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Cinnamon extract improves fasting blood glucose and glycosylated hemoglobin level in Chinese patients with type 2 diabetes

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ARTICLE INFO

Article history:
Received 19 November 2011
Revised 9 April 2012
Accepted 14 May 2012

Keywords:
Cinnamon
Type 2 diabetes
Fasting blood glucose
HbA_{1c}
Blood lipids
Human

ABSTRACT

For thousands of years, cinnamon has been used as a traditional treatment in China. However, there are no studies to date that investigate whether cinnamon supplements are able to aid in the treatment of type 2 diabetes in Chinese subjects. We hypothesized cinnamon should be effective in improving blood glucose control in Chinese patients with type 2 diabetes. To address this hypothesis, we performed a randomized, double-blinded clinical study to analyze the effect of cinnamon extract on glycosylated hemoglobin A_{1c} and fasting blood glucose levels in Chinese patients with type 2 diabetes. A total of 66 patients with type 2 diabetes were recruited and randomly divided into 3 groups: placebo and low-dose and high-dose supplementation with cinnamon extract at 120 and 360 mg/d, respectively. Patients in all 3 groups took gliclazide during the entire 3 months of the study. Both hemoglobin A_{1c} and fasting blood glucose levels were significantly reduced in patients in the low- and high-dose groups, whereas they were not changed in the placebo group. The blood triglyceride levels were also significantly reduced in the low-dose group. The blood levels of total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and liver transaminase remained unchanged in the 3 groups. In conclusion, our study indicates that cinnamon supplementation is able to significantly improve blood glucose control in Chinese patients with type 2 diabetes.

1. Introduction

The number of patients with type 2 diabetes is rapidly increasing throughout the world, rising from approximately 171 million in 2000 to a projected 366 million in 2030. In China, it was estimated that approximately 90 million people were having type 2 diabetes with over 150 million people being prediabetic in 2010 [1]. Because diabetes is a prolonged chronic metabolic disease that causes many other complications, such as cardiovascular diseases, expenses spent on its treatment have placed a huge burden upon the economy and health systems worldwide. Therefore, developing an

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; FBG, fasting blood glucose; HbA_{1c}, glycosylated hemoglobin A_{1c}; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

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doi:10.1016/j.nutres.2012.05.003

economical, efficient, and simple strategy to prevent and treat diabetes is a major challenge.

Cinnamon, a plant of the laurel family Lauraceae, has been used in China for thousands of years to treat many diseases, such as the "thirsty disease," which was an old term for diabetes in China before the term *diabetes mellitus* was coined in modern medicine. Recent studies demonstrated that cinnamon is effective in improving blood glucose control in patients with type 2 diabetes. In 2003, Khan et al [2] first reported that cinnamon was able to reduce the fasting blood glucose (FBG) level and improve hyperlipidemia in human patients with type 2 diabetes. Since then, a series of clinical studies have been conducted in a variety of countries, not including China, and revealed the potential effectiveness of cinnamon or cinnamon extract in improving blood glucose control in patients with type 2 diabetes in different countries. In Germany in 2006, Mang et al [3] reported that cinnamon extract could reduce FBG level in type 2 diabetic patients. This same year, Ziegenfuss et al [4] reported that cinnamon extract could decrease FBG among patients of metabolic syndrome in the United States. A randomized study performed in 2009 in the United States indicated that cinnamon was able to improve hemoglobin A_{1c} (HbA_{1c}) levels in type 2 diabetic patients [5]. Similarly, a study performed in the United Kingdom demonstrated that cinnamon was capable of reducing the level of HbA_{1c} in type 2 diabetic patients [6]. However, a few studies have revealed that cinnamon has no effect in improving blood glucose control. In 2007, Blevins et al [7] from the United States reported that cinnamon could not alter the levels of FBG and HbA_{1c} in type 2 diabetic patients. Two other studies comparing healthy subjects and those with impaired FBG demonstrated that cinnamon had no effect in decreasing FBG level [8,9]. These conflicting outcomes might be due to the differences in prescribed antidiabetic medication, the type of cinnamon administered, the duration of the study, and the studied population. In addition, only a few of these studies used HbA_{1c} to monitor the blood glucose homeostasis, and HbA_{1c} is better than FBG as a parameter in gauging the long-term change of hyperglycemia.

