European Journal of Clinical Investigation (2006) **36**, 340–344

Effects of a cinnamon extract on plasma glucose, HbA_{1c}, and serum lipids in diabetes mellitus type 2

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Abstract

Background According to previous studies, cinnamon may have a positive effect on the glycaemic control and the lipid profile in patients with diabetes mellitus type 2. The aim of this trial was to determine whether an aqueous cinnamon purified extract improves glycated haemoglobin A1c (HbA_{1c}), fasting plasma glucose, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triacylglycerol concentrations in patients with type 2 diabetes.

Methods A total of 79 patients with diagnosed diabetes mellitus type 2 not on insulin therapy but treated with oral antidiabetics or diet were randomly assigned to take either a cinnamon extract or a placebo capsule three times a day for 4 months in a double-blind study. The amount of aqueous cinnamon extract corresponded to 3 g of cinnamon powder per day.

Results The mean absolute and percentage differences between the pre- and post-intervention fasting plasma glucose level of the cinnamon and placebo groups were significantly different. There was a significantly higher reduction in the cinnamon group (10·3%) than in the placebo group (3·4%). No significant intragroup or intergroup differences were observed regarding HbA_{1c}, lipid profiles or differences between the pre- and postintervention levels of these variables. The decrease in plasma glucose correlated significantly with the baseline concentrations, indicating that subjects with a higher initial plasma glucose level may benefit more from cinnamon intake. No adverse effects were observed.

Conclusions The cinnamon extract seems to have a moderate effect in reducing fasting plasma glucose concentrations in diabetic patients with poor glycaemic control.

Keywords Cinnamon extract, diabetes mellitus type 2, fasting plasma glucose, HbA_{1c}, serum lipids.
Eur J Clin Invest 2006; 36 (5): 340–344

Introduction

Cinnamon has long been used as a herbal medicine in Asia, whereas it is known mainly as a spice in Western countries. Several *in vitro* and animal studies published since 1990 have indicated that cinnamon may mimic insulin effects and thus may improve glucose utilization [1–6]. It has been assumed that the methylhydroxychalcone polymer is the active substance [4]. Anderson *et al.* [7] used various aqueous cinnamon extracts and showed insulin-enhancing properties *in vitro* in adipocytes, suggesting that isolated A-type doubly linked procyanidin oligomers of the catechins and/or epicatechins from cinnamon may be responsible for the observed effect. *In vitro* studies have shown that cinnamon enhances glucose uptake by activating insulin receptor (IR) kinase activity, autophosphorylation of IR, glycogen synthesis and glycogen synthase activity [4]. *In vivo*, cinnamon extract enhances glucose utilization in rats in a dose-dependent fashion by potentiating insulin-stimulated tyrosine phosphorylation of (IR)-β, IR substrate (IRS)-1 and the IRS-1 association with phosphatidylinositol (PI) 3-kinase [8]. Owing to these results a beneficial role of cinnamon in the glycaemic control of diabetics has been

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Received 18 January 2005; accepted 14 February 2006

postulated [7,9], which could be demonstrated in a study with diabetic patients [9]. Furthermore cinnamon may inhibit hepatic HMG-CoA reductase activity and lower blood lipids in animals [10] and humans [9]. However, a cholesterol-increasing effect has also been shown in rats in a previous study [11].

As a consequence of the results obtained by Khan *et al.* [9] with cinnamon powder (Cinnamomum cassia), many diabetics are already taking cinnamon products even though our knowledge remains limited. To date, there has only been one randomized, controlled trial investigating the effect of different dosages of cinnamon powder on plasma glucose concentrations and blood lipids in patients with diabetes mellitus type 2 [9]. In this study supplementation of 1, 3, or 6 g of cinnamon for 40 days caused positive effects on fasting serum glucose and blood lipids. However, the results of this study, which was performed in Pakistan, may not be valid for Western populations. The data indicate that these diabetics were not adequately treated according to evidence-based recommendations [12] because the mean fasting serum glucose concentrations of 11·4–16·7 mmol L^{-1} were quite high before the cinnamon intake. The authors did not state the mean HbA_{1c} of the sample but the glucose concentrations indicated correspond to HbA_{1c} values of approximately 8·0–10·5% [12]. Such high fasting serum glucose concentrations are unusual in Western diabetics. The current guidelines set targets of HbA_{1c} of less than 7% and ≤ 6·9 mmol L^{-1} of fasting plasma glucose [12]. Although these low targets are not achieved in Western countries, most patients with diagnosed diabetes mellitus (> 60%) exhibit HbA_{1c} levels < 8·0%, as indicated in a recent report [13].

