Effects of 1 and 3 g cinnamon on gastric emptying, satiety, and postprandial blood glucose, insulin, glucose-dependent insulinotropic polypeptide, glucagon-like peptide 1, and ghrelin concentrations in healthy subjects

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ABSTRACT

Background: A previous study of healthy subjects showed that intake of 6 g cinnamon with rice pudding reduced postprandial blood glucose and the gastric emptying rate (GER) without affecting satiety.

Objective: The objective was to study the effect of 1 and 3 g cinnamon on GER, postprandial blood glucose, plasma concentrations of insulin and incretin hormones [glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide 1 (GLP-1)], the ghrelin response, and satiety in healthy subjects.

Design: GER was measured by using real-time ultrasonography after ingestion of rice pudding with and without 1 or 3 g cinnamon. Fifteen healthy subjects were assessed in a crossover trial.

Results: The addition of 1 or 3 g cinnamon had no significant effect on GER, satiety, glucose, GIP, or the ghrelin response. The insulin response at 60 min and the area under the curve (AUC) at 120 min were significantly lower after ingestion of rice pudding with 3 g cinnamon (P = 0.05 and P = 0.036, respectively, after Bonferroni correction). The change in GLP-1 response (ΔAUC) and the change in the maximum concentration (ΔCmax) were both significantly higher after ingestion of rice pudding with 3 g cinnamon (P = 0.0082 and P = 0.0138, respectively, after Bonferroni correction).

Conclusions: Ingestion of 3 g cinnamon reduced postprandial serum insulin and increased GLP-1 concentrations without significantly affecting blood glucose, GIP, the ghrelin concentration, satiety, or GER in healthy subjects. The results indicate a relation between the amount of cinnamon consumed and the decrease in insulin concentration.

INTRODUCTION

Changes in lifestyle, such as increases in energy intake and decreases in physical activity, are causing overweight and obesity and leading to an epidemic increase in type 2 diabetes. Diets with a low glycemic index (GI) and/or a low glycemic load diets are associated with a reduced risk of type 2 diabetes and heart disease (1), comparable with the reduction in risk observed with a high intake of dietary fiber and whole-grain products. Measurements of the blood glucose response 2 h after eating have been shown to be a better predictor of death from cardiovascular disease than fasting blood glucose (2).

Gastric emptying, together with other factors, regulates the postprandial blood glucose response, and a reduction in the gastric emptying rate (GER) leads to a lower postprandial blood glucose concentration. Gastrointestinal hormones, such as glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide 1 (GLP-1), are secreted by the K and L cells, respectively, of the intestinal wall (3). GLP-1 is known to be an incretin, and it stimulates glucose-dependent insulin secretion (3). Exogenous administration of GLP-1 delays gastric emptying with secondary effects on the glucose concentration (4–8) and decreases the postprandial feeling of hunger (7, 8). GIP also stimulates glucose-dependent insulin secretion (9). The gastrointestinal hormone ghrelin has been shown to stimulate gastric emptying and hunger in healthy subjects (9).

Cinnamon has been shown to improve the insulin receptor function in rats, which leads to enhanced cellular glucose uptake (10, 11). A recent short-term study in healthy subjects showed lower postprandial blood glucose concentrations and improved insulin sensitivity when 5 g cinnamon was eaten 12 h before, or ingested at the same time as, an oral-glucose-tolerance test was performed (12). A long-term study of nondiabetic women with polycystic ovary syndrome also showed a significant reduction in insulin resistance after the intake of 1 g cinnamon/d for 8 wk before an oral-glucose-tolerance test was performed (13). However, a recent meta-analysis of 5 long-term studies of subjects with type 1 and type 2 diabetes showed that the intake of cinnamon did not significantly improve glycated hemoglobin (Hb A1c), fasting blood glucose, or lipid variables (14). It is

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therefore still uncertain whether the intake of cinnamon can help prevent diabetes.

