

Review

Cinnamon Improves Glycated Haemoglobin and Body Mass Index, but Not Inflammatory Parameters in Patients with Type 2 Diabetes: Evidence from a Systematic Review and Meta-Analysis of Randomised Controlled Trials

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Abstract: Background: Type 2 Diabetes (T2D) is increasingly becoming a critical healthcare priority globally. Medical interventions are primary strategies for managing diabetes, but more recently, diet/nutrition therapy, including the use of functional food products such as cinnamon and/or cinnamon products, has garnered considerable attention. The focus of this systematic review and meta-analysis is to examine whether cinnamon improves blood glucose parameters, body mass index, and inflammatory markers in people with T2DM. Method: PRISMA and PICOS frameworks were used for the review. EBSCOhost was used to search for relevant literature in health science research databases, while EMBASE and reference lists were used to access other relevant articles. Results: For systematic review and meta-analysis, 14 and 12 studies, respectively, were included (five from Iran, two each from the USA and India, and one each from the UK, China, Germany, Portugal, and Iraq). All participants had T2DM with ages ranging from ≥ 30 –65 years. The effect of cinnamon on glycaemic control and other parameters did not follow a regular pattern. Effect on HbA1c (nine studies and 605 participants; MD of -0.07 (95% CI, -0.13 , -0.01 , $p = 0.02$), postprandial blood glucose (PBG) and BMI showed significant ($p < 0.05$) reductions. However, cinnamon exhibited no significant ($p > 0.05$) impact on FBG (MD of -1.73 (95% CI, -3.98 , 0.52 , $p = 0.13$), CRP, TNF- α , and IL-6 in people with T2D; neither did the sensitivity test reveal any change in relation to these parameters. Conclusions: Cinnamon or cinnamon extracts/products are significantly effective in diabetes management through reduction in HbA1c, PBG, and BMI.

Keywords: cinnamon; glycated haemoglobin; type 2 diabetes; body mass index; inflammatory parameters; postprandial blood glucose; systematic review; meta-analysis



Academic Editor: Daniela Foti

Received: 8 September 2024

Revised: 19 December 2024

Accepted: 7 January 2025

Published: 9 January 2025

Citation: Ojo, O.; Otunola, G.A.; Oshungade, O.R.; Joshua, B. Cinnamon Improves Glycated Haemoglobin and Body Mass Index, but Not Inflammatory Parameters in Patients with Type 2 Diabetes: Evidence from a Systematic Review and Meta-Analysis of Randomised Controlled Trials. *Endocrines* **2025**, *6*, 3. <https://doi.org/10.3390/endocrines6010003>

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1. Introduction

Type 2 diabetes (T2D) prevalence is rapidly increasing on a global scale [1,2]. In 1980, the number of people having T2D was 108 million, and by 2014, this number had risen to 422 million, and the number of people with T2D will reach 642 million by 2040 [1,2]. There is evidence that controlling levels of postprandial glucose is useful in the management of T2D, which results from the dysfunction of the beta cells of the pancreas and resistance to the action of insulin, leading to high blood glucose levels [3].

Preventing and managing diabetes and related complications is mainly through appropriate medication, lifestyle and dietary modifications, and increased physical activity [4]. Several oral medications used for treating diabetes may produce serious effects that are unintended (including risk of hypoglycaemia in sulfonylureas) and may be contraindicated during pregnancy. These antihyperglycaemic agents are also expensive, resulting in a large number of people with diabetes in developing economies using herbal medicines in the management of diabetes [5,6]. Due to the side effects that those with diabetes experience, coupled with the rising costs of these drugs, the existing treatment strategies and anti-diabetic medications are deemed unsatisfactory. Thus, there is a need to have more antidiabetic agents from plant sources, such as foods with functional properties that are effective [7].

1.1. Description of the Intervention

The role of diet and functional foods in managing people with T2D at the population level is significant. For example, plant-based foods such as whole grains, fruits, and vegetables have been shown to improve health in people with T2D [8]. Furthermore, prebiotics have been used to promote eubiosis of gut microbiota and to maintain glucose homeostasis in people with T2D [2]. There has also been a growth in the use of functional foods for managing chronic conditions such as T2D as a result of the hypoglycaemic, antioxidant, hypolipidemic, anti-inflammatory, and anti-hypertensive properties they possess [9]. Cinnamon has been identified as one of the effective spices with functional properties [7,10]. Cinnamon contains phytochemicals, including flavonoids, which are useful in promoting health [11]. In addition, the dry bark of the cinnamon tree is rich in polyphenol, which is effective in enhancing general health, including T2D [12].

Milner [13] noted that functional foods include any products potentially beneficial to health, encompassing any food or food ingredients that have been modified that could promote health beyond the nutrients it traditionally contains. Functional foods have been identified as foods that are fortified, enriched, or enhanced and whole foods that have the potential to be beneficial to health when consumed regularly at levels that are effective and as a component of a balanced diet [7]. Therefore, functional foods may be fortified, enriched, altered products, and enhanced commodities [14].

Cinnamon [*Cinnamomum verum* (Lauraceae)] and its derivatives have been shown to be significantly beneficial for human health as a result of the anti-hypertriglyceridemic and anti-diabetic properties [7,15,16]. Apart from its culinary uses, cinnamon promotes the secretion of insulin, enhances its sensitivity, and regulates insulin receptors kinase [17].

1.2. How This Intervention Might Work

The possible mechanism of action of cinnamon in lowering blood glucose in people with T2D may include increasing glucose uptake in the cells through enhanced insulin receptor phosphorylation and the translocation of glucose transport-4 to the plasma membrane. Polyphenolic compounds have been implicated as the active compounds in this process [12,18]. The mechanism of action of cinnamon may also involve increased insulin sensitivity by promoting the expression of peroxisome proliferator-activated receptors. Cinnamon has been shown to possess an inhibitory effect on intestinal glucosidases and pancreatic amylase. Furthermore, it inhibits gluconeogenesis, stimulates glycogen synthesis, and delays gastric emptying while causing a reduction in postprandial blood glucose [12,18].