We planned a study in a randomized, placebo-controlled, double-blind design and investigated the effects of the daily intake of an aqueous cinnamon extract (Cinnamomum cassia) over 4 months on HbA_{1c}, fasting plasma glucose, and serum lipids in type 2 German diabetic patients. An aqueous purified extract with < 0·1% coumarins and < 0·1% essential oil was chosen because of the known allergic potential of cinnamon [14] and the fact that coumarins in the lipophilic fraction may affect blood coagulation [15,16].

Methods

Study design and included patients

A total of 79 patients with diagnosed diabetes mellitus type 2 were recruited in the region of Hannover, Germany, and randomly assigned to take either one cinnamon extract or one placebo capsule three times a day with a meal in a double-blind design. Only patients treated with oral antidiabetics or diet were included in the study. Two subjects were excluded because of weight changes ≥ 5% during the 4 months of intervention and 12 subjects were excluded owing to withdrawal of consent (n = 7), serious disease (n = 4) or irregular intake of the study preparation (n = 1). Thus the data of 65 subjects were included in the evaluation.

One cinnamon capsule contained 112 mg of the aqueous cinnamon extract TC112 prepared by Finzelberg (Andernach, Germany), corresponding to 1 g of cinnamon. The placebo capsules looked identical but contained microcrystalline cellulose only. Both capsules were donated by Truw Arzneimittel Vertriebs GmbH (Diabetruw®, Gütersloh, Germany). Patients were instructed to take the capsules for 4 months. Compliance was monitored by capsule count and diary in which the patient had to mark the day he/she had forgotten to take one or more capsules. All subjects gave written informed consent. The study was approved by the Ethics Committee of the Medizinische Hochschule Hannover, Hannover, Germany.

Blood sampling and analytical methods

After informed consent was obtained, blood samples were drawn after an overnight fast at baseline and after 4 months of intervention. Anthropometric data were determined on the day of blood sampling. For plasma preparation blood samples, taken with a heparin-containing blood sample system, were directly centrifuged at 2665 × g for 10 min at 19 °C. Blood samples for serum preparation were stored for blood coagulation (20 min) and then centrifuged under the same conditions. For the determination of HbA_{1c}, EDTA blood was used. EDTA blood, serum and plasma aliquots were stored at 4 °C and transported to the laboratory (Department of Clinical Chemistry of the Medizinische Hochschule, Hannover, Germany) within 5 h. HbA_{1c} was assessed by immunoturbidimetric determination (Roche-Tina-quant II [a], Roche Diagnostics, Mannheim, Germany). Fasting plasma glucose was measured by the hexokinase method (Gluco-quant, Roche Diagnostics, Mannheim, Germany). Serum concentrations of triacylglycerol and total cholesterol were measured using the GPO-PAP kit and the CHOD-PAP kit, respectively (Roche Diagnostics, Mannheim, Germany). Low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol were measured enzymatically (Wako Chemicals, Neuss, Germany).

Statistical analyses

Data were analyzed using SPSS 13·0 (SPSS Inc., Chicago, IL). Data are shown as mean ± standard deviation. The independent-sample t-test was used to reveal significant differences between the cinnamon extract group and the placebo group. In order to detect significant differences in the same group at two different times the t-test for dependent variables was used. Owing to the skewed distribution of triacylglycerol concentrations the Mann–Whitney U-test was applied for detection of intergroup differences and the Wilcoxon test for intragroup differences for this variable. Correlation between fasting plasma glucose levels at baseline and the absolute differences of fasting glucose were analyzed with the Pearson method. P-values < 0·05 were considered statistically significant.