Therefore, based on the proposed history of cinnamon bark being used to treat diabetes, we hypothesized that cinnamon would improve blood glucose in patients with type 2 diabetes. To test this hypothesis, we performed a randomized, double-blind clinical study to analyze the effect of cinnamon extract on the levels of FBG and HbA_{1c} in Chinese patients with type 2 diabetes. To minimize the potential confounding effects of different medications, all subjects took the same kind of prescribed antidiabetic medication.

2. Methods and materials

2.1. Subjects

All subjects were outpatients from Xuhui Central Hospital, Shanghai. Sixty-nine patients (including 44 women and 25 men with age >48 years) with type 2 diabetes and who had levels of HbA_{1c} greater than 7.0% and FBG greater than 8.0 mmol/L were randomly divided into 3 groups: placebo, low-dose, and high-dose groups. The low- and high-dose groups took either 2 or 6 cinnamon tablets, respectively, with each tablet containing 60 mg of cinnamon extract. The placebo group took 2 control tablets a day with the same size, shape, and color as the cinnamon-containing tablet. The cinnamon or placebo tablets were taken just before breakfast. All of the participating patients were taking gliclazide (Diamicron, 30 mg per tablet) during the study period. All patients were informed of the study and signed the consent form. The study was approved by the ethics committee of Xuhui Central Hospital. The subjects received weekly telephone calls from the hospital's medical staff to communicate about their medication. During the 3-month study period (on average of 91 days), 3 subjects withdrew from the study. A total of 66 subjects successfully completed the study. This was a double-blinded study with neither the physician nor the patient knowing whether the tablet contained cinnamon extract.

2.2. Cinnamon extract

The cinnamon tablets used in the study were developed by Shanghai Yitian Bio-Scientific Co, Ltd (Shanghai, China), and produced by Shanghai Jinsijia Health-Care Food Co, Ltd (Shanghai, China), batch number 20090901. Cinnamon extract was prepared from the bark of Chinese Cinnamomum aromaticum, which is produced in Guangxi province using methods previously reported [10]. Each cinnamon tablet contains 60 mg of cinnamon extract isolated from 2.4 g of cinnamon. The cinnamon tablet from Shanghai Yitian Bio-Scientific Co, Ltd, was approved for human use in 2011 by the State Food and Drug Administration of China with the approval number G20110080.

2.3. Analyses of blood samples

After fasting for at least 10 hours, blood samples were obtained from the subjects in the morning. Hemoglobin A_{1c} was measured by high-performance liquid chromatography. Fasting blood glucose concentration in the serum was determined by the hexokinase method. Total cholesterol, triglyceride, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, aspartic transaminase, and glutamic transaminase of the serum were analyzed with an automatic biochemical analyzer of Siemens ADVIAII400 model (Tarrytown, NY). The serum samples were centrifuged for 10 minutes at a speed of 3000 rpm before the analyses.

2.4. Statistical analyses

The software R 2.11.0 (from http://www.R-project.org) was used for statistical analyses with our data. All of the measurements are expressed in means ± SD. The paired *t* test was used to compare all blood parameters between pre- and posttreatment, as shown in Table 1. Student *t* test was used to compare between different experimental groups. A value of 5% was used as the α error to define the significance.

