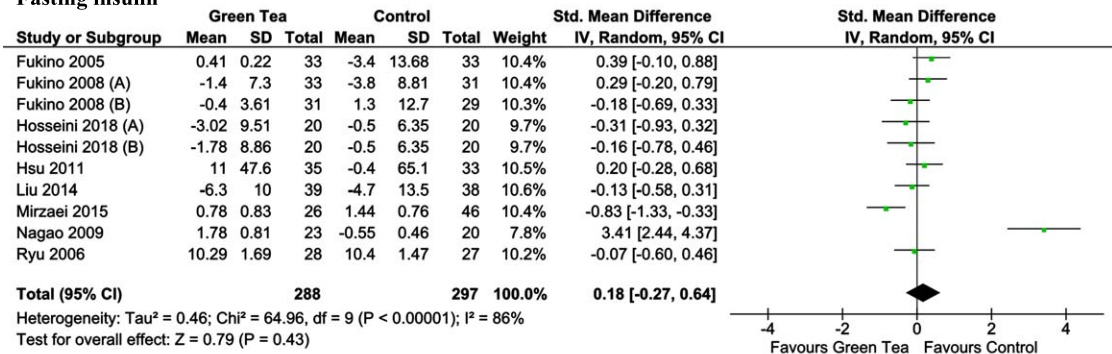
3.5.1.2. Fasting insulin. Ten studies assessed the effect of GT on the FBI level and involved 538 (257 males/281 females) participants who were included in the FBI analysis [38, 40, 46, 56, 61, 64, 65, 67]. Five studies assessed the effect of cocoa on the FBI level and involved 244 (63 males/181 females) participants who were included in the FBI analysis [58, 59, 68–70]. The results showed no significant difference for GT intervention (SMD: 0.18 ; 95% CI: -0.27 to 0.64 ; $P=0.43$) also no statistical difference for cocoa intervention (SMD: -0.80 ; 95% CI: -1.92 to 0.31 ; $P=0.16$). The forest plot of the meta-analysis for the FBI level is shown in Figs. 4, 5.

3.5.1.3. HbA1c. Ten studies reported the HbA1c level as an outcome after GT consumption and involved 526 (253 males/273 females) participants who were included in the HbA1c analysis [38, 40, 46, 55, 56, 61, 62, 65, 66]. Six studies reported the HbA1c level as an outcome after cocoa consumption

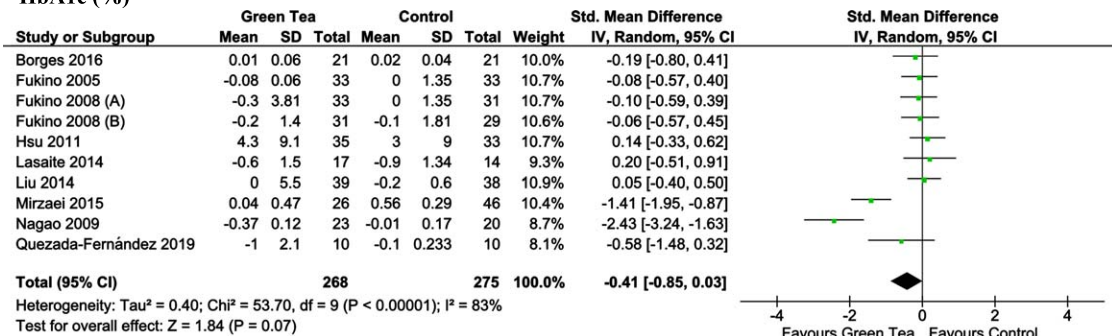
Fasting glucose



Fasting insulin



HbA1c (%)