Results

Data from 65 subjects were included in the evaluation. The characteristics of the study population are shown in Table 1. Forty-four men and 21 women took part in the study. There were no significant differences between the cinnamon group and the placebo group in respect to the distribution between the sexes or the anthropometric variables. The duration of diabetes was also similar: 6·8 ± 4·7 years for the placebo group and 7·1 ± 6·2 years for the cinnamon group. In respect to drug treatments, 27·7% of the study population took metformin, 12·3% sulphonylureas, 4·6% glinides, 1·5% glitazones and 30·8% received combination therapies. For those not taking drugs, 23·1% of the study population were only treated with basic therapy such as diet and/or physical activity. In addition, 49·2% took antihypertensive medication and 20·0% received drugs against dyslipidaemia. Table 2 shows the fasting plasma glucose concentrations, HbA_{1c}, serum lipids and the corresponding differences of these variables for the cinnamon and placebo groups. While the fasting plasma glucose of the cinnamon group was significantly reduced after the intervention compared with baseline, no such effect was observed in the placebo group. The mean absolute and percentage differences of fasting glucose between the cinnamon group and the placebo group were significantly different. The mean percentage difference calculated from the individual glucose concentrations was 10·3 ± 13·2% in the cinnamon group and 3·37 ± 14·2% in the placebo group ($P = 0·046$). Fasting plasma glucose concentrations at baseline showed a significant correlation with the decrease of the fasting plasma glucose levels ($r = 0·685$; $P < 0·001$). No significant changes or intergroup differences of HbA_{1c}, total cholesterol, LDL, HDL or triacylglycerol concentrations were observed.

Blood coagulation variables did not change significantly during the intervention period (data not shown). No adverse effects of the cinnamon extract were reported by the participants.

Table 1 Characteristics of the study population*

Variable	Cinnamon group ($n = 33$)	Placebo group ($n = 32$)
Gender		
Men (%)	63·6 ($n = 21$)	71·9 ($n = 23$)
Women (%)	36·4 ($n = 12$)	28·1 ($n = 9$)
Time since diagnosis of diabetes type 2 (y)	7·1 ± 6·2	6·8 ± 4·7
Age (year)	62·8 ± 8·37	63·7 ± 7·17
Height (m)	1·72 ± 0·09	1·73 ± 0·07
Weight (kg)	88·5 ± 19·1	89·9 ± 14·1
BMI (kg m^{-2})	29·6 ± 4·64	30·1 ± 5·22
Waist circumference (cm)	100·5 ± 15·0	102·7 ± 11·2

*Data are means ± SD.

Table 2 Variables of glucose and lipid metabolism at baseline and after the intervention period*

Variable	Cinnamon group ($n = 33$)	Placebo group ($n = 32$)
Fasting plasma glucose at baseline (mmol L^{-1})	9·26 ± 2·26	8·66 ± 1·47
Fasting plasma glucose postintervention (mmol L^{-1})	8·15 ± 1·65†	8·31 ± 1·62
Differences‡ of fasting glucose (mmol L^{-1})	1·11 ± 1·59§	0·35 ± 1·29
HbA_{1c} at baseline (%)	6·86 ± 1·00	6·71 ± 0·73
HbA_{1c} postintervention (%)	6·83 ± 0·83	6·68 ± 0·70
Differences‡ of HbA_{1c} (%)	0·05 ± 0·43	0·03 ± 0·61
Total cholesterol at baseline (mmol L^{-1})	5·38 ± 0·89	5·25 ± 0·79
Total cholesterol postintervention (mmol L^{-1})	5·29 ± 0·89	5·17 ± 0·75
Differences‡ of total cholesterol (mmol L^{-1})	0·09 ± 0·50	0·08 ± 0·49
LDL at baseline (mmol L^{-1})	3·48 ± 0·71	3·59 ± 0·69
LDL postintervention (mmol L^{-1})	3·52 ± 0·75	3·60 ± 0·64
Differences‡ of LDL-cholesterol (mmol L^{-1})	–0·03 ± 0·30	–0·01 ± 0·39
HDL at baseline (mmol L^{-1})	1·44 ± 0·49	1·34 ± 0·31
HDL postintervention (mmol L^{-1})	1·46 ± 0·52	1·33 ± 0·30
Differences‡ of HDL-cholesterol (mmol L^{-1})	–0·02 ± 0·16	0·02 ± 0·21
Triacylglycerol at baseline (mmol L^{-1})	1·96 ± 1·65	1·66 ± 0·78
Triacylglycerol postintervention (mmol L^{-1})	1·81 ± 1·58	1·73 ± 0·70
Differences‡ of Triacylglycerol (mmol L^{-1})	0·16 ± 0·83	–0·08 ± 0·56

*Data are means ± SD.
†Significantly different from baseline ($P < 0·001$).
‡Differences between pre- and postintervention values.
§Significantly different from the placebo group ($P = 0·038$).

