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Review

Cinnamon in glycaemic control: Systematic review and meta analysis

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SUMMARY

Background & aims: Cinnamon seems to be highly bioactive, appearing to mimic the effect of insulin through increased glucose uptake in adipocytes and skeletal muscles. This systematic review and Meta analysis examined the effect of cinnamon on glycaemic control in patients with Type 2 Diabetes mellitus.
Methods: A systematic literature search was conducted from the earliest possible date through to 01 August 2011. Search terms included free text terms, MeSH and Medline medical index terms such as: "*cinnamon*", "*cinnamomum*", "*cinnamomum cassia*", "*cinnamomum zeylanicum*", "type 2 diabetes mellitus". Each was crossed with the term "diabetes mellitus". In addition, references of key articles were hand searched.
Results: A total of 6 clinical trials met the strict inclusion criteria and considered a total of 435 patients; follow up between 40 days–4 months, doses ranging from 1 g to 6 g per day. Meta-analysis of RCTs showed a significant decrease in mean HbA1c [0.09%; 95% CI was 0.04–0.14] and mean FPG [0.84 mmol/l; 95% CI was 0.66–1.02].
Conclusions: Use of cinnamon showed a beneficial effect on glycaemic control (both HbA1c and FPG) and the short term (<4 months) effects of the use of cinnamon on glycaemic control looks promising.

1. Introduction

Research has suggested that cinnamon may have potentially useful pharmacological effects for the treatment of diabetes.[1,2] Although there are different species of cinnamon, *Cinnamomum zeylanicum* is categorised as true cinnamon when referred to as a spice, but the glucose lowering effect of *Cinnamomum cassia* spices is thought to be superior.[3] Early studies suggested that cinnamon can be used effectively to lower blood glucose[1,2] and cholesterol[1] levels in type 2 diabetes mellitus [T2DM]. However, recent studies reported that cinnamon did not seem to improve glycaemic control in type 2[4,5] or type 1 diabetic patients.[6] In contrast, studies in people with pre diabetes/insulin resistance and metabolic syndrome revealed that cinnamon has the potential to improve glycaemic control and insulin sensitivity.[7,8]

The blood glucose lowering potential and pharmacological properties of cinnamon has been demonstrated previously *in vitro* and *in vivo* animal studies.[9–14] Cinnamon polyphenols display insulin like properties and stimulate glucose uptake in skeletal muscle and adipose tissue.[9,11,15] More recently nutritional research on diabetes has increased and producing higher quality RCTs. It is therefore possible to appraise new evidence on the effectiveness of dietary intervention of cinnamon supplementation on the management of glycaemic control in T2DM. Providing a new emphasis on managing T2DM by using an effective dietary intervention might prove to be an attractive option given the dramatic increase in the incidence of T2DM. The aim of this review is to investigate whether cinnamon has a potential effect on glycaemic control in patients with T2DM.

2. Materials and methods

A systematic electronic literature search was carried out to identify and analyze all relevant literature providing information regarding the glucose lowering effect of cinnamon. All human intervention studies of RCTs of cinnamon and T2DM conducted from earliest possible date and August 2011 were included. Using these criteria, a search of the following databases was conducted:

- All EBM reviews –Cochrane Database of Systematic Reviews, ACP Journal Club, DARE, CCTR, CMR, HTA and NHSEED, Allied and Complementary Medicine
- EMBASE and Ovid MEDLINE(R)
- JAMA, BMJ, High wire Press and Lancet databases January 2000 to March 2011.

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Medical subject headings (MeSH) used for searching were 'type 2 diabetes', 'diabetes', 'cinnamon' 'glycaemic control' and 'blood glucose'. The literature search was confined to English language articles only. Fig. 1 provides the inclusion and exclusion criteria used in this review. A total of 322 articles were identified, of these 6 studies met the strict inclusion criteria for RCTs of cinnamon and T2DM. The methods and results sections of all 322 selected papers were reviewed independently by two authors. Out of these 322 articles, 303 were excluded either due to duplicates, *in vivo* animal studies, *in vitro* studies, not published in English language, did not have an abstract or author's name, or did not include a proper intervention method. From the remaining studies ($n = 19$) of *in vivo*