HOMA-IR

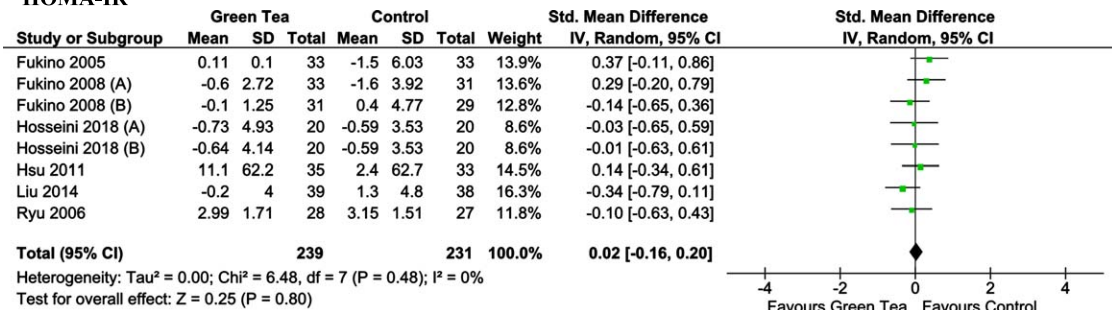
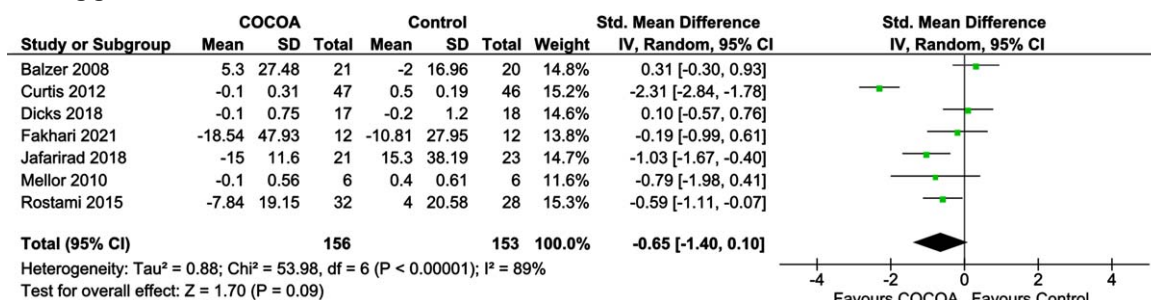
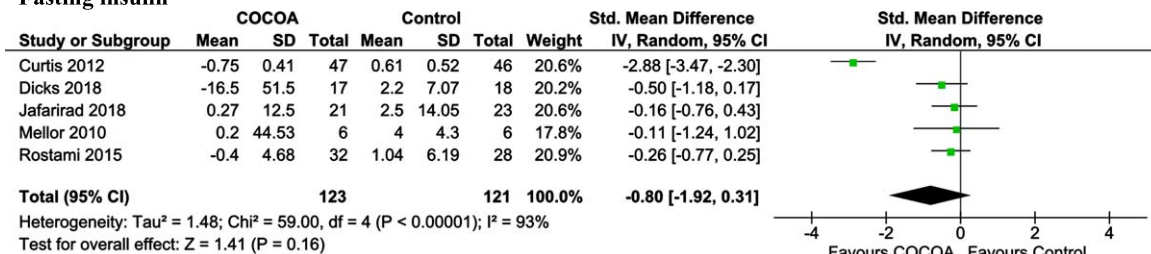


Fig. 4. Meta-analysis results of green tea for each assessed outcome.

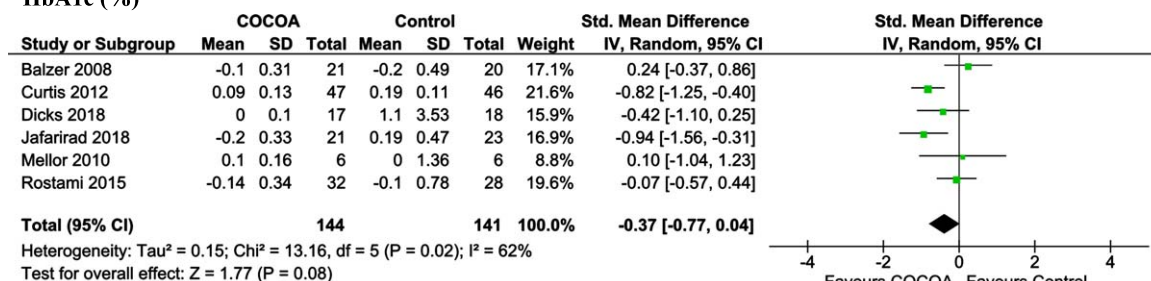
Fasting glucose



Fasting insulin



HbA1c (%)



