2020

Lowering HbA1c Levels in Type 2 Diabetics with Cinnamon Supplementation

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PAL 5600-5680 Elective: Capstone to Publication

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October 16, 2020

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Introduction

Cinnamon has been evaluated in clinical studies, including RCTS, for its glycemic-lowering effects. The studies have been small and produced conflicting results. The objective of this paper is to provide an updated systematic review that evaluates the relationship between cinnamon supplementation and A1c levels among individuals with Type 2 diabetes mellitus (T2DM).

T2DM, the most common type of diabetes, is a complex metabolic disease characterized by high levels of blood glucose. In T2DM, there is an inability of cells to respond normally to insulin or an inadequate production of insulin to maintain glucose control. T2DM is a global health problem with more than 500 million prevalent cases worldwide, and the incidence is increasing around the world[1]. Those with T2DM have an increased risk for several serious health problems, including cardiovascular disease, kidney failure, blindness, limb amputation, depression, and cognitive decline[3]. It is the seventh leading cause of death among adults older than 45 years of age in the United States [2]. While there is no cure for diabetes, lifestyle modifications, drug therapy, and dietary changes are mainstays in management. Medication therapy however poses a significant economic burden, with medical costs being twice as high compared to those without diabetes[2]. Other cost-effective strategies that improve glycemic control are worth investigating.

Research has shown that several dietary supplements have similar effects on insulin action. Carnation, walnut, green tea, and the spice cinnamon are examples. Cinnamon, because it is among the bioactive of these products, has garnered interest for use in hyperglycemic conditions, such as T2DM. It has a rich history as a traditional remedy for several ailments and has become a natural supplement of interest. Consumption of cinnamon is associated with statistically significant reductions in fasting plasma glucose, total cholesterol, LDL-C, and triglycerides and an increase in HDL-C levels. The review found no significant effects on A1c levels. In a 2017 systematic review of cinnamon supplementation on blood lipid levels, significant reductions in blood TGs and total cholesterol were observed without significant effects on HDL-C or LDL-C. It has been suggested that cinnamon's insulin-potentiating effects can be attributed to its active component cinnamaldehyde[6]. Such hypoglycemic effects have been investigated in in-vitro and in-vivo trials and demonstrated that cinnamaldehyde enhances glucose uptake by activating insulin receptor kinase activity, glycogen synthesis, and autophosphorylation of insulin receptors[7].

Several clinical trials have been conducted to explore cinnamon's efficacy on glucose levels; however, they report conflicting results[8-13]. Consumption of cinnamon doses between 1 to 6 gram/daily reported reductions in fasting blood glucose (FBG) and in A1c[8,10,12,15]. However, other studies showed that consumption of 1 to 1.2 gram/daily was associated with increases in FBG and A1c[11]. A recent meta-analysis did not reveal any statistically significant changes in A1c or fasting blood glucose[14]. Identifying safe, effective, low cost treatments for hyperglycemia in T2DM remains important to help patients on a budget to reach glucose targets.

Methods

A systematic review of published studies reporting the effects on blood glucose of cinnamon supplementation was conducted following the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines. A literature search was conducted in the following databases: PubMed and CINHAL. A search strategy was performed to include the following combination of keywords: HbA1c, hemoglobin A1c, cinnamon, *cinnamonum cassia*, type 2 diabetes, and diabetes mellitus type 2. Trials that were selected in this systematic review were randomized control trials (RCTs) that evaluated the use of oral cinnamon supplementation and reported data on hemoglobin A1c endpoints. Studies that included other endpoint parameters, such as lipids and fasting plasma glucose were also included. The data specific to HbA1c was then extracted. Study participants were limited to adult subjects. The type of cinnamon intervention was limited to the species *cinnamomum cassia.* Type 2 diabetics, excluding those taking insulin, of either gender or age were included. The formulation and dosage of cinnamon intervention was not restricted. The search included countries outside of the United States.

Results

A total of 5 RCTs met the inclusion criteria and were included in the systematic review. These 5 RCTs together considered a total of 313 patients who followed the study for a range of 40 to 90 days. All the RCTs administered cinnamon powder, specifically *cinnamomum cassia*, with the dose ranging from 1 to 6 grams per day. The characteristics of the study participants, study characteristics used in RCTs, and results of the selected studies are reported in Table 1, Table 2, and Table 3, respectively.

The results of the first human RCT reported that the addition of 1, 3, or 6 g of cinnamon led to significant decreases in serum glucose levels after 40 days. All three doses of cinnamon

reduced the mean fasting plasma glucose (FPG) ranging from 18 to 29% (Table 3). The response to all three levels of cinnamon was similar suggesting that there is no evident dose response. The second RCT failed to detect any significant effect in A1c or serum glucose levels after addition of 1 g of cinnamon daily for 90 days (Table 3). The third RCT reported that a daily intake of 2 g of cinnamon for 12 weeks showed significant reduction in A1c. The fourth RCT suggested that intake of 1.5 g of cinnamon per day was associated with reduction in A1c levels (Table 3). The fifth RCT was unable to recommend cinnamon for the treatment of T2DM as it failed to improve A1c levels (Table 3).