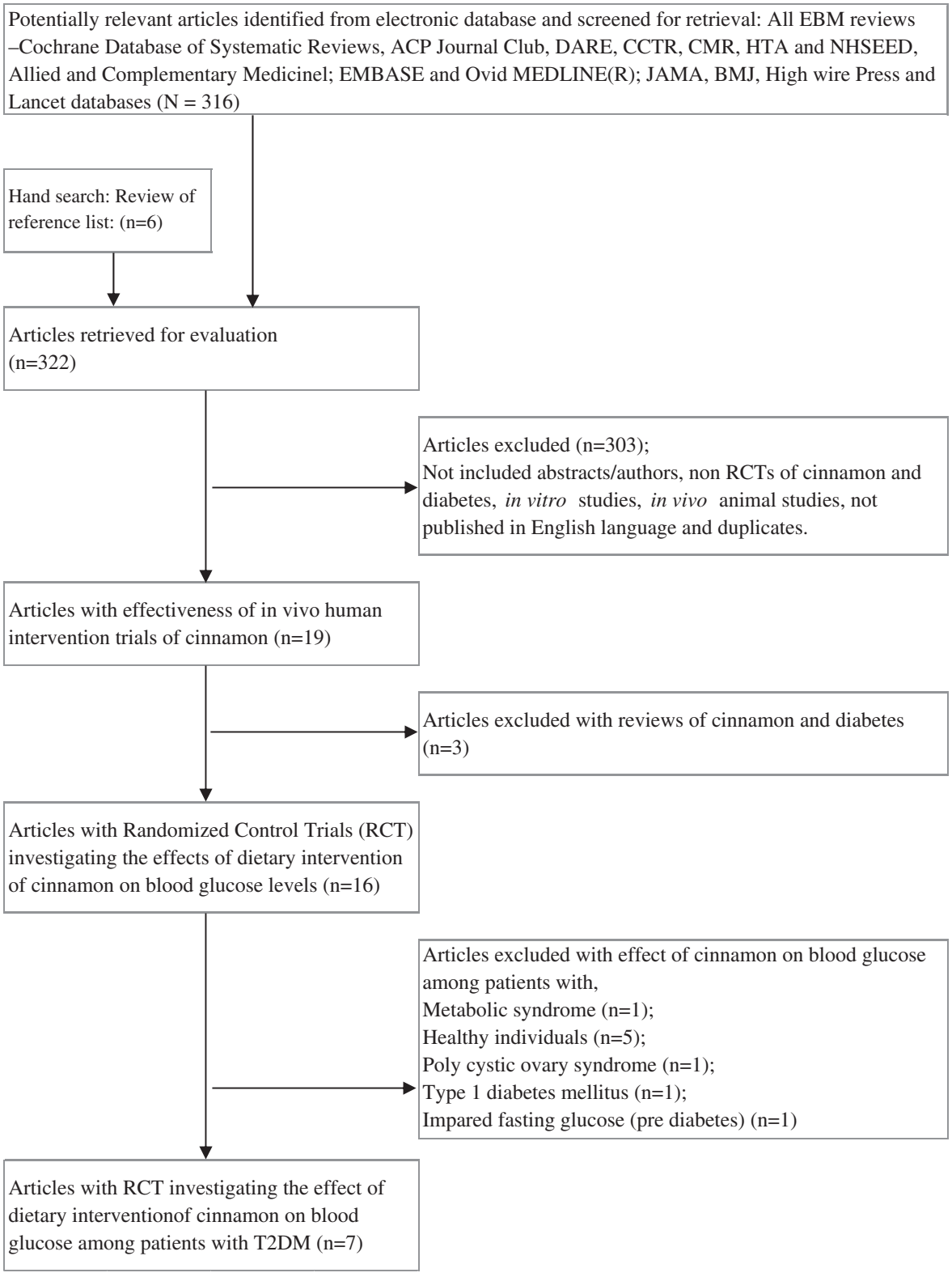

Fig. 1. Systematic review flow diagram; n = number of articles, RCT − randomized control trials.

human intervention trials of cinnamon, 12 studies were excluded; as they were duplicates,[16–18] studies with cinnamon and metabolic syndrome,[8] RCT for cinnamon and type 1 diabetes,[6] studies of cinnamon and healthy individuals,[7,19–22] cinnamon and polycystic ovary syndrome,[23] and cinnamon and impaired fasting glucose/pre-diabetes.[24] As a result, six RCTs were included for further review. These trials were analysed in detail for participant numbers, population characteristics, methodology, data analysis and results in order to explore whether cinnamon may lower blood glucose in T2DM.

Rev Man5.0 was used for meta-analysis (Cochrane collaboration). The mean change (baseline vs. Post intervention) was treated as a continues variable, outcomes were analysed by weighted mean difference, as difference between the means in the control (placebo) and treatment (cinnamon) groups (fixed effect model). Chi square test ($\alpha = 0.05$) was used for heterogeneity test, and weighted mean difference was also calculated (95% CI). The results of meta-analysis were explained by forest plot (Fig. 1). Statistical heterogeneity was addressed using the I^2 statistic.