Ingestion of 6 g cinnamon together with rice pudding has been shown to reduce postprandial blood glucose concentrations and GER in healthy subjects, although the reduction in blood glucose concentrations was much more pronounced than the lowering of GER, which was unexpected (15). Six grams of cinnamon is not a quantity ordinarily used in food. The primary objective of this study was to determine whether adding 3 g cinnamon to a meal would change GER, satiety, or postprandial blood glucose, insulin, GIP, and GLP-1 concentrations. If this was the case, the secondary objective was to establish whether adding 1 g cinnamon to a meal would change GER, satiety, and postprandial blood glucose, insulin, GIP, and GLP-1 concentrations. This study was therefore designed to determine whether changes in insulin response explain lower postprandial blood glucose concentrations and whether a change in GIP, GLP-1, or ghrelin response could explain the change in insulin secretion or the change in GER in healthy subjects after cinnamon consumption. We also studied the dose-response relation with respect to the effect on GER, satiety, and postprandial blood glucose, insulin, GIP, GLP-1, and ghrelin responses in healthy subjects.

SUBJECTS AND METHODS

Subjects

Fifteen healthy subjects [9 men and 6 women; mean (±SD) age: 24.6 ± 1.9 y (range: 20–27 y); body mass index (in kg/m²): 22.5 ± 2.7 (range: 19.3–27.5)] with no symptoms and no history of gastrointestinal disease, abdominal surgery, or diabetes mellitus were included in this crossover study. The subjects had no connective tissue disease or cerebrovascular or endocrine disease, and none was taking any medications other than oral contraceptives (n = 1 woman). Two subjects were smokers, and one was a snuff user. All subjects were recruited from the population of southern Sweden. All subjects gave their written informed consent. The study was approved by the Ethics Committee of Lund University and was performed according to the Helsinki Declaration. The study started on 29 May 2007 and ended on 12 December 2007.

Methods

The subjects were examined between 0730 and 1030 after an 8-h fast. Smoking and snuff use were prohibited 8 h before and during the test. The fasting blood glucose concentration of each subject was checked on the day of the examination to ensure that it was normal. If the subjects reported gastrointestinal symptoms (diarrhea or constipation) on the day of the study, the examination was postponed.

The test meal consisted of 300 g rice pudding (AXA Goda Grö10 Rigsrynsgröt; Lantmänn AXA, Järna, Sweden) mixed with 1 or 3 g cinnamon (Cinnamomum cassia; Santa Maria AB, Mölndal, Sweden). The total caloric value of the meal was 330 kcal: 10% from protein (9 g), 58% from carbohydrates (48 g), and 32% from fat (12 g). The reference meal consisted of 300 g rice pudding without cinnamon. The meals were served in random order at 1-wk intervals. Randomization was performed by using a table of random numbers. The meals were ingested within 5 min. The total test duration did not exceed 2 mo, except for one subject (5.5 mo).

GER was estimated by using an ultrasound method described previously (16). The sonographic examination was performed with a 3.5-MHz abdominal transducer (Acusone Sequio 512; Siemens Medical Solutions, Mountain View, CA) and an imaging system (Siemens Elegra; Siemens Medical Solutions). Measurements of the gastric antrum were performed by the same radiologist, who was blinded with respect to the meals. The abdominal aorta and the left lobe of the liver were used as internal landmarks in each measurement of the gastric antrum. The subjects were examined in the supine position, but were allowed to sit up between examinations. Measurements were made 15 and 90 min after the meal had been consumed, and the degree of gastric emptying was expressed as the percentage change in the antral cross-sectional area between these 2 measurements. At each examination, the longitudinal and anteroposterior diameters (d1 and d2, respectively) were measured 3 times, and the mean values were used to calculate the cross-sectional area of the gastric antrum. GER (%) was calculated by using the following equation:

\[
\text{GER} = \left[1 - \left( \frac{\text{antrum area at 90 min/antrum area at 15 min}}{100} \right) \right]
\]