HOMA-IR

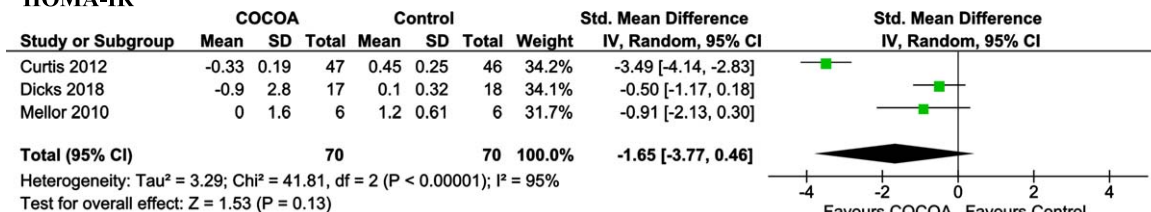


Fig. 5. Meta-analysis results of cocoa for each assessed outcome.

and involved 295 (83 males/212 females) participants who were included in the HbA1c analysis [57–59, 68–70]. The results of the HbA1c analysis showed no significant reduction after GT and cocoa consumption (SMD: -0.41 ; 95% CI: -0.85 to 0.03 ; $P = 0.07$ and SMD, -0.37 ; 95% CI, -0.77 to 0.04 ; $P = 0.08$, respectively). The forest plot of the meta-analysis for the HbA1c level is shown in Figs. 4, 5.

3.5.1.4. HOMA-IR. Amongst the included studies, eight RCTs assessed the effect of GT on HOMA-

IR levels [38, 40, 61, 64, 65, 67], while three RCTs assessed the effect of cocoa on HOMA-IR levels [58, 59, 68]. The GT and cocoa studies that involved 406 (222 males/184 females) and 140 (25 males/115 females) participants, respectively, were included in the HOMA-IR analysis. The results of the meta-analysis showed no significant difference in HOMA-IR levels following GT and cocoa consumption compared to the control group (SMD: 0.02 ; 95% CI: -0.16 to 0.20 ; $P = 0.80$ and SMD: -1.62 ; 95% CI,

−3.77 to 0.46; $P=0.13$, respectively). The forest plot of the meta-analysis for the FBG level is shown in Figs. 4, 5.

3.5.2. Subgroup analysis

We stratified studies based on the type of intervention (beverage, capsule, solid chocolate in cocoa) and (beverage, capsule in GT) duration of intervention (≥ 12 and <12 weeks), flavanols dosage (≥ 500 and <500 mg/day) and baseline of FBG (high, >7.1 mmol/l and standard, 4–7 mmol/l). Subgroup analysis showed that cocoa consumption longer than three months resulted in a highly significantly reduce in HbA1c levels (SMD: -0.71 ; 95% CI: -1.07 to -0.35 ; $P=0.0001$). Additionally, solid chocolate consumption resulted in a highly significant decrease in FBG and HbA1c (SMD: -1.01 ; 95% CI: -1.82 to -0.20 ; $P=0.01$ in FBG) and (SMD: -0.50 ; 95% CI: -1.00 to -0.02 ; $P=0.04$ in HbA1c). The dose (<500 mg/day) consumption resulted in a significant decrease in HOMA-IR (SMD: -0.60 ; 95% CI: -1.19 to -0.01 ; $P=0.05$). However, It can be seen that studies who started with baseline of FBG within the normal range (4–7 mmol/l) had highly significant difference in FBG levels following GT and cocoa consumption compared to the group who started with FBG within the high range (>7.1 mmol/l) (SMD: -2.44 ; 95% CI: -3.25 to 1.63 ; $P=0.0001$ and SMD: -0.62 ; 95% CI, -1.10 to -0.15 ; $P=0.01$, respectively). As shown in Tables 3, 4.