3. Results

Since 2000 to date, six RCTs on the effects of cinnamon on Type 2 diabetes have been reported.[1,2,4,5,25,26] These 6 RCT's together considered a total of 375 patients who were followed up for a period of between 40 days and 4 months. In all seven RCT's the same cinnamon species of *Cinnamomum cassia* was administered and the dose ranged from 1 to 6 g grams per day. Five RCT's administered cinnamon powder,[1,4,5,25,26] and one RCT administered cinnamon extract.[2] The Baseline characteristics of the study participants, summary of methodologies used in RCTs and results of selected RCTs are given in Table 1, Table 2 and Table 3 respectively.

Khan et al,[1] reported the results of the first human intervention trial and demonstrated that addition of 1, 3 and 6 g of cinnamon led to significant decreases ($p < 0.05$) in FPG levels ranging from 18 to 29% after 40 days (Tables 1–3). The second RCT reported by Vanschoonbeek et al,[5] failed to detect any effect on plasma glucose level, HbA1c and insulin sensitivity in postmenopausal women with diabetes. There were no time and treatment interactions for whole body insulin sensitivity or oral glucose tolerance (Tables 1–3). A third publication from a German group of scientists[2] reported that daily intake of cinnamon extract showed significant reduction in FPG, but not HbA1c. The patients who had the highest FPG at the baseline of the trial experienced the greatest reductions (Tables 1–3).

Blevins et al,[4] (4th RCT), suggested that cinnamon cannot be generally recommended for the treatment of T2DM as it failed to improve HbA1c and FPG (Tables 1–3). A fifth RCT in USA conducted by Crawford (2009)[25] demonstrated that cinnamon could be useful for lowering serum HbA1c in type 2 diabetic patients. This study suggested that cinnamon significantly lowered HbA1c by 0.83% compared with usual care (0.37%) alone (Tables 1–3). In agreement with Crawford (2009),[25] we published the results of the first UK study recently,[26] and demonstrated that administration of 2 g of cinnamon showed significant reduction in HbA1c, but not FPG (Tables 1–3).

Improvement on HbA1c: One of the 6 RCTs,[1] did not report HbA1c were excluded. The remaining 5 RCTs were included, and the effect size for Meta analysis was weighted mean difference (WMD). Heterogeneity test showed ($P < 0.00001$), so the null hypothesis that all five RCTs were homogenous was rejected. The results suggested that cinnamon significantly improved the HbA1c compared to placebo [WMD = 0.09; 95% CI was 0.04–0.14, and did not include 0] (Fig. 2).

Improvement on FPG: One of the 6 RCTs,[25] did not report the effect of cinnamon on FPG and were excluded. Of the remaining 5 RCTs, the heterogeneity test showed ($P < 0.00001$), suggesting that all five RCTs were heterogeneous. The results suggested that

Table 1
The baseline characteristics of the participants in RCTs of cinnamon and T2DM.

Variable	Khan *et al 2003* $N = 60$		Mang *et al 2006* $N = 65$		Vanschoonbeek *et al* 2006 $N = 25$		Blevins *et al 2007* $N = 58$		Crawford 2009 $N = 109$		Akilen *et al* 2010 $N = 58$	
Treatment	Cinnamon	Placebo	Cinnamon	Placebo	Cinnamon	Placebo	Cinnamon	Placebo	Cinnamon	Placebo	Cinnamon	Placebo
N	$n = 30$	$n = 30$	$n = 33$	$n = 32$	$n = 13$	$n = 12$	$n = 28$	$n = 30$	$n = 55$	$n = 54$	$n = 30$	$n = 28$
Men %	50%	50%	63.6%	71.9%	0%		Not known		58%	59%	37%	54%
Women %	50%	50%	36.4%	28.1%	100%		Not known		42%	41%	63%	46%
Ethnicity	Ethnicity not noted but recruitment was from Pakistan		German		Ethnicity not noted but recruitment was from Maastricht, The Netherlands		68% Caucasian 16% Native American 7% African American 4% Hispanic 2% Asian 3% unknown		Recruitment from Florida, USA. White 76%, Black 14%, Latino 4% and Asian 6%.		Recruitment from London, UK; White 17%, Asian/Asian British 57% and Black or Black British 26%	
Time since diagnosis of diabetes (years)	7.10 ± 3.29	6.73 ± 2.32	7.1 ± 6.2	6.8 ± 4.7	7.6 ± 1.4	7.1 ± 1.6	–		–		5.8 ± 4.9	5.8 ± 4.2
Baseline FPG (mmol/L)[a]	12 ± 1.43	13.76 ± 1.40	9.26 ± 2.26	8.66 ± 1.47	8.37 ± 0.59	8.28 ± 0.33	7.38 ± 0.51	8.04 ± 0.57	–		8.82 ± 3.45	8.77 ± 2.59
Mean age (y)	52 ± 5.85	52 ± 6.87	62.8 ± 8.37	63.7 ± 7.17	62 ± 2	64 ± 2	63.6	58	60.5 ± 10.7	59.9 ± 9.2	54.9 ± 10.1	54.4 ± 12.5
Mean height (m)	–		1.72 ± 0.09	1.73 ± 0 07	1.67 ± 0.02	1.65 ± 0 02	–		–		–	
Mean weight (kg)	–		88.5 ± 19.1	89.9 ± 14.1	85.4 ± 3.6	82.2 ± 4.0	–		–		87.6 ± 17.5	87.5 ± 20.2
Mean BMI (kg/m^2)	–		29.6 ± 4.64	30.1 ± 5.22	30.7 ± 1.1	30.1 ± 1.4	32.5 ± 1.7	32.0 ± 1.5	31.9 ± 6.4	32.9 ± 6.4	33.4 ± 4.2	32.1 ± 8.3
Mean waist circumference (cm)	–		100.5 ± 15.0	102.7 ± 11.2	–		–		–		106.3 ± 11.8	105.0 ± 13.4