Venous blood samples were taken before and 15, 30, 45, 60, 90, 120, and 150 min after the start of the meal for the measurement of glucose, insulin, GIP, GLP-1, and ghrelin concentrations. Blood glucose concentrations were measured with the HemoCue Glucose system (HemoCue AB; Angelholm, Sweden). The precision of the HemoCue Glucose system was better than 0.3 SD from 0 to 22.2 mmol/L. Insulin concentrations were measured by using an immunoassay with an alkaline phosphatase conjugate (Access Ultrasensitive Insulin; Beckman-Coulter AB, Bromma, Sweden). The sensitivity of the insulin immunoassay was 0.03 mU/L (mU/L), and the intraassay CV was <10% from 0.03 to 300 mU/L. Plasma ghrelin concentrations were measured by using a radioimmunoassay kit (GHRT-89k) manufactured by Linco Research (St Charles, MO), which measures total ghrelin (intact as well as desoctanoylated ghrelin). The sensitivity obtained was 100 pg/mL, and the intraassay CV was <10%. Quality controls were always within acceptable limits. GIP and GLP-1 concentrations in plasma were measured after extraction of plasma with 70% ethanol (vol:vol, final concentration). For the GIP radioimmunoassay (17) the C-terminally directed antisera R 65 was used, which cross-reacts fully with human GIP but not with the so-called GIP 8000, the chemical nature and relation of which to GIP secretion are uncertain. It reacts fully with the primary metabolite, GIP 3–42. Human GIP and iodine-labeled human GIP (70 MBq 125I/μmol) were used for standards and tracer, respectively. The plasma concentrations of GLP-1 were measured against standards of synthetic GLP-1 7–36 amide by using antiseraum code no. 89390 (18), which is specific to the amidated C-terminus of GLP-1 and, therefore, does not react with GLP-1–containing peptides from the pancreas. The results of the assay accurately reflect the rate of secretion of GLP-1 because the assay measures the sum of intact GLP-1 and the primary metabolite, GLP-1 9–36 amide, into which GLP-1 is rapidly converted (19). For both assays, the sensitivity was...
<1 pmol/L, the intraassay CV was <6% at 20 pmol/L, and the recovery of the standard added to plasma before extraction was ≈100% when corrected for losses inherent in the plasma extraction procedure.

A validated satiety scoring scale was used according to the method of Haber et al (20) based on a scoring system from −10 (extreme hunger) to 10 (extreme satiety). Satiety scores were estimated before the meal (0 min) and 15, 30, 45, 60, 90, and 120 min after the start of the meal.

**Statistical analysis**

Median values and quartiles (Q1 and Q3) are presented for GER. The areas under the curves (AUCs) were measured for blood glucose, insulin, GIP, GLP-1, and ghrelin in each subject. The AUC was calculated above zero. The change in AUC (ΔAUC) was defined as the AUC above the baseline value. The AUC and ΔAUC values are expressed as means ± SEMs. The maximum concentration observed is denoted as Cmax, and the maximum increase compared with the baseline value is denoted as ΔCmax.

Differences in values were tested by pairwise comparisons using the Wilcoxon’s signed rank sum test (R, version 2.6; The R Foundation for Statistical Computing c/o Institut für Statistik und Wahrscheinlichkeitstheorie, Technische Universität Wien, Wiedner Hauptstrasse 8–10/1071,1040 Vienna, Austria). The level of statistical significance was set at P ≤ 0.05 after Bonferroni correction. A 2-factor method developed for repeated measures of ordinal scale data (21) using SAS statistical software version 8.2 (SAS Institute, Cary, NC) was used to elucidate differences in the satiety data.