4. Discussion

This systematic review identified the studies that evaluated the effect of GT and/or cocoa intake on improving glycaemic control and insulin sensitivity in patients with T2DM. To the best of our knowledge, this is the first systematic review and meta-analysis to compare the effects of GT and cocoa consumption on individuals with chronic T2DM for a period of more than four weeks. However, the results of the FBG, FBI, HbA1c, and HOMA-IR analyses showed no significant reduction in T2DM after GT and cocoa consumption. Though extensive studies have been conducted over the past few decades, the efficacy of polyphenols from GT and cocoa on reducing the incidence of complications and improving glycaemic control and insulin sensitivity in adult patients with T2DM has not been well-established. The findings of this systematic review are consistent with the findings

of a previous systematic review and meta-analysis regarding the efficacy of polyphenols from GT and cocoa on improving glycaemic control and insulin sensitivity (see, for example, [31, 44], and [47] in green tea, and partially with [10] in cocoa). Though a [10] meta-analysis revealed that cocoa consumption significantly reduced FBG, no significant improvement was found in FBI and HbA1c. In addition, despite the inclusion criterion (studies that examined T2DM outcomes), the review's strength may be demonstrated in the number of papers it carefully reviewed between 2005 and 2021, including RCTs with either a parallel or crossover design, which were included in this study. According to [3], because of their lower intraparticipant variability, crossover trials are typically considered more robust than parallel trials. After excluding the studies that did not meet the inclusion criteria, fifteen studies on GT and seven on cocoa were included. There were 738 participants (348 male/390 female) in the GT studies and 331 (83 male/ 248 female) in the cocoa studies with T2DM. The GT studies used a dose ranging from 80 to 1200 mg/day of polyphenols for different periods (either 30 days, three months, or \geq one year); the cocoa studies used a dose ranging from 16.6 to 850 mg/day of polyphenols for different periods (30 days, two months, three months).

Even among the researchers who advocate polyphenol consumption, the effect of GT and/or cocoa consumption on T2DM remains uncertain. A meta-analysis of seven RCTs by [44] found that GT consumption did not decrease FBG, FBI, HbA1c, or HOMA-IR levels in populations at risk of T2DM. In the results of six RCTs, no evidence was found to support the suggestion that consuming GT/GTE could reduce HbA1c, HOMA-IR, FBG, or FBI levels in adults with prediabetes and T2DM [31]. The meta-analysis indicated that the supplementary intake of GT had no significant effect on FPG, FBI, HbA1c, or HOMA-IR in patients with T2DM [47]. Moreover, the systematic studies and meta-analyses that focused on the link between GT and cocoa intake, insulin resistance, and glycaemic control have produced conflicting results. Another meta-analysis of 22 RCTs revealed that the administration of GT with or without caffeine significantly reduced FBG; still, the results did not reveal a positive effect on FBI, HbA1c, or HOMA-IR in adults with T2DM [45]. In 27 RCTs, short-term GT supplementation significantly reduced FBG but did not significantly affect FBI or HbA1c in T2DM patients [3].

Table 3
Result of subgroup analysis of included studies in the meta-analysis for green tea.