1.3. Why It Is Important to Do This Review

Evidence from literature suggests that cinnamon has an effect on blood glucose parameters, although the results are varied. While extracts from cinnamon containing polyphenol type-A polymers have been found to have insulin-mimetic properties, not all studies have

reported the beneficial effects of cinnamon [10]. In addition, there remains a paucity of evidence, including reviews conducted on the role of cinnamon, its extracts, and products on glyco-metabolic and inflammatory parameters in people with T2D. Therefore, more research is needed to clearly establish the effect of cinnamon in people with T2D.

The aim of this systematic review and meta-analysis is to examine the effects of cinnamon on blood glucose and inflammatory parameters in people with T2D.

Research question: How effective is cinnamon in improving blood glucose parameters and markers of inflammation in people with T2D?

2. Methods

The preferred reporting items for systematic review and meta-analysis (PRISMA) were relied upon to conduct the review [19]. The systematic review and meta-analysis protocol was registered with Prospero (Registration Number: CRD42023442330).

The types of studies included were only Randomised Control Trials (RCT), while the participants/population were people with T2D. With respect to the types of intervention, cinnamon, its extracts, and products were compared with a placebo or non-exposed control group.

Inclusion and exclusion criteria: RCT involving people with T2D aged 18 years and older were included. On the other hand, studies involving participants without T2D at baseline were excluded from the review.

2.1. Outcomes Measures

The primary outcomes included blood glucose parameters (glycated haemoglobin, fasting blood glucose, and postprandial blood glucose) and inflammatory indicators [C-reactive protein (CRP), interleukin-6 (IL-6), and tumour necrosis factor- α (TNF- α)]. On the other hand, the secondary outcome of interest was body mass index.

2.2. Search Strategy

The Health Sciences Research databases, which include other databases such as Academic Search Premier, MEDLINE, APA PsycINFO, CINAHL Plus with Full Text, Psychology and Behavioural Sciences Collection, and APA PsycArticles databases, were searched through EBSCOhost for articles. Furthermore, EMBASE and the reference list of articles were also searched for relevant articles. The Population, Intervention, Comparator, Outcomes, and Study (PICOS) (Table 1) framework was used to define the research question.

The search terms were drawn from Synonyms and Medical Subject Headings and combined using Boolean Operators (OR/AND). The searches were conducted by one researcher (OO) and independently verified by another researcher (GAO). Differences in terms of the search results/outcomes of the searches were resolved through a joint review of the search strategy by the two researchers. Searches were conducted from database inception until 10/08/23. Search results were de-duplicated in EndNote.

Table 1. Search Strategy.

Patient/Population	Intervention	Outcome (Primary)	Study Designs	Combining Search Terms
Patients with T2D	Cinnamon	Glucose and inflammatory parameters	RCT	
Patients with diabetes OR diabetes OR type 2 diabetes OR diabetes mellitus OR diabetes complications OR type 2	Cinnamon OR cinnamon extracts OR cinnamon products OR extracts of cinnamon	Glycated haemoglobin OR fasting blood glucose OR lipid profile OR inflammatory parameters	#1 controlled clinical trial OR randomised controlled trial OR trial OR randomised OR drug therapy OR placebo OR randomly OR groups#2 "Animals" NOT "Humans" #3 #1 NOT #2	Columns 1, 2, 3, and 4 were combined using 'AND'.

2.3. Data Collection and Analysis

Studies identified through searches of databases and reference lists of articles were assessed for eligibility on the basis of a set criteria (Figure 1).

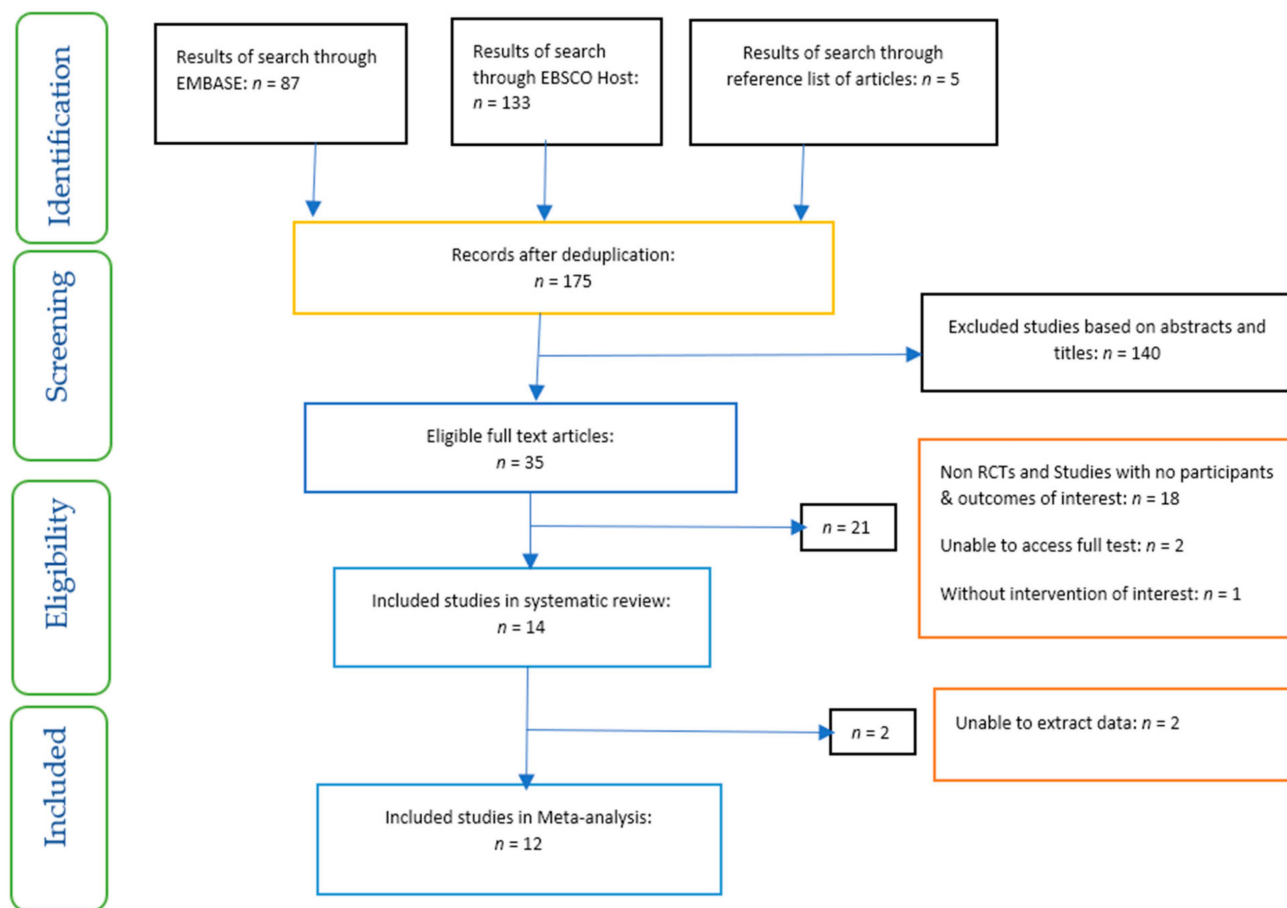


Figure 1. PRISMA flow chart of studies included.