**RESULTS**

**Postprandial blood glucose response**

The mean AUCs 120 min after the ingestion of rice pudding, rice pudding with 1 g cinnamon, and rice pudding with 3 g cinnamon were 601 ± 24, 593 ± 17, and 586 ± 18 mmol·min⁻¹·L⁻¹, respectively, whereas the mean AUCs 150 min after the meals were 730 ± 28, 715 ± 18, and 708 ± 21 mmol·min⁻¹·L⁻¹, respectively. No significant differences were seen in blood glucose responses at different postprandial times in terms of the AUCs for postprandial blood glucose, Cmax, or ΔCmax between the different meals (Figure 1).

**Postprandial plasma insulin response**

Ingestion of rice pudding with 3 g cinnamon resulted in a significantly lower plasma insulin response 60 min postprandially than did the reference meal (P = 0.05 after Bonferroni correction) (Figure 2). The ingestion of rice pudding with 3 g cinnamon also resulted in a significantly lower AUC at 120 min than did the reference meal (P = 0.036 after Bonferroni correction) (Table 1). No significant differences in the ΔAUC, Cmax, and ΔCmax for insulin were observed between the reference meal and the puddings with cinnamon (Table 2).

**Postprandial plasma GIP response**

No significant differences in the AUC, Cmax, or ΔCmax for plasma GIP responses at the different postprandial time points were observed between the different meals (Figure 3).

**Postprandial plasma GLP-1 response**

No significant differences in the AUCs for postprandial plasma GLP-1 responses at the different postprandial time points were observed between the different meals (Figure 4). Ingestion of rice pudding with 3 g cinnamon resulted in a significantly higher ΔCmax for GLP-1 (P = 0.0138 after Bonferroni correction) than did the reference meal (Table 2). The mean ΔAUC value after ingestion of the reference meal was −151.0 ± 191.1 pmol/L and was not significantly different from that after the ingestion of rice pudding with 1 g cinnamon (772.5 ± 246.3 pmol/L; P = 0.092 after Bonferroni correction) and significantly lower than the ingestion of rice pudding with 3 g (838.5 ± 267.0 pmol/L; P = 0.0082 after Bonferroni correction).

**FIGURE 1.** Mean (±SEM) blood glucose concentrations in 15 healthy subjects after the ingestion of meals consisting of rice pudding without cinnamon (●, reference meal), with 1 g cinnamon (■), and with 3 g cinnamon (▲). No significant differences were found between meals, P > 0.05 (Wilcoxon’s signed rank sum test after Bonferroni correction).

**FIGURE 2.** Mean (±SEM) plasma insulin concentrations in 15 healthy subjects after the ingestion of meals consisting of rice pudding without cinnamon (●, reference meal), with 1 g cinnamon (■), and with 3 g cinnamon (▲). Significantly different from the response to the reference meal, P ≤ 0.05 (Wilcoxon’s signed rank sum test after Bonferroni correction).
Postprandial plasma ghrelin response

No significant differences were seen in plasma ghrelin responses between the different meals at different times, in terms of the areas under the postprandial ghrelin curves, \( C_{\text{max}} \) or \( AC_{\text{max}} \) (Figure 5).

Gastric emptying rate

No significant differences in gastric antral cross-sectional areas were found. No significant differences in GER were observed in response to the rice pudding with 1 g cinnamon, the rice pudding with 3 g cinnamon, and the reference meal (Figure 6). The median GER value after the reference meal was estimated to be 40 ± 20% (range: 6–82%; Q1 = 27%, Q3 = 54%), that after rice pudding containing 1 g cinnamon was estimated to be 60 ± 22% (range: 13–79%; Q1 = 31%, Q3 = 67%), and that after rice pudding with 3 g cinnamon was estimated to be 55 ± 25% (range: -9% to 78%; Q1 = 41%, Q3 = 67%).

Satiety

No significant differences were recorded in satiety after the different meals (Figure 7). However, significant changes in satiety over time were observed after ingestion of all the meals \((P < 0.05)\).