Data are means ± SD; N corresponds to the number of participants for which data was available upon completion of each study.
As no dose–response relationship was found between 1 g, 3 g and 6 g in the study by Khan et al. (2003).

Table 2
Summary of methodology used in studies of RCTs of cinnamon and T2DM.

Variable	Khan *et al 2003*	Mang *et al 2006*	Vanschoonbeek *et al 2006*	Blevins *et al 2007*	Crawford 2009	Akilen *et al* 2010
Study design	Single-blind randomized placebo controlled trial	Double-blind randomized placebo controlled trial	Double-blind, placebo controlled trial	Double-blind randomized placebo controlled trial	Randomized placebo controlled trial (no blind/open)	Double-blind randomized placebo controlled trial
Matched pairs	Matched for age	Not matched	Matched for age, BMI, years since diagnosis, baseline FBG and medication	Stratified by gender and randomized	Blocked randomization method	Not matched
Type of cinnamon used	*C. cassia* powder	*C. cassia* aqueous extract	*C. cassia* powder	*C. cassia* powder	*C. cassia powder*	*C. cassia* powder
Dose of cinnamon	1 g, 3 g and 6 g	3 g	1.5 g	1 g	1 g	2 g
Study duration	40 days intervention 20 days washout	4 months	6 weeks	3 months	90 days	12 weeks
Dietary control	Not mentioned other than participants consumed usual diet	Not mentioned	2 day food diary Pre-OGTT exercise control and standardized meal pre-OGTT	Diet monitored with a 3 day food diary	Not mentioned	Diet monitored with 3 days diet diary at baseline and post intervention
Diabetes medication taken by participants	All sulphonylureas	27.7% metformin, 12.3% sulphonylureas, 4.6% glinides, 1.5% glitazones, 30.8% combination therapy, 23.1% diet	Sulphonylureas with metformin ($n = 14$), metformin ($n = 3$), thiazolidinediones with/without metformin ($n = 6$), diet only ($n = 4$)	$^{3}/_{4}$ metformin, Over $^{1}/_{3}$ thiazolidinedione ½ hydroxymethylglutaryl-CoA reductase inhibitor. Diet only: 23% (cinnamon group), 9% placebo group	Not mentioned. However the dosage of diabetic medication not changed during the study period	Metformin ($n = 44$, 76%), Sulphonylureas ($n = 7$, 12%) and both Metformin and Sulphonylureas ($n = 7$, 12%)
Other medication	No other medications taken	49.2% anti-hypertensive medication 20% dyslipidaemia medication	None reported	55% cinnamon group and 48% placebo group took dyslipidaemia medication	Not mentioned	22% anti-hypertensive medication, 20% statins, 12% both statins and anti-hypertensive's

cinnamon significantly reduces the FPG compared to placebo in type 2 diabetic patients [WMD = 0.84; 95% CI was 0.66–1.02, and did not include 0] (Fig. 2).

4. Discussion

The baseline characteristics of the 6 RCTs including Gender, age, years since diagnosis of T2DM, baseline FPG or HbA1c and BMI were varied across all RCTs and there is a likelihood of heterogeneous factors contributing to the contrasting results. There were differences in ethnicity which may have also contributed to the heterogeneity of results. Furthermore, it remains unclear why potential changes in HbA1c were not measured by Khan et al,[1] because HbA1c remains the most important long term predictor of complications in both Type 1 and T2DM, the effect of any intervention on HbA1c is critical in determining its clinical usefulness.[6] The differences in patient outcome in Vanschoonbeek study[5] may be attributed to the inclusion of overweight postmenopausal women and using a range of oral anti diabetic drugs like metformins, sulfonylureas and thiazolidinediones. Furthermore, the duration of this study was 6 weeks and perhaps this shorter duration could contribute to a false negative result in HbA1c measurements. Because the lifespan of red blood cells is 120 days, it is believed that at least a minimum of 2–3 months is required to demonstrate an effect of cinnamon on HbA1c levels.[6]

Interestingly, recent interventions by Crawford (2009)[25] and Akilen et al,[26] has shown a clinically significant reduction in HbA1c due to cinnamon supplementation. This could be attributed to the fact that, studied only patients with poorly controlled type 2 diabetes (HbA1c $\geq$ 7%). Though, there are some major weaknesses in Crawford (2009)[25] study. Firstly, they used standard, off the shelf cinnamon capsules that patients would find at their local stores or on the internet, this may cause serious bias that different brand of cinnamon capsules might have different purity and active compounds. Secondly, they did not use a standard placebo group or blinding, but instead they used a group of patients received standard care as control.