	Sub-grouped by	Change in FBG			Change in FBI			Change in HbA1c			Change in HOMA-IR		
		Trials (n)	Std. Mean Difference IV, Random, 95%CI	P for effect size	Trials (n)	Std. Mean Difference IV, Random, 95%CI	P for effect size	Trials (n)	Std. Mean Difference IV, Random, 95%CI	P for effect size	Trials (n)	Std. Mean Difference IV, Random, 95%CI	P for effect size
Type of intervention	Beverage	5	-0.09[-0.77,0.58]	0.78	4	0.59[-0.36,1.53]	0.22	3	-0.87[-2.15,0.42]	0.19	3	-0.02[-0.30,0.26]	0.89
	Capsule	5	-0.05[-0.34,0.25]	0.76	4	-0.13[-0.51,0.25]	0.51	6	-0.24[-0.67,0.19]	0.27	3	0.09[-0.19,0.36]	0.55
Duration	≥12 weeks	5	-0.34[-0.98,0.29]	0.29	4	0.62[-0.20,1.44]	0.14	7	-0.32[-0.78,0.14]	0.18	3	-0.02[-0.30,0.26]	0.89
	<12 weeks	5	0.12[-0.28,0.52]	0.56	4	-0.19[-0.62,0.23]	0.38	2	-0.74[-2.04,0.56]	0.26	3	0.09[-0.19,0.36]	0.55
Flavanols dose	≥500 mg/dl	6	-0.13[-0.77,0.52]	0.70	4	0.43[-0.50,1.37]	0.36	4	-0.87[-1.93,0.18]	0.11	3	-0.11[-0.39,0.17]	0.45
	<500 mg/dl	4	0.03[-0.20,0.26]	0.82	4	0.03[-0.20,0.26]	0.80	5	-0.10[-0.34,0.13]	0.40	3	0.12[-0.12,0.36]	0.32
Country	Western	1	-0.54[-1.44,0.35]	0.24	NA	NA	NA	3	-0.14[-0.55,0.27]	0.50	NA	NA	NA
	Asian	9	-0.05[-0.41,0.32]	0.81	8	0.18[-0.27,0.64]	0.43	6	-0.51[-1.08,0.06]	0.08	6	0.02[-0.16,0.20]	0.80
Study design	Parallel	8	-0.11[-0.58,0.37]	0.66	6	0.29[-0.39,0.97]	0.40	8	-0.51[-1.07,0.06]	0.08	4	0.02[-0.23,0.27]	0.86
	Crossover	2	0.07[-0.29,0.42]	0.71	2	0.02[-0.27,0.32]	0.88	1	-0.08[-0.43,0.27]	0.65	2	0.03[-0.27,0.32]	0.86
Baseline FBG	High (>7.1 mmol/l)	8	0.09[-0.19,0.37]	0.53	6	-0.08[-0.36,0.20]	0.57	8	-0.21[-0.54,0.11]	0.20	5	0.04[-0.16,0.24]	0.69
	Normal (4–7 mmol/l)	2	-2.44[-3.25,1.63]	0.0001	2	1.65[-1.76,5.05]	0.34	1	-2.43[-3.24, -1.63]	0.0001	1	-0.10[-0.63,0.43]	0.72
Overall bias	Low risk	3	0.09[-0.31,0.49]	0.66	2	0.02[-0.30,0.35]	0.90	4	-0.03[-0.30,0.25]	0.85	2	-0.11[-0.57,0.36]	0.65
	Some concerns	5	-0.16[-0.85,0.54]	0.65	4	0.44[-0.62,1.50]	0.42	3	-1.28[-2.56,0.00]	0.05	2	0.15[-0.17,0.48]	0.35
	High risk	2	0.07[-0.29,0.42]	0.71	2	0.02[-0.27,0.32]	0.88	2	-0.03[-0.34,0.29]	0.87	2	0.03[-0.27,0.32]	0.86

FBG, fasting blood glucose; FBI, fasting blood insulin; HbA1c, glycated haemoglobin; HOMA-IR, homeostatic model assessment of insulin resistance; NA, not applicable.

Table 4
Result of subgroup analysis of included studies in the meta-analysis for cocoa.