2.3.1. Extraction of Data and Management

The author/s names, study design, aim of study, participants, size of sample, age, intervention type, and results were the information extracted from the studies included.

One researcher (ORO) extracted the data and was independently verified by two other researchers (OO and BJ). Resolution of differences was through discussion.

2.3.2. Data Analysis

The Review Manager was used to carry out the meta-analysis [20]. The level of consistency of the results was assessed by conducting a sensitivity analysis that involved removing studies one after the other from the meta-analysis. The I^2 statistic was used as a measure of heterogeneity, and statistical significance of heterogeneity was set at $p = 0.10$. Mean Difference (MD) and Fixed Effects Model were used to carry out the meta-analysis, except with respect to CRP, where the Standardised Mean Difference (SMD) was used because the units of measurements of the included studies were different. In addition, data reporting standard errors were converted to standard deviations, and the units of measurement for FBG and PBG were converted from mmol/L to mg/dL. The statistical significance of the effect of the intervention was set at $p < 0.05$. Furthermore, forest plots were used to represent the results of the meta-analysis.

In order to conduct the Risk of Bias (Quality) Assessment, the studies included were evaluated using the domain-based evaluation tool. The domains that were assessed included attrition bias, allocation concealment (selection bias), reporting bias, detection bias, selection bias, and performance bias.

3. Results

There were fourteen studies included in the systematic review and twelve studies in the meta-analysis (Figure 1). The studies' characteristics are shown in Table 2. Five of the fourteen studies [4,11,16,21,22] were carried out in Iran, while two studies each were carried out in the USA [23,24] and India [25,26]. One study each was conducted in the UK [18], China [27], Germany [28], Portugal [3], and Iraq [12]. All the participants had T2D, with ages ranging from ≥ 30 years to 65 years.

Table 2. Characteristics of studies included.

Author/Date	Country of Study	Study Design	Aim	Participants	Sample Size	Mean Age (Years)	Type of Interventions	Result/Findings
Akilen et al. [18]	UK	RCT	To evaluate the effect of cinnamon on blood glucose and lipid parameters and BP in people with T2D.	People with T2D.	58 participants Cinnamon: $n = 30$ Placebo: $n = 28$	Cinnamon: 54.90 ± 10.14 Placebo: 54.43 ± 12.53	Therapeutic	After intervention, there was a significant decrease in mean glycated haemoglobin (HbA1c) in the intervention group compared to the placebo group. Cinnamon supplementation may be used as an additional dietary supplement in managing BG levels in addition to conventional medications in people with T2D.
Azimi et al. [11]	Iran	RCT	To examine the effects of cinnamon, cardamom, saffron, and ginger in people with T2D.	People with T2D.	204 Cinnamon: $n = 40$ Control: $n = 39$	Cinnamon: 54.33 ± 0.5 Control: 53.64 ± 1.3	Therapeutic	Cinnamon did not have significant effects on glycaemic control, anthropometric markers of inflammation, or oxidative stress following 8 weeks of intervention. With respect to within-group comparisons, intake of cinnamon decreased FBG significantly.
Blevins et al. [23]	USA	RCT	To examine the effects of cinnamon on glucose and lipid parameters in people with T2D.	People with type 2 diabetes.	58 Cinnamon: $n = 30$ Placebo: $n = 28$	Cinnamon: 63.6 Placebo: 58.0	Therapeutic	1 g per day of cinnamon taken for 3 months had no effect on fasting blood glucose (FBG) and HbA1c levels.
Crawford [24]	USA	RCT	To assess if cinnamon has an effect on HbA1c in patients with T2D.	Patients with T2D, >18 years.	109 subjects Cinnamon: $n = 55$ Control: $n = 49$	Cinnamon: 60.5 ± 10.7 Control: 59.9 ± 9.2	Therapeutic	There was significant lowering of HbA1c in the cinnamon group compared with usual care.

Table 2. Cont.

Author/Date	Country of Study	Study Design	Aim	Participants	Sample Size	Mean Age (Years)	Type of Interventions	Result/Findings
Davari et al. [21]	Iran	RCT	To examine the role of daily cinnamon supplementation on inflammatory parameters, levels of plasma Sirtuin-1 (SIRT) and NF-kB, in people with T2D.	Adult patients with T2D.	44 participants Cinnamon: $n = 20$ Placebo: $n = 19$	Cinnamon: 58.9 ± 7.93 Placebo: 56.26 ± 9.46	Therapeutic	This study found that supplementation with cinnamon was not beneficial in reducing inflammatory parameters, SIRT1 and NF-kB, in people with T2D. In addition, the effect of cinnamon on FBG was not significant.
Hendre et al. [25]	India	RCT	To assess the role of cinnamon on insulin resistance and BG in people with T2D.	Patients with T2D aged 35–65 years.	200 Cinnamon: $n = 100$ Control: $n = 100$	35–65 years	Therapeutic	There was a significant reduction in FBG and postprandial blood glucose (PBG). There was also a significant difference in serum insulin after 3 months, while HOMA-IR also showed significant changes.
Lu et al. [27]	China	RCT	To examine the role of extracts from cinnamon on HbA1c and FBG levels in people with T2D.	Men and women > 48 years with type 2 diabetes.	69 subjects High-dose cinnamon: $n = 23$ Placebo: $n = 20$	High-dose cinnamon: 58.8 ± 6.4 Placebo: 60 ± 5.9	Therapeutic	The extract from cinnamon when supplementing gliclazide effectively lowered HbA1c and FBG in people with T2D.
Mang et al. [28]	Germany	RCT	To assess whether an aqueous cinnamon-purified extract improves HbA1c and FBG in people with T2D.	Patients with diagnosed T2D.	79 Cinnamon: $n = 33$ Placebo: $n = 32$	Cinnamon: 62.8 ± 8.37 Placebo: 63.7 ± 7.17	Therapeutic	The effect of cinnamon extract in reducing FBG levels in patients with T2D with poor glycaemic control was moderate.