DISCUSSION

This study showed that the ingestion of 3 g cinnamon reduces postprandial insulin and increases GLP-1 concentrations without significantly affecting satiety, GER, or concentrations of blood glucose, GIP or ghrelin in healthy subjects. The reduced postprandial plasma insulin concentration observed after the ingestion of 3 g cinnamon was not the result of delayed delivery of nutrients into the duodenum. The data suggest a slight reduction in the postprandial insulin response after the ingestion of 1 g cinnamon, but there were no significant differences in the insulin response, probably because of the low number of study subjects. The reduction in postprandial insulin response after the ingestion of 3 g cinnamon was more pronounced than that after the ingestion of 1 g cinnamon. Our finding that cinnamon decreases the insulin demand, despite the lack of change in blood glucose concentrations, was probably due to enhanced glucose uptake via stimulation of the insulin receptor. This finding is consistent with the results of previous studies.

Various herbs and medicinal plants have been investigated, and cinnamon has been shown to be one of the most effective at regulating blood glucose (22). A water-soluble polyphenol type-A polymer isolated from cinnamon has been shown to enhance insulin activity (23). Cinnamon has also been shown in vitro to stimulate the insulin receptor by activating the insulin receptor kinase and inhibiting the insulin receptor phosphatase, which increases insulin sensitivity (24). In vivo, cinnamon has been shown to enhance glucose utilization in rats in a dose-dependent manner by potentiating insulin-stimulated tyrosine phosphorylation of the insulin receptor-\(\beta\) and the insulin receptor substrate-1 and its association with phosphatidylinositol (PI) 3 kinase (10). When insulin-resistant rats were fed cinnamon for 3 wk, their

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<td>Postprandial plasma insulin area under the curves (AUCs) in healthy subjects after the ingestion of meals consisting of rice pudding without cinnamon (reference meal) and with 1 or 3 g cinnamon.</td>
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1 All values are means ± SEMs; \( n = 15 \).
2 Significantly different from the reference meal, \( P = 0.036 \) (Wilcoxon’s signed rank sum test after Bonferroni correction).

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<td>Maximum observed concentration ( (C_{\text{max}}) ) and the maximum change from baseline ( (AC_{\text{max}}) ) in insulin and glucagon-like peptide 1 (GLP-1) in healthy subjects after the ingestion of meals consisting of rice pudding without cinnamon (reference meal) and with 1 or 3 g cinnamon.</td>
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<td>Insulin (mU/L)</td>
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1 All values are means ± SEMs; \( n = 15 \).
Insulin resistance decreased, as measured by using a euglycemic clamp; the explanation given was the improved insulin signaling pathway described above (11). In women with polycystic ovary syndrome without diabetes, a dietary supplement of 333 mg cinnamon extract, 3 times/d for 8 wk, decreased insulin resistance and fasting glucose concentrations (25).