	Sub-grouped by	Change in FBG			Change in FBI			Change in HbA1c			Change in HOMA-IR		
		Trials (n)	Std. Mean Difference IV, Random, 95%CI	P for effect size	Trials (n)	Std. Mean Difference IV, Random, 95%CI	P for effect size	Trials (n)	Std. Mean Difference IV, Random, 95%CI	P for effect size	Trials (n)	Std. Mean Difference IV, Random, 95%CI	P for effect size
Type of intervention	Beverage	1	0.31[-0.30,0.93]	0.32	NA	NA	NA	1	0.24[-0.37,0.86]	0.44	NA	NA	NA
	Capsule	1	0.10[-0.57,0.76]	0.77	1	-0.50[-1.18,0.17]	0.14	1	-0.42[-1.10,0.25]	0.22	1	-0.50[-1.17,0.18]	0.15
	Solid chocolate	5	-1.01[-1.82, -0.20]	0.01	4	-0.87[-2.29,0.54]	0.23	4	-0.50[-1.00, -0.02]	0.04	2	-2.26[-4.78,0.27]	0.08
Duration	≥12 weeks	2	-1.11[-3.47,1.24]	0.35	2	-1.70[-4.03,0.63]	0.15	2	-0.71[-1.07, -0.35]	0.0001	2	-1.99[-4.93,0.94]	0.18
	<12 weeks	5	-0.43[-0.93,0.07]	0.09	3	-0.21[-0.57,0.16]	0.26	4	-0.19[-0.74,0.35]	0.48	1	-0.91[-2.13,0.30]	0.14
Flavanols dose	≥500 mg/dl	3	-1.02[-2.55,0.51]	0.19	2	-1.52[-4.19,1.14]	0.26	3	-0.52[-1.21,0.17]	0.14	1	-3.49[-4.14, -2.83]	0.0001
	<500 mg/dl	4	-0.34[-0.70,0.03]	0.07	3	-0.32[-0.71,0.06]	0.10	3	-0.16[-0.54,0.22]	0.40	2	-0.60[-1.19, -0.01]	0.05
Country	Western	4	-0.68 [-2.09,0.74]	0.35	3	-1.20 [-3.03, 0.63]	0.20	4	-0.30[-0.85,0.26]	0.30	3	-1.65[-3.77,0.46]	0.13
	Asian	3	-0.65 [-1.07,0.22]	0.003	2	-0.22[-0.61,0.17]	0.26	2	-0.48[-1.33,0.37]	0.27	NA	NA	NA
Study design	Parallel	6	-0.63 [-1.46,0.19]	0.13	4	-0.95[-2.23,0.33]	0.14	5	-0.41[-0.85,0.03]	0.07	2	-1.99[-4.93,0.94]	0.18
	Crossover	1	-0.79 [-1.98, 0.41]	0.20	1	-0.11[-1.24,1.02]	0.85	1	0.10[-1.04,1.23]	0.87	1	-0.91[-2.13,0.30]	0.14
Baseline FBG	High (>7.1 mmol/l)	5	-0.64[-1.68,0.41]	0.23	3	-1.19[-2.92,0.55]	0.18	4	-0.50[-1.02,0.01]	0.05	2	-1.99[-4.93,0.94]	0.18
	Normal (4–7 mmol/l)	2	-0.62[-1.10, -0.15]	0.01	2	-0.24[-0.70,0.23]	0.32	2	-0.04[-0.50,0.42]	0.87	1	-0.91[-2.13,0.30]	0.14
Overall bias	Low risk	2	-0.28[-0.95,0.39]	0.41	2	-0.35[-0.76, 0.06]	0.09	2	-0.20[-0.60,0.21]	0.34	1	-0.50[-1.17,0.18]	0.15
	Some concerns	2	-0.36[-1.68,0.96]	0.59	1	-0.16[-0.76,0.43]	0.59	2	-0.35[-1.50,0.81]	0.56	NA	NA	NA
	High risk	3	-1.13[-2.62,0.36]	0.14	2	-1.54[-4.26,1.17]	0.27	2	-0.52[-1.37,0.33]	0.23	2	-2.26[-4.78,0.27]	0.08

FBG, fasting blood glucose; FBI, fasting blood insulin; HbA1c, glycated haemoglobin; HOMA-IR, homeostatic model assessment of insulin resistance; NA, not applicable.