Table 2. Cont.

Author/Date	Country of Study	Study Design	Aim	Participants	Sample Size	Mean Age (Years)	Type of Interventions	Result/Findings
Rachid et al. [3]	Portugal	RCT	To assess the role of aqueous cinnamon extract on levels of PBG in people with T2D mellitus.	People with T2D.	36 subjects Cinnamon: $n = 18$ Control: $n = 18$	Cinnamon: 63.5 ± 1.6 Control: 62.06 ± 2.4	Therapeutic	The data revealed that aqueous cinnamon extract had no significant effect in influencing the response of postprandial glucose in patients with T2D during an OGTT.
Sahib [12]	Iraq	RCT	To evaluate the effect of cinnamon on blood glucose parameters and markers of oxidative stress in poorly controlled people with T2D.	Male and female patients with T2D.	25 patients Cinnamon: $n = 13$ Placebo: $n = 12$	49.1 ± 6.0	Therapeutic	There was a significant reduction in FBG after 6 and 12 weeks of treatment compared to baseline value and to the placebo group. In the cinnamon group, HbA1c reduced by 2.625% and 8.25% after 6 and 12 weeks, respectively. However, compared to baseline, these reductions were not significant.
Sharma et al. [26]	India	RCT	To evaluate the efficacy of cinnamon supplementation on BG and HbA1c in patients with T2D.	People with T2D.	150 patients with T2D Cinnamon (6 g dose): $n = 50$ Cinnamon (3 g dose): $n = 50$ Placebo: $n = 50$	≥ 30 years	Therapeutic	Cinnamon seems effective in managing hyperglycaemia in newly diagnosed patients with T2D without any adverse effect.
Talaei et al. [4]	Iran	RCT	To assess the effect of cinnamon on markers of glycaemic control in people with T2D.	Patients with T2D.	44 patients Cinnamon: $n = 20$ Control: $n = 19$	Cinnamon: 58.90 ± 7.93 Control: 56.26 ± 9.46	Therapeutic	Cinnamon supplementation was found to have no major effect on glycaemic control and markers of inflammation in people with T2D.

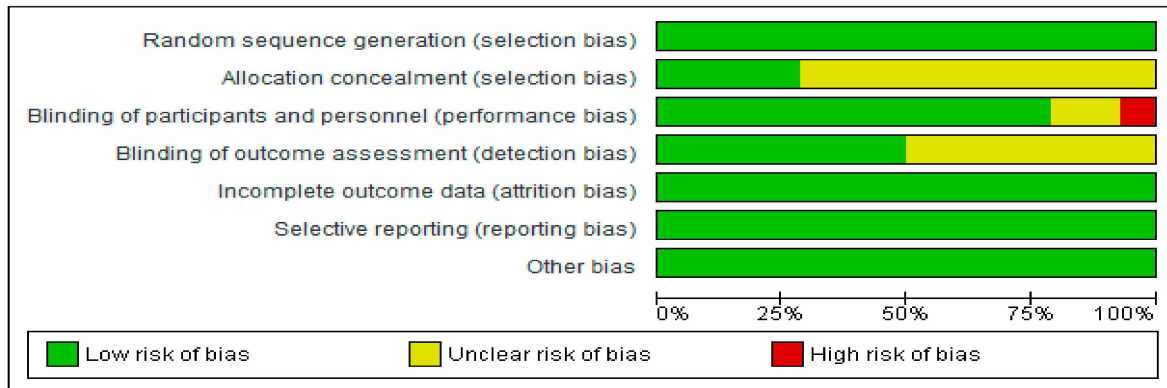
Table 2. Cont.

Author/Date	Country of Study	Study Design	Aim	Participants	Sample Size	Mean Age (Years)	Type of Interventions	Result/Findings
Vafa et al. [22]	Iran	RCT.	To examine the effects of cinnamon over eight weeks on glycaemic indicators and body composition in people with T2D.	Individuals with T2D.	44 subjects Cinnamon: $n = 19$ Placebo: $n = 18$	Cinnamon: 54.11 ± 10.37 Placebo: 55.67 ± 7.98	Therapeutic	Significant differences were not observed in glycaemic and anthropometric parameters between the groups at the end of the intervention. However, significant differences were found between baseline and 8 weeks in relation to fasting blood glucose and glycated haemoglobin in the cinnamon group, but not within the placebo group.
Zare et al. [16]	Iran	RCT.	To assess the impact of cinnamon supplementation on anthropometric and glycaemic outcomes in people with T2D.	People with T2D.	140 patients Cinnamon: $n = 69$ Placebo: $n = 69$	Cinnamon: 52.1 ± 9.7 Placebo: 53.2 ± 8.5	Therapeutic	All anthropometric parameters (BMI, TBF, and VF) and glycaemic indicators (FPG, HbA1C, fasting insulin, and insulin resistance) demonstrated improvements following cinnamon supplementation.

Abbreviations: blood glucose (BG); body mass index (BMI); blood pressure (BP); fasting blood glucose (FBG); fasting plasma glucose (FPG); glycated haemoglobin (HbA1c); high-sensitivity C-reactive protein (hs-CRP); homeostatic model assessment for insulin resistance (HOMA-IR); interleukin-6 (IL-6); nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B); oral glucose tolerance test (OGTT); Sirtuin-1 (SIRT1); total body fat (TBF); tumour necrosis factor alpha (TNF- α); type 2 diabetes (T2D); visceral fat (VF).