A study in Pakistan by Khan et al (26) showed that the ingestion of 1, 3, and 6 g cinnamon daily for 40 d lowered concentrations of fasting glucose, triglyceride, LDL cholesterol, and total cholesterol in women and men with type 2 diabetes receiving oral blood-glucose-lowering treatment. Treating women and men with type 2 diabetes with oral blood-glucose-lowering medication or diet and/or physical activity and supplementation with 3 g cinnamon/d for 4 mo resulted in a reduction in fasting plasma glucose concentrations, whereas no difference was observed in Hb A1c, total cholesterol, LDL, HDL, or triacylglycerol concentrations (13). However, no improvement was seen in Hb A1c, fasting glucose or insulin concentration, triacylglycerol, LDL, HDL, total cholesterol, or insulin resistance or sensitivity in overweight, postmenopausal women with type 2 diabetes taking oral blood-glucose-lowering medication or consuming controlled diets supplemented with 1.5 g cinnamon/d for 6 wk (12). In a study performed in the United States, no significant changes were seen in fasting glucose, lipid, Hb A1c, or insulin concentrations in persons with type 2 diabetes when 1 g cinnamon was consumed daily for 3 mo (27). These results suggest that those with poorly controlled diabetes may benefit from cinnamon intake more than those receiving adequate treatment. No significant differences in
this study did not stimulate insulin release or slow gastric emptying. We, and others, have failed to observe stimulatory effects of GLP-1 on postprandial insulin (6, 32–35). A lower infusion rate of GLP-1, similar to physiologic concentrations of \( \approx 25 \text{ pmol/L} \), suppressed postprandial glycemia and insulinemic responses explained by a slowing of gastric emptying in healthy subjects (6, 33). Another study showed that infusion of GLP-1 at plasma concentrations \( \approx 25 \text{ pmol/L} \) reduced meal-related increases in glucose, insulin, and glucagon concentrations (33). Unfortunately, GER was not measured in that study. A dose-dependent deceleration of gastric emptying and a reduction in the postprandial insulin response was also found in patients with type 2 diabetes when GLP-1 was infused at higher doses, despite a decline in postprandial blood glucose concentrations (34). Our understanding of the effects of GLP-1 is mainly based on studies using exogenous GLP-1, whereas little is known about the effects of endogenously released GLP-1. Our findings that cinnamon increases GLP-1 concentrations and decreases insulin concentrations, despite the lack of change in blood glucose concentrations or gastric emptying, support the previously described stimulation of the insulin receptor by cinnamon. The stimulatory effects of cinnamon on GLP-1 could be due to a direct effect on the L cells in the intestine. Unfortunately, postprandial glucagon concentrations were not measured in the present study. Infusion of ghrelin has been shown to stimulate gastric emptying and hunger (10). The results of the present study suggest a lower ghrelin response after ingestion of 3 g cinnamon, but the difference was not significant. The different doses of cinnamon used in the previous studies to evaluate the impact on glucose and plasma lipids in patients with type 2 diabetes may have also contributed to the differences in results. However, it appears that lower intakes of cinnamon may also be of benefit. The ability of cinnamon to control blood glucose concentrations in patients with type 1 and type 2 diabetes has not yet been fully evaluated. Treatment of type 2 diabetes mellitus based on enhanced glucose uptake by stimulation of the insulin receptor with cinnamon may improve glycemic control and decrease the insulin demand, with secondary effects on the \( \beta \) cell mass and prevention of the loss of \( \beta \) cell function. Clearly, a long-term clinical trial involving a larger number of diabetes patients is needed to evaluate the effects of cinnamon supplementation in type 2 diabetes.

This study showed that the ingestion of 3 g cinnamon reduced postprandial serum insulin and increased GLP-1 concentrations but had no effect on postprandial GER, satiety or blood glucose, GIP, or ghrelin concentrations in healthy subjects. A relation between the amount of cinnamon consumed and the decrease in insulin concentrations in healthy subjects was also shown in this study. Higher doses of cinnamon are apparently required to influence GER and postprandial blood glucose concentrations.

Hb A1c, total daily insulin intake, or the number of hypoglycemic episodes were observed between patients with type 1 diabetes treated with 1 g cinnamon/d for 3 mo and the placebo group (28). This may be explained by the fact that cinnamon decreases insulin resistance, which is not a mechanism of type 1 diabetes pathophysiology. However, a recent meta-analysis of the abovementioned 5 randomized, placebo-controlled trials in patients with type 1 and type 2 diabetes did not show any significant changes in Hb A1c, fasting blood glucose, or lipid concentrations (14).