Table 1. Characteristics of Participants in included RCTs of systematic review

Variable	**Khan et al.**	**Blevins et al.**	**Akilen et al.**	**Tangvarasittichai et al.**	**Talaei et al.**
Treatment	**Placebo/Cinnamon**	**Placebo/Cinnamon**	**Placebo/Cinnamon**	**Placebo/Cinnamon**	**Placebo/Cinnamon**
N	30 30	28 29	28 30	50 49	19 20
Gender	M&W	M&W	M&W	M&W	M&W
Time since diagnosis of DM (y)	6.73 ± 2.32 7.10 ± 3.29	N/A	5.84 ± 4.23 5.76 ± 4.93	8.14 ± 2.75 9.04 ± 4.76	N/A
Mean Age (y)	52.0 ± 6.87 52.0 ± 5.85	58.0 63.6	54.43 ± 12.53 54.90 ± 10.14	56.9 ± 1.2 57.2 ± 1.11	56.29 ± 9.49 57.61 ± 8.70
Mean BMI	N/A	32.0 ± 1.5 32.5 ± 1.7	32.13 ± 8.31 33.36 ± 4.20	24.7 24.7	29.02 ± 5.53 26.41± 3.06

Table 2. Summary of methodology in included RCTs of systematic review

Study	Year	Location	Study Type	Type of Cinnamon (Treatment)	Dosage of Cinnamon (grams)	Type of Placebo (Control)	Duration (day)
Khan et al.	2003	Pakistan	RCT, double-blind	C. cassia	1, 3, 6	Unknown	40
Blevins et al.	2007	USA	RCT, placebo-controlled, double-blind	C. cassia	1	Wheat flour	90
Akilen et al.	2010	England	RCT, double-blind	C. cassia	2	Starch	84
Tangvarasittichai et al.	2015	Thailand	RCT, double-blind	C. cassia	1.5	Unknown	60
Talaei et al.	2017	Iran	RCT, double-blind	C. cassia	3	Microcrystalline cellulose	56

Table 3. Results of included RCTs in systematic review

Study	Baseline a1c (Treatment	Post-trial a1c (treatment)	Baseline a1c (Control)	Post-trial a1c (control)
Khan et al. 2003	8.9 ± 2.7	7.1 ± 2.6	12.2 ± 2.3	9.4 ± 2.3
Blevins et al. 2007	7.2 ± 0.3	7.4 ± 0.4	7.1 ± 0.2	7.2 ± 0.4
Akilen et al.	8.2 ± 1.1	7.86 ± 1.42	8.55 ± 1.8	8.68 ± 1.83

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Tangvarasittichai et al. 2015	8.0	7.6	7.7	8.0
Talaei et al. 2017	10.04 ± 1.30	10.11 ± 1.49	10.31 ± 1.86	10.30 1.70

Discussion

In this systematic review of studies assessing glycemic control, consumption of cinnamon, specifically the *cinnamonum cassi*a formulation, of at least 1 gram daily may reduce HbA1c in T2DM patients. When comparing changes in serum glucose to the dosage of supplementation given, as in Khan[12], a decrease in serum glucose was observed across all three groups. This suggests that there is no significant dose response associated with degree of glycemic control. In general, cinnamon was well-tolerated, and no side effects were documented. A systematic review by Namazi et al[17] showed that cinnamon can reduce levels of glucose in serum with no changes in other glycemic parameters. However, it was stated that the studies' high heterogeneity should be interpreted lightly.

A limitation of this analysis is in the quality of the interventions performed. Multiple characteristics of the 5 RCTs including gender, age, ethnicity, years of diagnosis of T2DM, baseline HbA1c, and baseline BMI were all varied suggesting a degree of heterogeneity contributing to the results. Other factors such as diet at baseline or during the experimental period were not reported which may have also contributed to the heterogeneity of the results. Another limitation is the lack of documentation of compliance to supplementation by pill counts was only achieved by one study.

To conclude, the data suggests that cinnamon supplementation, when used as an adjunct to diabetic management, may provide some lowering effects on HbA1c. However, it is not recommended as a replacement for hypoglycemic medications, exercise, or proper diet. Given the increasing prevalence of T2DM and the economics of our pharmaceutical system, it is within reason to consider safe adjuncts, especially if it can help improve glycemic control. For diabetics on a tight budget, cinnamon may serve as a cost-effective adjunct to standard therapy to help patients reach glucose targets and attain their goal HbA1c level.

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