3.1. Assessment of Risk of Bias

There was low risk of bias in all the studies in relation to selection bias (random sequence generation), attrition bias, selective reporting, and other bias (Figure 2a,b). While there were unclear risks of bias in some of the studies in respect of allocation concealment [3, 4,11,12,21,22,25–28], performance bias [11,25], and blinding of outcomes [3,11,12,25–28], only one study [24], in respect of performance bias, showed high risk of bias.



(a)

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Akilen et al 2010	+	+	+	+	+	+	+
Azimi et al 2014	+	?	?	?	+	+	+
Belvin et al 2007	+	+	+	+	+	+	+
Crawford 2009	+	+	-	+	+	+	+
Davari et al 2020	+	?	+	+	+	+	+
Hendre et al 2019	+	?	?	?	+	+	+
Lu et al 2012	+	?	+	?	+	+	+
Mang et al 2006	+	?	+	?	+	+	+
Rachid et al 2022	+	?	+	?	+	+	+
Sahib 2016	+	?	+	?	+	+	+
Sharma et al 2012	+	?	+	?	+	+	+
Talaei et al 2017	+	?	+	+	+	+	+
Vafa et al 2012	+	?	+	+	+	+	+
Zare et al 2019	+	+	+	+	+	+	+

(b)

Figure 2. Showing (a) risk of bias and (b) risk of bias summary of studies included [3,4,11,12,16,18,21–28].

Following a narrative synthesis and meta-analysis, three distinct areas were identified as follows:

Glycaemic control, inflammatory parameters, and BMI.

3.2. Glycaemic Control

The effects of cinnamon, cinnamon extract, or cinnamon products on glycaemic control in the studies included varied from moderate and significant effects [26] to effects that were not significant. Four studies [16,18,24,27] found improvement and/or significant reduction in HbA1c in the cinnamon group compared to control, following intervention. In contrast, the reduction in HbA1c by cinnamon was not significant in other studies [12,23]. Furthermore, there was no significant difference between the intervention and control groups in some of the studies with respect to glycaemic control [4,11,22].

The analysis of the effect of cinnamon on HbA1c had nine studies and 605 participants. The reduction in HbA1c in the cinnamon group compared with control was significant, with an MD of -0.07 (95% CI, $-0.13, -0.01$, $p = 0.02$) (Figure 3). After the sensitivity analysis, there was consistency in the result ($p < 0.05$), which only changed when the Zare et al. [16] study was removed from the analysis, and then, the effect of cinnamon on HbA1c was not significant ($p > 0.05$).

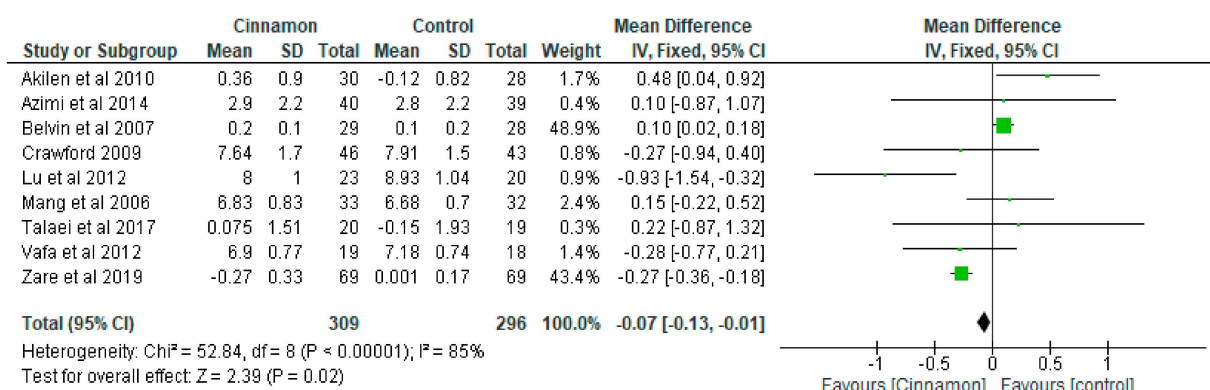


Figure 3. The effect of cinnamon on HbA1c (%) [4,11,16,18,22–24,27,28].

In relation to FBG, while there were moderate [28] and significant reductions [12,16,25,27] in FBG after intervention, two other studies [21,23] showed that cinnamon did not have a significant effect on FBG.

Nine studies and 716 participants were analysed with respect to FBG (Figure 4). The effect of cinnamon on FBG in people with T2D was not significant, with an MD of -1.73 (95% CI, $-3.98, 0.52$, $p = 0.13$). After the sensitivity test, the result remained consistent, except when Blevins et al. [23] and Zare et al. [16] studies were removed one by one from the meta-analysis, at which point the difference was significant between the groups.

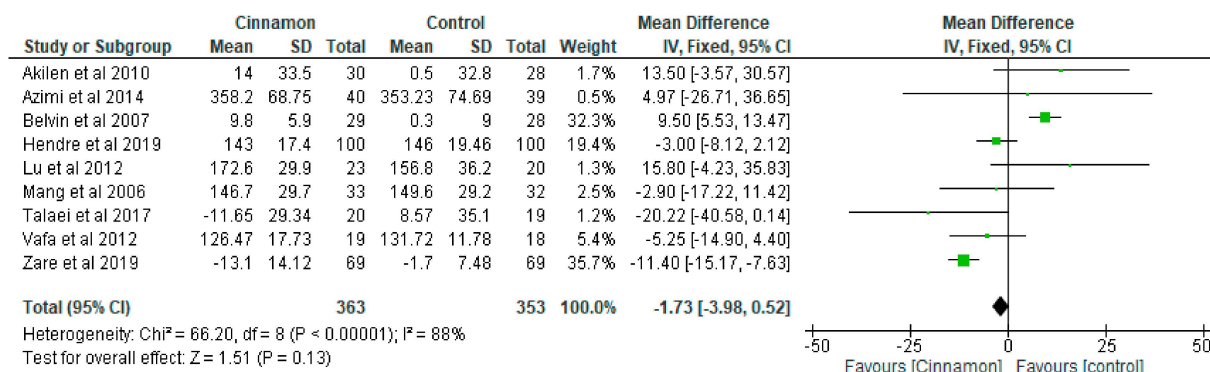


Figure 4. The effect of cinnamon on FBG (mg/dL) [4,11,16,18,22,23,25,27,28].