Table 1 – Parameters of the patients at baseline and posttreatment

	Placebo	Low dose (120 mg/d)	High dose (360 mg/d)
Age	60 ± 5.9	62.4 ± 7.9	58.9 ± 6.4
No.	20	23	23
Sex			
Male	8	8	9
Female	12	15	14
Gliclazide tablet/d	2.25 ± 0.44	2.26 ± 0.45	2.22 ± 0.42
HbA_{1c} (%)			
Pre	8.93 ± 1.14	8.90 ± 1.24	8.92 ± 1.35
Post	8.93 ± 1.04	8.23 ± 0.99	8.00 ± 1.00
Δ (95% CI)	0.00 (−0.61 to 0.61)	−0.67 (−1.09 to −0.25) **	−0.93 (−1.38 to −0.47) **
Fasting glucose (mmol/L)			
Pre	8.92 ± 1.21	9.00 ± 1.23	11.21 ± 2.21
Post	8.71 ± 2.01	7.99 ± 1.05	9.59 ± 1.66
Δ (95% CI)	−0.22 (−1.34 to 0.91)	−1.02 (−1.61 to −0.42) **	−1.62 (−2.32 to −0.93) **
Triglyceride (mmol/L)			
Pre	1.68 ± 0.67	2.93 ± 2.08	1.74 ± 1.05
Post	1.82 ± 0.88	2.15 ± 1.19	1.84 ± 1.16
Δ (95% CI)	0.15 (−0.19 to 0.49)	−0.78 (−1.32 to −0.23) **	0.10 (−0.20 to 0.41)
Total cholesterol (mmol/L)			
Pre	4.60 ± 1.04	4.96 ± 1.35	5.18 ± 0.78
Post	4.83 ± 1.11	4.63 ± 1.09	4.91 ± 0.85
Δ (95% CI)	0.23 (0.01 to 0.45) *	−0.33 (−0.70 to 0.04)	−0.27 (−0.61 to 0.07)
HDL-cholesterol (mmol/L)			
Pre	1.43 ± 0.50	1.23 ± 0.36	1.56 ± 0.49
Post	1.39 ± 0.48	1.23 ± 0.28	1.59 ± 0.85
Δ (95% CI)	−0.04 (−0.17 to 0.09)	0.00 (−0.08 to 0.08)	0.03 (−0.34 to 0.40)
LDL-cholesterol (mmol/L)			
Pre	2.70 ± 0.86	2.65 ± 0.76	3.14 ± 0.60
Post	2.78 ± 0.68	2.66 ± 0.72	3.01 ± 0.54
Δ (95% CI)	0.08(−0.10 to 0.26)	0.01 (−0.23 to 0.25)	−0.13 (−0.37 to 0.11)
AST (U/L)			
Pre	21.72 ± 6.03	21.81 ± 6.16	25.27 ± 11.16
Post	22.83 ± 7.34	21.00 ± 6.64	21.05 ± 4.58
Δ (95% CI)	1.11 (−1.74 to 3.96)	−0.81 (−3.43 to 1.81)	−4.23 (−9.14 to 0.69)
ALT (U/L)			
Pre	17.61 ± 7.06	20.45 ± 7.56	25.91 ± 8.55
Post	23.72 ± 11.97	19.00 ± 8.65	23.18 ± 11.50
Δ (95% CI)	6.11 (1.05 to 11.17) *	−1.45 (−4.42 to 1.52)	−2.73 (−7.35 to 1.90)

All the data are presented as means ± SD. Δ (95% CI) indicates that the difference between pretreatment and posttreatment and 95% confidence interval. CI indicates confidence interval; Pre, pretreatment; Post, posttreatment.
* $P < .05$ between pre- and posttreatment as analyzed by paired t test.
** $P < .01$ between pre- and posttreatment as analyzed by paired t test.

3. Results

3.1. Characteristics of the subject

To explore the effect of cinnamon on blood glucose control, we performed a randomized, double-blind clinical study in Chinese patients with type 2 diabetes. A total of 66 patients completed the study. The inclusion criteria were that the subjects are type 2 diabetic patients and that they took only gliclazide as the prescribed medication to treat their diabetes. This was to minimize the potential interference of different medications. The criteria of exclusions included type 1 diabetes; use of insulin; serious pathology, including medical problems in major organs such as the heart, lung, endocrine, and kidney; concomitant medication (except for gliclazide) or herbal medicines; and/or allergies to cinnamon. As shown in Table 1, there were no significant differences in sex, age, and dosage of gliclazide among the 3 groups of patients.

3.2. Effect of cinnamon extract on HbA_{1c} and FBG

The levels of HbA_{1c} and FBG of the patients were measured in the beginning of the experiment (pretreatment) and at the end of the 3 months of treatment (posttreatment). As shown in Table 1, the levels of HbA_{1c} and FBG were not significantly altered in the placebo group with HbA_{1c} changing from 8.92% to 8.93% and FBG from 8.92 to 8.71 mmol/L and no significant differences between pre- and posttreatment. However, both the HbA_{1c} and FBG levels were significantly reduced in posttreatment in the low- and high-dose groups (Table 1). The HbA_{1c} level was decreased from 8.90% to 8.23% in the low-dose group with an average reduction of 0.67% ($P = .003$) and from 8.92% to 8.00% in the high-dose group with an average reduction of 0.92% ($P = .0004$). Meanwhile, the FBG level had a