Over the past few years different clinical trials have demonstrated conflicting results related to the glucose lowering effects of cinnamon.[4,26] Current guidelines for the treatment of diabetes recommend maintaining normal or near normal glycaemia at an HbA1c level of <7%.[27,28] This suggests that in well controlled type 2 diabetic patients (HbA1c of <7%) the effects of cinnamon on HbA1c may be minimum. This might be the reason why Crawford (2009)[25] and Akilen et al,[26] studies demonstrated a significant reduction in HbA1c in the cinnamon group, as their baseline HbA1c was approximately more than 8.2% (Fig. 3). Other RCTs[2,4,5] did not demonstrated a significant reduction in HbA1c in the cinnamon group, as their baseline HbA1c was well controlled and ranged approximately from 6.8 to 7.1% (Fig. 3). Therefore, we suspect that it is most likely that the therapeutic dose of cinnamon may depend upon the subjects' baseline HbA1c rather than there being a significant dose-dependent effect (Fig. 3). In contrast, studies conducted with pre diabetes men and women[8] reported an 8.4% reduction in FPG in subjects with mean baseline FPG of 6.46 mmol/l and treated with 10 g of cinnamon. This illustrates that even higher cinnamon doses may bring about a significant reduction in blood glucose ($P < 0.01$) in subjects with lower baseline FPG, and suggests a possible relationship between baseline FPG or HbA1c, dose of cinnamon and % reduction in glycaemic levels which might be tested in future studies. However, our main question is the tolerability and compliance of high dose of cinnamon along with anti diabetic medication and these needs to be studied further. Furthermore, the effects of cinnamon on blood glucose levels differ by population (ethnicity), their habitual diet, BMI, baseline glucose levels and dose of cinnamon,[4] and further studies are necessary to address these facts.

Cinnamon also reported to delay gastric emptying,[20] this may reduce postprandial glucose (PPG) and HbA1c levels in type 2 diabetic patients. It has emerged that at a certain dose, cinnamon is able to lower blood glucose, but whether there is a lasting therapeutic

Table 3
Results of RCTs of cinnamon and T2DM; FPG, HbA1c and serum lipids at base line and after intervention period.