Discussion

To our knowledge this is the first study evaluating the effect of an aqueous cinnamon extract on fasting plasma glucose, $HbA1_c$ and serum lipids in Western type 2 diabetics. Similar to the results of Khan *et al.* [9], who showed a significant reduction of fasting glucose after 40 days of intervention with cinnamon powder, we also observed a significant reduction of plasma glucose after 4 months of treatment in the cinnamon group but not in the placebo group. The differences of pre- and postintervention fasting glucose concentrations showed a significantly higher reduction in the cinnamon group than in the placebo group. Whereas Khan and coworkers [9] reported a strong reduction of 18–29% of fasting serum glucose in the three cinnamon groups independently of the ingested dosages of 1, 3, or 6 g of cinnamon, we observed a reduction of 10% in the cinnamon group, probably owing to the lower initial fasting glucose concentrations compared with the Pakistani diabetics. Initial mean fasting plasma glucose levels in our study were comparable to the postintervention concentrations of the Pakistani diabetics [9]. No significant intragroup or

intergroup differences were observed in the HbA_{1c} values in our study.

The high mean fasting glucose concentrations of the Pakistani diabetics suggest a poor control of diabetes in that study population. According to the current guidelines recommended for the treatment of diabetes, normal or near-normal glycaemia with a $HbA_{1c} < 7\%$ should be achieved [12]. On average our study sample attained the recommended value, as the mean HbA_{1c} of the total study population was 6·79% at baseline. The smaller reduction of fasting glucose concentrations in our study compared to Khan *et al*. [9] and the lack of effect on the HbA_{1c} values may indicate that in well-treated diabetics weak effects of cinnamon only can be achieved. The positive correlation between baseline plasma glucose and the decrease of plasma glucose in our study and the strong decrease of serum glucose in the poorly controlled Pakistani diabetics suggest that subjects with poor glycaemic control may benefit more from cinnamon intake.

There were no changes regarding the lipid profiles after the intervention compared with baseline in our study. Khan *et al.* [9] reported significant decreases of triacylglycerol (23–30%) and serum cholesterol (12–26%) concentrations in the various cinnamon groups. LDL levels were also significantly reduced (7–27%) in the 3- and 6-g groups. Insulin resistance leads to the overproduction of very low-density lipoproteins (VLDLs) and to reduced lipoprotein-lipase activity, thereby resulting in dyslipidaemia [17,18]. Therefore, attainment of better glycaemic control may improve the lipid profile [19,20]. Obviously, the decrease of plasma glucose concentrations in our study was not sufficient to induce an improvement of the lipoprotein concentrations.

The lower decrease of plasma glucose compared with Khan *et al*. [9] most probably did not result from using an aqueous extract instead of cinnamon powder. As shown, *in vitro* and *in vivo* aqueous extracts of cinnamon exhibit insulin-enhancing properties. Furthermore the substances proposed to be responsible for this are part of the aqueous fraction [6,7]. Using an aqueous extract of cinnamon, which is nearly free of lipophilic substances, may be safer than the powder because Cinnamomi cassiae cortex is known to cause allergic reactions owing to components of the volatile oil, particularly of cinnamic aldehyde [14,21,22], and may decrease blood coagulation [15,16] owing to the coumarins.

In conclusion, our study shows that in Western type 2 diabetics treated in accordance with the current guidelines [12], the intake of an aqueous cinnamon extract leads to a moderate effect on fasting plasma glucose, but not on HbA_{1c}, serum lipids or blood coagulation parameters.

Acknowledgements

We are indebted to Prof. Hartmut Hecker for statistical expertise and to Olaf Hülsmann, Gudrun Gläser and Heike Kohrs for assistance. We thank all the volunteers who participated in this study.

The study was supported by grants from Truw Arzneimittel GmbH (Gütersloh, Germany) and Finzelberg GmbH & Co. KG (Andernach, Germany).

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