Hendre et al. [25] and Zare et al. [16] reported that cinnamon significantly reduced PBG levels in patients with T2D. However, Rachid et al. [3] noted in their study that cinnamon extract (aqueous) did not have a substantial effect on PBG in people with T2D.

Following meta-analysis, the evidence indicated that the effect cinnamon had on PBG was significant compared with the control group, with an MD of -6.18 (95% CI, -9.93 , -2.43 , $p = 0.001$) (Figure 5). Three studies and 375 participants were involved in the meta-analysis. After the sensitivity analysis, the difference between the cinnamon and control groups remained significant ($p < 0.05$) with respect to PBG.

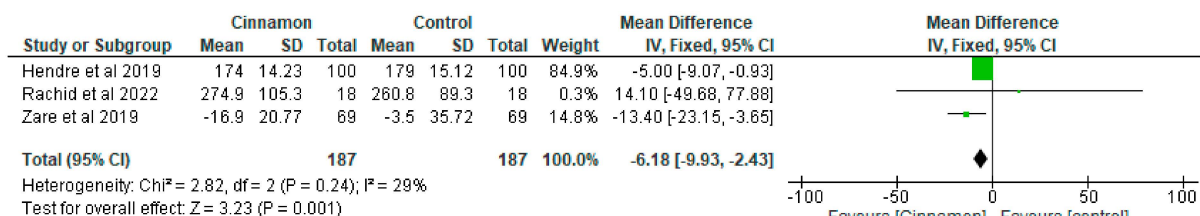
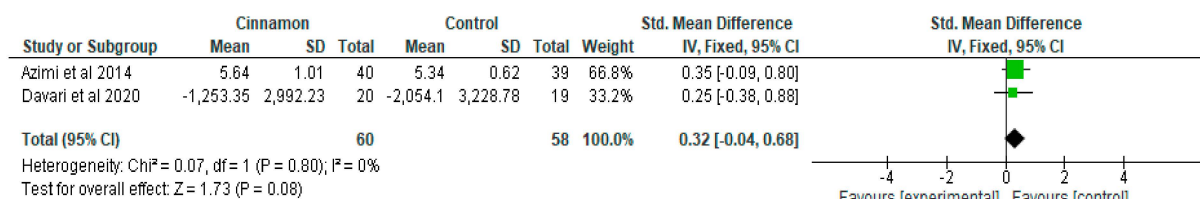


Figure 5. The effect of cinnamon on PBG (mg/dL) [3,16,25].

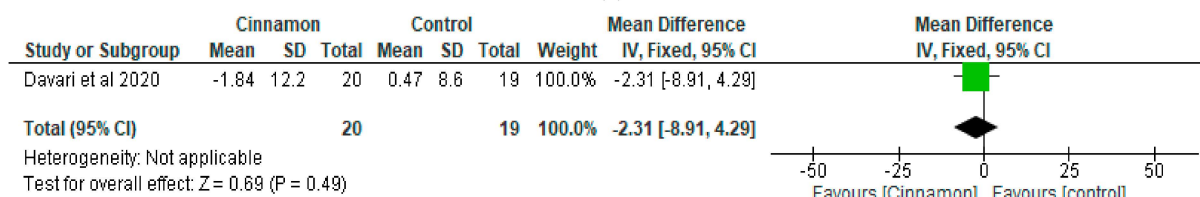
3.3. Inflammatory Parameters

Three studies [4,11,21] observed that cinnamon had no significant or beneficial effects in reducing inflammatory parameters, including CRP, IL-6, and TNF- α levels, in patients with T2D.

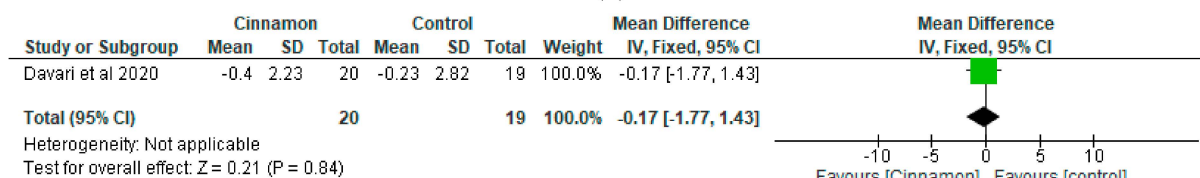
The analysis of the effect of cinnamon on CRP, TNF- α , and IL-6 did not show any significant difference ($p > 0.05$) between the cinnamon and control groups (Figure 6a–c). The sensitivity test did not reveal any change in relation to the effect of cinnamon on CRP ($p > 0.05$).



(a)



(b)



(c)

Figure 6. The effect of cinnamon on (a) CRP (StD. Mean Difference) [11,21], (b) TNF- α (pg/mL) [21], and (c) IL-6 (pg/mL) [21].

3.4. Body Mass Index

Zare et al. [16] reported that anthropometric and body composition indicators such as BMI, TBF, and VF in the cinnamon group compared with the control were significantly reduced. However, Vafa et al. [22] and Akilen et al. [18] found no significant differences between the cinnamon and control groups with respect to BMI after the intervention.

Five studies and 369 participants were analysed in respect of BMI. The result revealed that BMI was significantly reduced by the intervention compared with control, with MD of -0.31 (95% CI, -0.38 , -0.24 , $p = 0.001$) (Figure 7). After the sensitivity analysis, cinnamon remained significantly effective ($p < 0.05$) in reducing BMI compared to the control group in people with T2D.

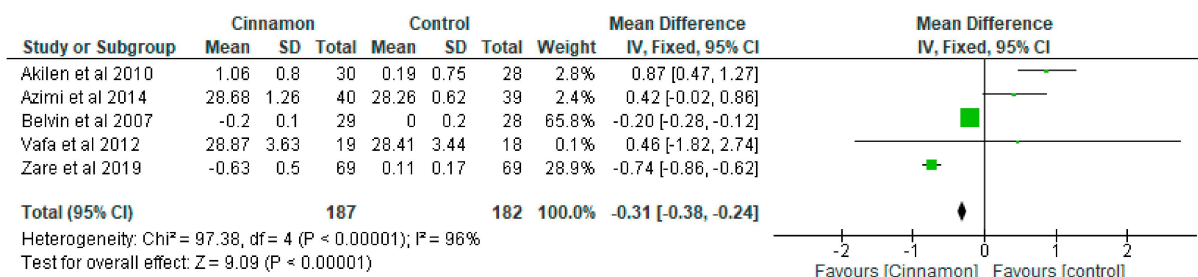


Figure 7. The effect of cinnamon on BMI (kg/m^2) [11,16,18,22,23].