It was recently shown that 5 g cinnamon ingested 12 h before, or in conjunction with, an oral-glucose-tolerance test in healthy men reduced the blood glucose response and improved insulin sensitivity, but no difference was observed in the insulin response (29). The intake of 6 g cinnamon with rice pudding was found to reduce postprandial blood glucose and delay gastric emptying in healthy subjects (15). However, in the present study, an intake of 3 g cinnamon reduced postprandial insulin concentrations more noticeably than did the ingestion of 1 g cinnamon, without affecting postprandial blood glucose or GER. There seems to be a relation between the amount of cinnamon consumed, the delay in gastric emptying, and the reduction in postprandial blood glucose concentrations. The previously described reduction in postprandial blood glucose concentrations after the ingestion of 6 g cinnamon was much more noticeable than was the lowering of GER (15). Gastric emptying, as well as other factors, regulates the postprandial blood glucose response, and a delay in gastric emptying leads to a lower postprandial blood glucose concentration (30, 31). Unfortunately, neither postprandial insulin nor GLP-1 concentrations were measured in the previous study.

As mentioned in the Introduction, infusion of GLP-1 delays the rate of gastric emptying with secondary effects on glucose concentrations (4–8) and also decreases the postprandial feeling of hunger (7, 8). The late phase of the GLP-1 response was clearly stimulated by cinnamon. Surprisingly, the increase in GLP-1 concentrations after the ingestion of cinnamon, seen in this study did not stimulate insulin release or slow gastric emptying. We, and others, have failed to observe stimulatory effects of GLP-1 on postprandial insulin (6, 32–35). A lower infusion rate of GLP-1, similar to physiologic concentrations of \( \approx 25 \text{ pmol/L} \), suppressed postprandial glycemia and insulinemic responses explained by a slowing of gastric emptying in healthy subjects (6, 33). Another study showed that infusion of GLP-1 at plasma concentrations \( \approx 25 \text{ pmol/L} \) reduced meal-related increases in glucose, insulin, and glucagon concentrations (33). Unfortunately, GER was not measured in that study. A dose-dependent deceleration of gastric emptying and a reduction in the postprandial insulin response was also found in patients with type 2 diabetes when GLP-1 was infused at higher doses, despite a decline in postprandial blood glucose concentrations (34). Our understanding of the effects of GLP-1 is mainly based on studies using exogenous GLP-1, whereas little is known about the effects of endogenously released GLP-1. Our findings that cinnamon increases GLP-1 concentrations and decreases insulin concentrations, despite the lack of change in blood glucose concentrations or gastric emptying, support the previously described stimulation of the insulin receptor by cinnamon. The stimulatory effects of cinnamon on GLP-1 could be due to a direct effect on the L cells in the intestine. Unfortunately, postprandial glucagon concentrations were not measured in the present study. Infusion of ghrelin has been shown to stimulate gastric emptying and hunger (10). The results of the present study suggest a lower ghrelin response after ingestion of 3 g cinnamon, but the difference was not significant. The different doses of cinnamon used in the previous studies to evaluate the impact on glucose and plasma lipids in patients with type 2 diabetes may have also contributed to the differences in results. However, it appears that lower intakes of cinnamon may also be of benefit. The ability of cinnamon to control blood glucose concentrations in patients with type 1 and type 2 diabetes has not yet been fully evaluated. Treatment of type 2 diabetes mellitus based on enhanced glucose uptake by stimulation of the insulin receptor with cinnamon may improve glycemic control and decrease the insulin demand, with secondary effects on the \( \beta \) cell mass and prevention of the loss of \( \beta \) cell function. Clearly, a long-term clinical trial involving a larger number of diabetes patients is needed to evaluate the effects of cinnamon supplementation in type 2 diabetes.

This study showed that the ingestion of 3 g cinnamon reduced postprandial serum insulin and increased GLP-1 concentrations but had no effect on postprandial GER, satiety or blood glucose, GIP, or ghrelin concentrations in healthy subjects. A relation between the amount of cinnamon consumed and the decrease in insulin concentrations in healthy subjects was also shown in this study. Higher doses of cinnamon are apparently required to influence GER and postprandial blood glucose concentrations.
REFERENCES