Table 2 – Comparison of our study with other clinical studies

Study	Subject type	Country	Y	Dose/d	Form	Duration (wk)	FBG (mmol/L)				HbA_{1c} (%) control treated	
							n	Pre/Post	n	Pre/Post	Pre/Post	Pre/Post
Khan et al [2]	Type 2 diabetes	Pakistan	2003	1-6 g	Cinnamon	5.5	10	12.2 ± 1.0 12.4 ± 1.1	10	13.0 ± 1.4 9.20 ± 1.5 *	N/A	
Mang et al [3]	Type 2 diabetes	Germany	2006	6 g equivalent	Extract	16	32	8.7 ± 1.9 8.3 ± 1.6	33	9.3 ± 2.3 8.2 ± 1.7 **	6.7 ± 0.7 6.7 ± 0.7	6.9 ± 1.0 6.8 ± 0.8
Vanschoonbeek et al [11]	Type 2 diabetes	Netherland	2006	1.5 g	Cinnamon	6	13	8.3 ± 1.2 5.0 ± 0.4	12	8.4 ± 2.0 7.9 ± 2.5	N/A	
Ziegenfuss et al [4]	Met. Syndrome	United States	2006	500 mg	Extract	12	10	6.2 ± 0.6 6.3 ± 0.8	12	6.4 ± 0.7 5.9 ± 1.1 **	N/A	
Blevins et al [7]	Type 2 diabetes	United States	2007	2 g	Cinnamon	12	29	8.0 ± 0.6 NS	28	7.4 ± 0.5 NS	7.1 ± 0.2 NS	7.3 ± 0.3 NS
Roussel et al [9]	Impaired FBG	United States	2009	500 mg	Extract	12	11	6.2 ± 0.2 6.3 ± 0.3	11	5.7 ± 0.2 6.3 ± 0.1	N/A	
Crawford [5]	Type 2 Diabetes	United States	2009	1 g	Cinnamon	12	46	N/A	43	N/A	8.3 ± 1.3 7.9 ± 1.5	8.5 ± 1.8 7.6 ± 1.7 **
Akilen et al [6]	Type 2 diabetes	United Kingdom	2010	2 g	Cinnamon	12	28	8.8 ± 2.6 8.7 ± 3.1	30	8.8 ± 3.5 8.0 ± 3.1	8.6 ± 1.8 8.7 ± 1.8	8.2 ± 1.2 7.9 ± 1.4 **
This study [a]	Type 2 diabetes	China	2011	120 mg	Extract	13	20	8.9 ± 1.2 8.7 ± 2.0	23	9.0 ± 1.2 8.0 ± 1.1 **	8.9 ± 1.1 8.9 ± 1.0	8.9 ± 1.2 8.2 ± 1.0 **

The data of FBG and HbA_{1c} are presented as means ± SD. N/A indicates not available; NS, the actual data were not given in the study but were not significantly different from pretreatment.

[a] Only the data for low-dose group of our study are shown here.

* $P < .05$ between pre- and posttreatment as analyzed by paired t test.

** $P < .01$ between pre- and posttreatment as analyzed by paired t test.

statistically significant decrease from 9.00 to 7.99 mmol/L in the low-dose group with an average reduction of 1.01 mmol/L ($P = .002$) and from 11.21 to 9.59 mmol/L with an average reduction of 1.62 mmol/L in the high-dose group ($P = .00008$). We also measured the levels of triglyceride, total cholesterol, HDL cholesterol, LDL cholesterol, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) with the patients. Only the triglyceride level was significantly reduced in the low-dose group ($P = .007$). All other parameters were not significantly altered in any of the 3 groups between pre- and posttreatment, except that the levels of total cholesterol and ALT were slightly increased in the placebo group ($P = .042$ for total cholesterol and $P = .028$ for ALT). Collectively, these data indicate that supplementation of cinnamon extract at both 120 and 360 mg/d could significantly reduce the levels of HbA_{1c} and FBG in the type 2 diabetic patients. Meanwhile, low-dose cinnamon appears to have an effect in reducing triglyceride levels. In addition, both the low- and high-dose cinnamon tablets had no adverse effect on liver function, as monitored by the levels of AST and ALT.