4.1. Other factors that may influence the effectiveness of GT and cocoa on glycaemic control and insulin sensitivity

The changes in outcomes might be related to the different types of the population investigated (disease type), the clinical characteristics of patients (the severity of the disease), the type and dose of supplementation, the duration of intervention, and the sample size at the start of the study. Accordingly, several factors could help to show positive effects, including the duration of a diabetes diagnosis. This disparity might be more evident in diabetic patients who had a mean illness duration of approximately seven years. The majority of studies on cocoa reported that the duration of the disease or the time since diagnosis was less than seven years, while some studies on the effect of GT on T2DM reported the duration to be more than 12 years. For example, [70] found that cocoa led to lower levels of FBS and HbA1c compared to the control. However, while these changes were not high rates, they were considered significant compared to the control group. [40] found that GTE supplementation had a superior FBG-reducing impact in individuals with a diabetes history of fewer than five years than in those with a history of more than five years, while reduced insulin and lower HOMA-IR were only significant in people with illness for less than five years. Though a few studies have focused on the severity of T2DM (in terms of disease duration) in relation to the use of GT, the results have been difficult to ascertain. Accordingly, the clinical features of T2DM patients must be investigated in future research with a larger patient sample.

There may be a relationship between the dose amount and the extent of the effect on glycaemic control. However, the amount and type of polyphenols found in published research vary. [54] suggested that larger dosages may be required for diabetic individuals to detect clear results, such as drinking four cups of GT daily (1000 mg of flavanols). The number of polyphenols consumed, and the amount of insulin was also found to have a favourable association [61]. After 16 weeks of 856 mg EGCG, the HbA1c level and HOMA-IR index in the GTE group decreased significantly compared to the placebo group [65]. The GTE group (1344 mg of catechins) demonstrated substantial within-group alterations in the HOMA-IR index after 16 weeks of therapy, despite no significant changes in FBG or HbA1c [40]. [68] observed a significant reduction in HOMA-IR and an improve-

ment in insulin sensitivity following a significant decrease in FBI concentrations within two months associated with 850 mg of flavanols from cocoa. [59] reported that glucose and lipid metabolism was unaffected by the regular consumption of 2.5 g of cocoa (207.5 mg of flavanols) over three months. [69] indicated that cocoa with 450 mg of polyphenols is ineffective in improving the FBG, FBI, and HbA1c levels in diabetic adults compared to WCG. Moreover, [56] demonstrated no significant differences in the intervention group's FBG, HbA1c, and FBI levels within two months (with 240 mg of flavanols). From these studies it can be deduced that higher doses are more effective for T2DM, although researchers have reported that there were no restrictions on drinking GT in the control group. This could be the main reason for the results of the previous study.

4.2. Limitations of the review

This systematic review and meta-analysis have some limitations that must be addressed. First, T2DM is influenced by several variables, including genetic, metabolic, environmental, behavioural, social, and cultural factors, all of which may diminish the link between polyphenol consumption and T2DM outcomes. The selected studies focused on the impact of GT and cocoa on improving glycaemic control and insulin sensitivity in adults who are overweight/obese with T2DM. Therefore, the effectiveness of other sources of polyphenol in patients newly diagnosed with T2DM might not be determined in this review. Furthermore, since the majority of the RCTs selected included short-term interventions (up to 12 weeks), any long-term effects of the intervention were limited to expectations. In addition, this review's BMI range was 25–34.9 kg/m², so it was unable to identify the efficacy of GT or chocolate for people with a BMI of ≤ 24 kg/m². Therefore, the difference may be due to the degree of obesity or disease intensity, which merits further investigation. Consequently, most population groups from Asia and Africa may not have similar results compared to their counterparts in United States and Europe. Many participants (67%) were adult women, which limited the popularisation of the results. Moreover, significant differences in the feeding protocols between RCTs, short follow-up periods, small sample sizes, high dropout rates, the characteristics and number of participants, and the differences in the form of intervention make it difficult to determine which polyphenols are the most

effective for T2DM. There is a high degree of heterogeneity between the clinical and methodological RCTs included. For example, there was a substantial variation in macronutrient energy percentages. The probable influence of other lifestyle-related factors, which are not obvious in any of the studies included, is one of the biggest methodological challenges in any nutritional intervention. Nonetheless, the results of this meta-analysis may be limited because of the small number of eligible RCTs. Although a thorough search of the literature was conducted using limited search engines, there was bias in selecting RCTs that fit within the search engines' limited reach.