4. Discussion

Dietary interventions, including the use of functional foods, are on the rise as useful and important approaches for managing the high prevalence of T2D. Functional foods are food products that are enhanced with added nutrients or other substances that provide health benefits beyond their nutritional value [29]. Cinnamon has traditionally been used for managing diabetes with varying reported effects due to its functional properties. This review therefore assessed the effects of cinnamon, its extracts, or products on glyco-metabolic and markers of inflammation in people with T2D. All the studies investigated were RCT.

The included studies showed variations ranging from high to moderate to no significant effects of cinnamon, cinnamon extract, or cinnamon products on hyperglycaemia in T2D. The significant ($p > 0.5$) reduction in BG, including HbA1c and PBG, following the administration of cinnamon, its extracts, or products on people with T2D has been discussed extensively. Hlebowicz et al. [30] suggest that the substantial ($p < 0.5$) reduction in blood glucose could be attributed to improved function of the insulin receptor, activation of insulin receptor PI 3-kinase, and inhibition of tyrosine phosphates, which have an effect on cellular glucose uptake, while PBG response could be as a result of reduction in gastric emptying and controlled delivery of glucose to the small intestine [31]. Furthermore, the phytochemical constituents present in cinnamon, such as phenolic and volatile compounds, are useful in the antioxidant and anti-inflammatory activities that promote health [7].

4.1. Molecular Mechanisms of Cinnamon Action

There is evidence that cinnamon and its bioactive compounds, such as cinnamaldehyde, gallic acid, eugenol, and beta caryophyllene, have been associated with antihyperglycaemic, anti-lipidemic, and antioxidant effects [32–34]. The mechanisms of action of cinnamon may include the facilitation of glycogen synthesis in the liver, restoration of pancreatic islet function, deceleration of gastric emptying rates, and the augmentation of glucose absorption and enhancement of insulin sensitivity in skeletal muscle and adipose tissues as reviewed elsewhere [33].

For example, there is evidence that the mechanism of action of cinnamaldehyde, which is the principal active ingredient of cinnamon, on glycaemic control is based on its role in increasing glycogen synthesis and hindering gluconeogenesis [34]. Its roles in insulin signalling and glucose transport have also been reported [34]. Eugenol is another active ingredient of cinnamon that has been shown to have anti-hyperglycaemic, antioxidant, antibacterial, and anti-inflammatory properties, and its mechanism of action is through alteration in ghrelin secretion, influencing food intake and gastric emptying [34].

Beta caryophyllene and gallic acid are two other active ingredients found in cinnamon [34]. While beta caryophyllene has been reported to have anti-hyperglycaemic, antioxidant, anti-inflammatory, and anti-lipidemic properties through its role in increasing noradrenaline and thermogenic action, the antioxidant, antimicrobial, and anti-inflammatory effect of gallic acid is through increased insulin sensitivity [34].

In comparison, some of the studies reported only moderate or no observable impact ($p > 0.05$) on BG in people with T2D. These varying effects may be attributed to various forms of administration of cinnamon (food, extract, capsule, and supplement), doses, time, method/route, age, ethnicity, and use of other diabetic drugs [9,18,31]. Tables 2 and 3 provide highlights of the various doses of cinnamon, differences in the main inclusion criteria of included studies, such as body mass index, fasting blood glucose, glycated haemoglobin, age, and duration of diabetes; the different types of medications taken by participants; and differences in sample sizes of participants to explain differences in the results of the studies included and the findings of this review.

The impact of cinnamon on HbA1c in the studies reviewed followed the same trend as that for fasting blood glucose and postprandial glucose, ranging from high to not significant. For example, the use of cinnamon was beneficial in the reduction in HbA1c significantly [12,16,18,24–27]. These observations agree with reports of other studies, which showed that the cinnamon extracts given orally have a beneficial influence on BG and HbA1c levels [35–37]. On the other hand, the effect of cinnamon on HbA1c was not significant in some of the studies [3,11,23]. These findings are in agreement with some studies that showed that while there were relatively minor variations in HbA1c with respect to the consumption levels, differences in levels of HbA1c before and after the consumption of cinnamon were not significant [31,38]. However, the analysis of the studies (9 studies and 605 participants) showed that cinnamon reduced HbA1c significantly ($p < 0.05$) in the cinnamon group with MD of -0.07 (95% CI, -0.13 , -0.01 , $p = 0.02$). Even after the sensitivity analysis, there was consistency in the HbA1c result, except when Zare et al. [16] study was removed from the analysis. Overall, the existing evidence supports the capacity of cinnamon, cinnamon extracts, or products to positively modulate PBG and HbA1c in people with T2D.

In reviewing the inflammatory parameters, Azimi et al. [11], Talaei et al. [4], and Davari et al. [21] reported that the effect of cinnamon on inflammatory parameters in people with T2D was not significant. Cinnamon had no significant effect ($p > 0.05$) on CRP, TNF- α , and IL-6 compared to the control group (Figure 6a–c). The sensitivity test did not reveal any change in relation to the effect of cinnamon on CRP ($p > 0.05$). In contrast to these reports, however, other studies have demonstrated and reported significant effects of cinnamon on inflammatory parameters in people with T2D. These findings include the report that 600 mg of Ceylon cinnamon administered for 60 days reduced IL-6 significantly in the intervention group compared to the control group, as well as improved plasma concentration of CRP in chronic conditions [9,39,40]. According to Davari et al. [21], the diverging results could be due to differences in species/type of cinnamon used for the study, which could contain different active chemical properties, resulting in different pharmacological outcomes.

Table 3. Main inclusion criteria of included studies and types of medications taken by participants.