3.3. *Comparison of our studies with others*

We compared the results of our studies with other published data in which cinnamon or cinnamon extract was used in type 2 diabetes (Table 2). There are a total of 9 clinical studies, including ours. Among these studies, 5 have measured the HbA_{1c} level in the type 2 diabetic patients (Table 2). Interestingly, the 3 most recent studies (including ours) found that cinnamon or its extract was able to significantly reduce the HbA_{1c} level in the patients [5,6], whereas some the earlier studies revealed that cinnamon or cinnamon extract was able to improve FBG [2–4]. In support of our findings, most studies indicate that cinnamon is effective in improving blood glucose control.

4. Discussion

To our knowledge, this is the first clinical study to analyze the effect of cinnamon supplements on type 2 diabetes in China. Our results revealed that cinnamon extract, as a supplement to gliclazide, was effective in lowering HbA_{1c} and FBG levels in the patients. In comparison with previous studies in humans that investigated the effect of cinnamon, our study possessed several differences. First, all of the participating patients were taking the same type of prescribed antidiabetic medication to minimize the potential interference of different types of medications on the effect of cinnamon. Second, the baseline HbA_{1c} and FBG levels were relatively high in our study subjects in comparison with most other studies. Third, both HbA_{1c} and FBG levels were measured in our study, making the estimate of blood glucose control more accurate than some other studies. Lastly, our study duration was 3 months, a long enough interval to evaluate hyperglycemic status using HbA_{1c} as a biomarker.

Most of the available clinical studies using cinnamon in different countries are summarized in Table 2. The study of Khan et al [2] demonstrated that cinnamon was very effective in reducing FBG in a short period (5.5 weeks). However, HbA_{1c} was not measured in the study [2], thus making it difficult to evaluate the long-term effect of cinnamon on hyperglycemic control. The study of Mang et al [3] also revealed that cinnamon supplement was able to reduce FBG in type 2

diabetic patients. In the study of Blevins et al [7], cinnamon had no effect on either FBG or HbA_{1c}. However, the baseline levels of both of these parameters were much lower than those in our study. Interestingly, when the baseline level of HbA_{1c} was higher than 7.0%, cinnamon was effective in reducing the HbA_{1c}, as indicated in the studies by Crawford [5], Akilen et al [6], and ours. By comparing the results of our study with those of other studies, it appears that cinnamon supplements demonstrate a maximal effect on blood glucose control when the FBG and HbA_{1c} levels are relatively high at the beginning of the treatment.

It is noteworthy that the effect of cinnamon on blood glucose control is likely dependent on the form of cinnamon used for the patients. Furthermore, different extraction methods might affect the efficacy of cinnamon. We used cinnamon extract from the water-soluble fraction of cinnamon in this study [10]. It has been shown that the water-soluble polyphenol polymers from cinnamon could markedly increase insulin-dependent glucose metabolism in vivo as well as lead to an elevated antioxidant activity [12]. The aqueous extract from cinnamon was also able to enhance insulin signaling by inhibiting protein-tyrosine phosphatase 1B, a phosphatase that negatively regulates insulin action [13]. Furthermore, the water-soluble cinnamon extract could function as a dual activator of peroxisome proliferator–activated receptors γ and α, likely contributing to the antidiabetic effect of cinnamon [10]. In the future, it is important to further identify the active component of cinnamon and elucidate its molecular mechanism that is responsible for its effect on insulin sensitivity.

A limitation of this study was that the number of subjects in each group might be insufficient to identify the dose-dependent effect of cinnamon extract on blood glucose control. Nevertheless, our study has corroborated our hypothesis that cinnamon is able to improve blood glucose control in Chinese patients with type 2 diabetes. Based on our observations as well as other groups' reports, we propose that cinnamon be considered a promising supplement for the therapy of type 2 diabetes when hyperglycemia cannot be satisfactorily controlled by other strategies such as diet, exercise, and prescribed medication.

Acknowledgment

This study was funded by research grants from the Chinese Academy of Sciences (KSCX2-EW-R-08) and National Natural Science Foundation of China (30830037 and 81021002) to YC. The authors have stated that there was no conflict of interest.

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