Intervention		Fasting plasma glucose (mmol/l)		Fasting serum lipid profiles (mmol/l)								HbAlc (%)	
				Total cholesterol		HDL cholesterol		LDL cholesterol		Triglycerides			
		Baseline mean ± SD	Post intervention mean ± SD	Base line mean ± SD	Post intervention mean ± SD	Base line mean ± SD	Post intervention mean ± SD	Base line mean ± SD	Post intervention mean ± SD	Base line mean ± SD	Post intervention mean ± SD	Base line mean ± SD	Post intervention mean ± SD
Khan *et al.* (2003)	Placebo (1 g + 3 g + 6 g)	13.77 ± 1.13	13.97 ± 1.23	4.97 ± 0.33	5.09 ± 0.35	—	—	2.63 ± 0.26	2.71 ± 0.27	2.41 ± 0.32	2.47 ± 0.33	—	—
	Cinnamon (1 g + 3 g + 6 g)	12.0 ± 1.43	9.1 ± 1.40[b]	5.24 ± 0.25	4.35 ± 0.26[b]	—	—	2.77 ± 0.16	2.37 ± 0.15[b]	2.49 ± 0.35	1.83 ± 0.29[b]	—	—
Mang *et al.* (2006)	Placebo	8.66 ± 1.47	8.31 ± 1.62	5.25 ± 0.79	5.17 ± 0.75	1.34 ± 0.31	1.33 ± 0.30	3.59 ± 0.69	3.60 ± 0.64	1.66 ± 0.78	1.73 ± 0.70	6.71 ± 0.73	6.68 ± 0.70
	Cinnamon	9.26 ± 2.26	8.15 ± 1.65[†]	5.38 ± 0.89	5.29 ± 0.89	1.44 ± 0.49	1.46 ± 0.52	3.48 ± 0.71	3.52 ± 0.75	1.96 ± 1.65	1.81 ± 1.58	6.86 ± 1.00	6.83 + 0.83
Vanschoonbeek *et al.* (2006)	Placebo	8.28 ± 0.33	8.07 ± 0.36	4.91 ± 0.30	4.66 ± 0.31	1.29 ± 0.11	1.29 ± 0.09	3.04 ± 0.25	2.77 ± 0.24	1.28 ± 0.14	1.32 ± 0.18	7.1 ± 0.2	7.2 ± 0.2
	Cinnamon	8.37 ± 0.64	7.91 ± 0.71	5.05 ± 0.15	4.81 ± 0.19	1.42 ± 0.09	1.41 ± 0.09	3.06 ± 0.15	2.85 ± 0.16	1.25 ± 0.17	1.20 ± 0.13	7.4 ± 0.3	7.5 ± 0.3
Blevins *et al.* (2007)	Placebo[a]	8.04	8.02	4.56	4.63	2.2	—	2.72	2.79	1.76	1.58	7.1	7.2
	Cinnamon[a]	7.38	6.84	4.4	4.38	1.13	1.11	2.62	2.67	1.49	1.39	7.2	7.4
Crawford (2009)	Placebo	—	—	—	—	—	—	—	—	—	—	8.28 ± 1.3	7.91 ± 1.5
	Cinnamon	—	—	—	—	—	—	—	—	—	—	8.47 ± 1.8	7.64 ± 1.7[b]
Akiken *et al.* (2010)	Placebo	8.77 ± 2.59	8.74 ± 3.11	4.10 ± 0.87	4.25 ± 1.05	1.16 ± 0.19	1.14 ± 0.21	2.27 ± 0.75	2.34 ± 0.78	1.48 ± 1.04	1.66 ± 1.16	8.55 ± 1.82	8.68 ± 1.83
	Cinnamon	8.82 ± 3.45	8.04 ± 3.10[c]	4.31 ± 1.07	4.34 ± 1.09	1.18 ± 0.29	0.21 ± 0.31	2.47 ± 0.96	2.52 ± 1.00	1.65 ± 0.93	1.60 ± 0.83	8.22 ± 1.16	7.86 ± 1.42[b]

Data presented as mean plusmn SD; __ indicates data not measured.
[a] Shows data presented as only mean.
[b] Shows there is a significant difference at post intervention in the cinnamon group compared to placebo group.
[c] Shows the post intervention fasting plasma glucose levels were significantly lower compared to baseline in cinnamon group.

effect upon insulin resistance and sensitivity, with promise to improve the pathophysiology of diabetes requires further long term investigation. If there is an association between cinnamon efficacy and baseline FPG or HbA1c levels, or if cellular cinnamon-activated glucose uptake is limited in the presence of insulin, it may be hypothesized that anti-hyperglycaemic benefits are through delayed gastric emptying[20] and reduced glucose absorption[14] in subjects with lower blood glucose levels or less insulin resistance.

Understanding the blood glucose lowering mechanism of cinnamon is paramount important. Cao et al,[11] reported that purified cinnamon extracts (CE) and cinnamon polyphenols (CP) increased insulin receptor (IRβ) proteins and glucose transporter (GLUT4) proteins in 3T3-L1 adipocytes. These proteins are involved in the insulin signalling transduction pathway that functions in insulin receptor substrate activation, anti-inflammatory responses and insulin regulated glucose transportation respectively.[11] The 3T3-L1 cells are routinely used in signalling studies and are thought to demonstrate all of the features of adipocytes.[13] It is well established that insulin promotes the translocation of GLUT4 from the intracellular compartment to the plasma membrane.[29,30] Therefore the increase of GLUT4 protein by CP demonstrates a positive effect elicited by these compounds on the long term regulation of glucose transport and CP mimics insulin like activity. Insulin resistance has been attributed to decrease glucose transporter (GLUT4) activity, caused by inhibited insulin receptor substrate (IRS) tyrosine phosphorylation.[11,29,30] Methylhydroxychalcone polymer (MHCP) in cinnamon mimics insulin like activity.[13] MHCP stimulates the insulin receptor substrate (IRS) proteins-phosphoinositide 3-kinase (PI-3-K) pathway and up regulates glucose uptake and glycogen synthesis activity in 3T3-L1 adipocytes and down regulates glycogen synthase kinase-3 (GSK-3β) activity. GSK 3β is involved in phosphorylation and inactivation of glycogen synthase.[11,13,29]

Generally, cinnamon like dietary supplements may have greater use in countries where people believe orthodox treatment alone may less effective in controlling hyperglycaemia or as an initial treatment for newly diagnosed diabetics As significant results have been limited to specific and relatively small patient populations in this review, larger studies are required to detect statistically significant reductions in FPG or HbA1c following cinnamon supplementation, particularly within a Westernized diabetic population where blood glucose levels are tend to be lower.[4] We suspect that where blood glucose was reduced by cinnamon, this was not through increased insulin secretion but via gastrointestinal mechanisms through delayed gastric emptying[20] and glucose absorption, and through improved cellular uptake and glucose utilization, and that factor such as timing of cinnamon supplementation with meals may have a significant effect upon cinnamon's glucose lowering ability.