Some limitations of the included studies should be considered as well. Most of the studies focused on adults with T2DM aged between 18 and 65; hence, the findings of these studies may not hold for those with different ages and levels of health status and are thus limited in their generalisability. Some of the studies did not use a placebo: seven focused on GT [38, 54, 61, 62, 64, 66, 67], and two focused on cocoa [68, 70]. Consequently, it may be difficult to avoid bias. [66] and [58] identified the significant discrepancies in HbA1c levels (≥ 9), while all the other studies had discrepancies of ≤ 6 , which could affect the validity of the findings. Furthermore, since most studies on cocoa were based on small sample sizes and a minority number of male participants, it was difficult to ensure any impact related to gender. In contrast, the sample size for the GT studies was somewhat acceptable, and the ratio of males to females was equal. However, a large number of dropouts was noted in some studies: exceeding 21% for studies by [67] and [68] and 10% for the study by [66]. Despite these limitations, [68] offered the longest intervention to date for assessing the effects of cocoa flavonoids on patients with T2DM.

Some studies measured dietary intake/adherence using food records [38, 46, 54, 59, 61, 67]. Only a few studies have studied dietary intake, and their outcomes might be incorrect. According to [71] and [72], approximately 30% of overweight people underreport their food intake. Most of the participants were overweight and obese in this review, and a lack of substantial differences between the two groups might be due to the control group's lack of limits on GT consumption in [61]. Although dietary intake was monitored by a weekly intake questionnaire at each visit, this was not restricted in [60]. Some studies have reported that adherence to dietary restrictions was controlled by investigating nutrition status and nutritional intake, although physical activity was not

assessed [38, 46, 54, 59, 61, 67]. Therefore, the research may have been underpowered due to confounding effects from the lifestyle changes that may have altered outcome factors. However, in studies by [58–60, 68, 69], the participants were instructed to maintain a normal diet and engage in regular physical activity. In addition to the long duration, this results in ideal and more realistic situations. [38, 58, 64] were crossover trial studies in which there was more/some concern that individuals might be able to distinguish between the two preparations. In its study design, [69] did not have the possibility of double-blinding, and the participants were aware of the intervention grouping type. For [68] and [69], the amounts of serum polyphenols were not assessed at the start and conclusion, which might have influenced the outcomes in both groups. [60] reported that the diet of all patients was not the same 24 h before each blood sampling; moreover, during the trial, the patient's sleep, stress, and psychological condition were not examined as factors that could influence the findings. Moreover, some studies did not measure HbA1c and insulin resistance [46, 54–57, 59, 60, 62, 64, 66], which might have led to a less accurate evaluation of the changes in glycaemic control.

5. Conclusion

The effect of polyphenol intake in patients with T2DM is still uncertain. This systematic review has attempted to explore this by reviewing several studies. With regard to improving glycaemic control and insulin sensitivity, the evidence shows clearly that the short-term administration of cocoa or GT intake did not significantly reduce the level of FBG, FBI, HbA1c, and HOMA-IR. Overall, diabetes diagnosis should be performed regularly among the population at a high risk of T2DM. Combining increased screening, lifestyle changes, and polyphenols intake alongside anti-diabetic drugs may improve results for adults with T2DM if it is initiated early.

Based on the results of the systematic review, the heterogeneity of the findings of the included studies is attributed to the variability in dose, the severity of the disease, the duration of treatment, and the tools used to diagnose the disease. Consequently, further RCTs should consider larger sample size, dosage, duration or long-term follow-up, the timing of either GT or cocoa, the generalisation of the diet, the severity of the disease, and different methods of assessing the

hypotheses to investigate the effect of polyphenols on FBG, especially the long-term effects on FBI, HbA1c, and HOMA-IR.

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