Citation	Inclusion Criteria			Dose of Cinnamon	Types of Medications Participants Are Taking as Regular Medication
	BMI	FBG	HbA1c		
Akilen et al. [18]	Not Applicable	>7 mmol/L	HbA1c \geq 7%	18 years or older	2 gm cinnamon capsule/day for 12 weeks. Oral hypoglycaemic agents.
Azimi et al. [11]	\geq 25 Kg/m ²	\geq 126 mg/dL	Not Applicable	\geq 30 years	3 gm cinnamon/day for 8 weeks Oral hypoglycaemic agents (metformin and glibenclamide).
Blevins et al. [23]	Not Applicable	Not Applicable	6% or higher	Individuals of any age with type 2 diabetes	1 gm of cinnamon/day for 3 months Patients taking different hypoglycaemic drugs. Subjects were withdrawn if any of the following medicines were initiated, discontinued, or adjusted during the study: sulfonylureas, meglitinides, metformin, thiazolidinediones, α -glucosidase inhibitors, exenatide, hydromethylglutaryl-CoA reductase inhibitors, ezetimibe, niacin, or fibric acid derivatives
Crawford [24]	Not Applicable	Not Applicable	\geq 7% over the past 6 months.	>18 years	1 gm cinnamon daily for 90 days Patients were allowed to adjust their usual medications and doses as recommended by the doctor.
Davari et al. [21]	18.5–30 Kg/m ²	<180 mg/dL	Not Applicable	25–70 years Duration of diabetes: Newly diagnosed or had a history of <8 years	3 g of cinnamon extract/day for 8 weeks Patients on metformin.
Hendre et al. [25]	Not Applicable	Not Applicable	Not Applicable	35–65 years	500 mg/day of cinnamon for 90 days All patients were on one drug (metformin).

Table 3. Cont.

Citation	Inclusion Criteria			Dose of Cinnamon	Types of Medications Participants Are Taking as Regular Medication	
Lu et al. [27]	Not Applicable	Higher than 8.0 mmol/L	>7%	>48 years	120 mg/day or 360 mg/day of cinnamon extract for 90 days	All of the participating patients in the study were taking gliclazide during the study.
Mang et al. [28]	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Aqueous cinnamon extract equivalent to 3 g of cinnamon powder per day for 4 months	Patients were treated with oral antidiabetics or diet.
Rachid et al. [3]	Not Applicable	Not Applicable	Not Applicable	Aged between 35 and 77 years	Aqueous cinnamon extract (6 g/100 mL)	Not reported.
Sahib [12]	Not Applicable	Not Applicable	Not Applicable	Aged 40–65 years Duration of diabetes: 5–10 years	1 gm cinnamon/day for 12 weeks	Patients were on glibenclamide.
Sharma et al. [26]	Not Applicable	140–400 mg/dL	>6%	≥30 years Duration of diabetes: newly diagnosed	3 gm/day or 6 gm/day for 3 months	Not on oral hypoglycaemic agents and not on medications for other health conditions.
Talaei et al. [4]	18.5–30 Kg/m ²	<180 mg/dL	Not Applicable	25–70 years Duration of diabetes: <8 years old	3 gm/day cinnamon supplement for 8 weeks	Glycaemic control with metformin therapy.
Vafa et al. [22]	Not Applicable	126–160 mg/dL	6–8%	30–65 years	3 gm/day of cinnamon capsule for 8 weeks	Patients were using one of two hypoglycaemic drugs (metformin, gliclazide).
Zare et al. [16]	Not Applicable	126–250 mg/dL	Not Applicable	Not Applicable	1 gm/day of cinnamon capsule for 3 months	Not reported.

Abbreviations: body mass index (BMI); fasting blood glucose (FBG); glycated haemoglobin (HbA1c).

With regard to anthropometric indices, a significant reduction in BMI, TBF, and VF in the cinnamon group compared with the control was reported by Zare et al. [16], although Vafa et al. [22] and Akilen et al. [18] found no significant differences between the cinnamon and control groups in relation to BMI after the intervention. The meta-analysis (five studies, 369 participants) also showed that cinnamon reduced BMI significantly with an MD of -0.31 (95% CI, $-0.38, -0.24, p = 0.001$) (Figure 7). After the sensitivity analysis, cinnamon remained significantly effective ($p < 0.05$) in reducing BMI when compared to the control group in people with T2D. Evidence has demonstrated that the risk factors in the development of T2D include overweight and obesity and that weight loss is an effective strategy for improving glycaemic control [41,42]. However, studies have also reported that cinnamon has no major effect on anthropometric indicators and body composition [43]. Namazi et al. [6] found that BMI, waist circumference, and body weight were not affected significantly by cinnamon consumption.

4.2. Limitations

The high heterogeneity of some of the studies that were used for the meta-analysis would suggest that caution is needed when interpreting the results. However, we conducted sensitivity analysis in order to examine the effect of individual studies and to establish the level of consistency of the results/findings. This process was carried out by removing studies one after the other from the meta-analysis. In addition, the small sample size of some of the studies included and the small number of studies used for the meta-analysis in some of the outcomes of interest may limit the broader application of those results.

5. Conclusions

The results of the systematic review and meta-analysis have evidenced that cinnamon or cinnamon extracts are effective in significantly reducing ($p < 0.05$) HbA1c, PBG, and BMI compared to control in people with T2D. Furthermore, the results also indicate that the use of 1–3 gm/day of cinnamon for 12 weeks appears to have a significant effect on glycaemic control in people with T2D. However, cinnamon or cinnamon extracts did not have a significant effect ($p > 0.05$) on FBG and inflammatory markers in people with T2D. The sensitivity analysis demonstrated consistency with respect to PBG, BMI, and CRP, but not in respect to HbA1c and FBG. The evidence of this robust systematic review purports that cinnamon can be beneficial as a dietary adjuvant, supplement, or alternative therapy for the prevention, treatment, or management of T2D in humans.

However, for future research studies, it is important that key inclusion criteria, such as participants with a high cut-off of HbA1c, BMI, enough sample size, and the number of hypoglycaemic medications being taken by participants, are considered in order to fully evaluate the effectiveness of cinnamon in patients with type 2 diabetes.

Author Contributions: Conceptualization, O.O. and G.A.O.; methodology, O.O., G.A.O., O.R.O.; validation, O.O., G.A.O. and B.J.; formal analysis, O.O.; writing—original draft preparation, O.O. and G.A.O.; writing—review and editing, O.O., G.A.O. and B.J. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflicts of interest.

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