It's not clear whether both cinnamon extract and powder are equally effective, though the level of bioactive ingredients in the preparation is the important factor. It is hypothesized that studies reporting insignificant results did not supplement with a sufficient amount of the bioactive cinnamon components required to affect the associated baseline FPG or HbA1c. Based upon more recent studies, it appears that clarification of the bioactive components is progressing,[8,26] and continued analysis to determine the most active constituents of cinnamon may increase the likelihood of positive results in future studies. Although *Cinnamomum cassia* species was administered in all RCTs in this review, the precise consideration of purity of cinnamon, chemical composition or active ingredients and potency of derivatives of cinnamon may be influenced by the age of the cinnamon plant, the geographical location, the season of harvest, the method of drying and crude preparation. Therefore, a standardized method could eliminate this bias in future studies.

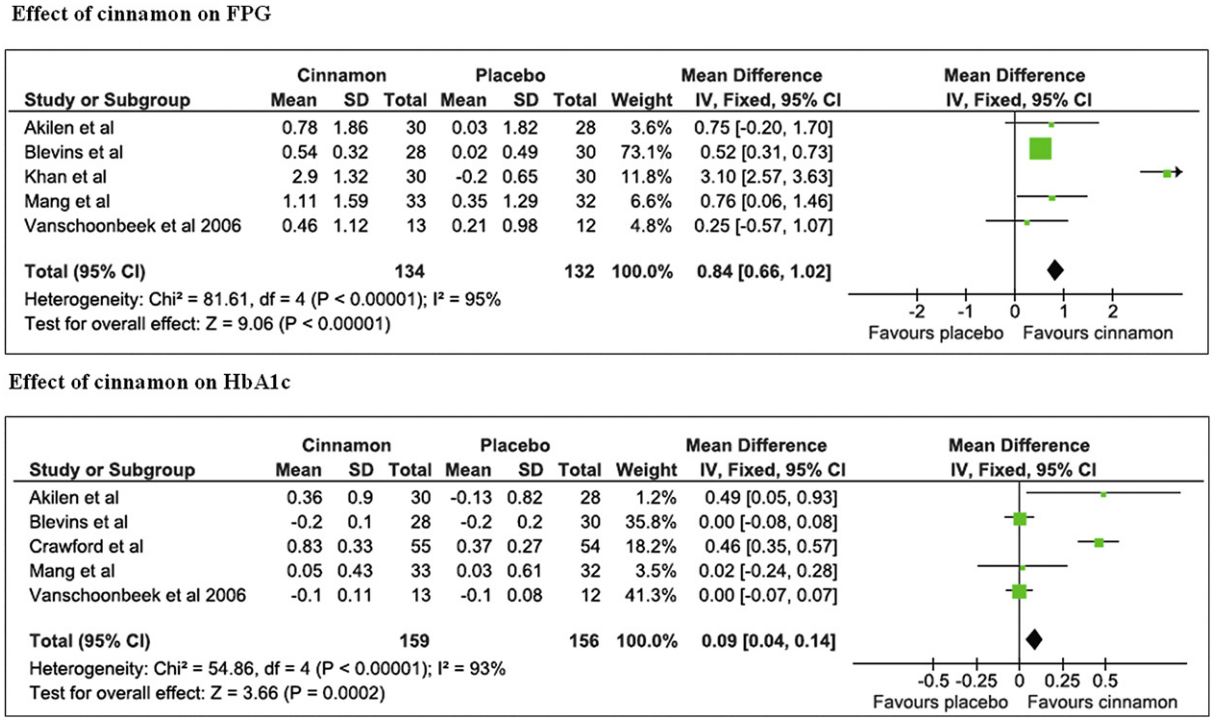

Fig. 2. Forest plot; Effect of cinnamon on fasting plasma glucose (FPG) and Glycated Haemoglobin (HbA1c).

It is hoped that the methodology illustrates no selection bias in this review, although the available literature search was confined to English language articles. Variations in population characteristics and methodology between cinnamon and diabetes (human trials) make comparisons problematic; therefore the diabetic studies are reviewed in depth to enable analysis of similar RCTs of cinnamon and T2DM with greater external validity.

If our findings are to be accepted, we need to address some limitations of the analysis. This Meta analysis only includes 6 RCTs (may be underpowered), the sample size is small and unpublished RCTs were not included, and these factors may cause bias. We have done our utmost to include all published studies to avoid selection bias. Except from one RCT,[2] none reported the randomization methods and allocation concealments clearly. Furthermore, this

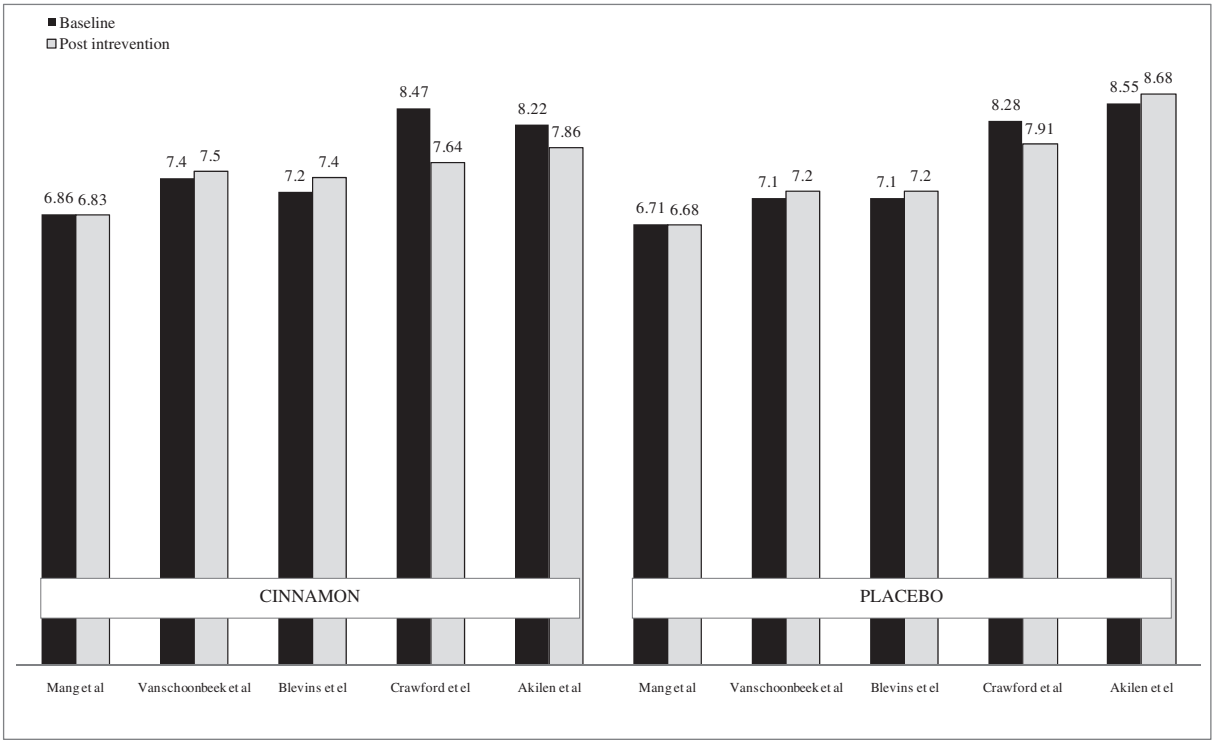

Fig. 3. RCTs reporting the effect of cinnamon on HbA1c; data presented as changes in HbA1c (%) at baseline and post intervention in cinnamon and placebo groups.

analysis only includes the short term interventions (<4 months) of 1 g, 1.5 g, 2 g, 3 g or 6 g of cinnamon and placebo controlled trials, and this requires further long term trials with different cinnamon dose levels. At present, cinnamon dosage, duration of RCTs, lack of verification of double blinding, differences in ethnicity, heterogeneous group of patients and concurrent glucose lowering medications are not consistent among the selected trials, which could bring many difficulties in data analysis.

Improvements in glycaemic control may also lower the risk for cardiovascular disease in persons with diabetes. As cardiovascular disease is the most common cause of death in persons with diabetes mellitus, additional long term trials are needed to decode the independent effect of cinnamon on HbA1c and glycaemic control. To date, randomized, controlled trials have not answered one of the most important questions: What are the long term tolerability, sustainability and safety of cinnamon and glycaemic control? However, our meta-analysis demonstrated that short term (<4 months) effects of the use of cinnamon on glycaemic control (both HbA1c and FPG) looks promising.

In summary, the majority of the studies investigating the effect of cinnamon on glycaemic control in people with T2DM showed no potential therapeutic benefits. However, considering the available information from the systematic review, cinnamon may be a viable addition to conventional diabetes management for patients with poorly controlled T2DM with an HbA1c more than 7%.

Statement of authorship

The authors declare that they have no conflict of interest. All my coauthors contributed to reviewing the manuscript and corrections, commenting and drafting tables and figures. Dr. Devasenan Devendra helped in statistical analysis of meta-analysis. Prof. Nicola Robinson and Dr Amalia Tsiami helped with systematic reviews and finding papers based on inclusion criteria.

Conflicts of interest

None declared.

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