Research Article

The Effect of *Tinospora crispa* on Serum Glucose and Insulin Levels in Patients with Type 2 Diabetes Mellitus

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Received 27 July 2011; Revised 15 August 2011; Accepted 25 August 2011

Academic Editor: Masa-Aki Shibata

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Objective. To determine the effects of *Tinospora crispa* on serum glucose and insulin levels in healthy subjects and patients with type 2 diabetes mellitus. **Method.** Serum from 10 healthy subjects and 10 diabetic participants, who had fasted overnight, were obtained every 30–60 minutes during the 3 hours of continued fasting and during the 3 hours after ingestion of 75 g of glucose with or without ingestion of 125 or 250 g of *Tinospora crispa* dry powder capsule. Glucose and Insulin levels were analyzed and the areas under the curve for mean serum glucose and insulin levels were calculated. **Result.** The areas under the curve of mean serum glucose and insulin levels in both healthy and diabetic participants were not significantly different between with or without *Tinospora crispa* dry powder capsule. In diabetic participants the area under the curve of glucose was slightly lesser when 250 mg of *Tinospora crispa* was ingested, but not reaching statistical significance (478 and 444 mg min/ml, resp., $P = 0.57$). **Conclusion.** The results suggest that *Tinospora crispa* ingestion cannot affect serum glucose and insulin levels in healthy subjects or patients with type 2 diabetes mellitus.

1. Introduction

Diabetes mellitus (DM), one of the major non-communicable diseases, has become a major public health problem and has increased prevalence in the modern world, even in developing countries such as Thailand [1]. As with other diseases, DM has been treated by oral administration of plant extracts based on traditional medicine since ancient times [2]. *Tinospora crispa* (*T. crispa*, Menispermaceae), a medicinal plant used to treat DM, was able to cause a reduction in serum glucose level in diabetic rats, and the hypoglycemic effect was probably due to its insulinotropic activity [3]. *T. crispa* also increased peripheral utilization of glucose and inhibited hepatic glucose release [4].

Sangsuwan et al. [5] showed that *T. crispa* had no efficacy for therapy in patients with type 2 DM who did not respond to an adequate dose of oral hypoglycemic drugs for at least 2 months and still had a glycosylated hemoglobin of greater than 8.5%. There were no significant changes in fasting serum glucose or glycosylated hemoglobin between those collected at baseline and during the study period in either group. In this study the author suggests that *T. crispa* did

not stimulate insulin secretion in poor controlled diabetes because these patients might not have ability to secrete insulin. Efficacy of *T. crispa* should be investigated in diabetic patient who responded to oral hypoglycemic drugs and did not use insulin therapy because pancreas in these patients might have ability of insulinotropic activity.

The objective of this study was to determine the effects of *T. crispa* on serum glucose and insulin levels in patients with type 2 DM and healthy subjects.

2. Material and Method

2.1. Subjects. After approval from the Ethics Committee for Human Studies of Ramathibodi Hospital, Mahidol University, 10 participants (7 women and 3 men) with type 2 DM between the ages of 32 and 64 years and 10 healthy participants (6 women and 4 men) with normal oral glucose tolerance test between the ages of 23 and 33 years were enrolled, type 2 DM participants responded to oral hypoglycemic drugs and discontinued oral hypoglycemic drugs at least 1 month. Patients with liver disease, heart disease, renal impairment, or those who previously received traditional medicine

TABLE 1: Baseline characteristics of the subjects in the study.

Characteristics	Diabetic participants ($n = 10$)	Healthy participants ($n = 10$)
Gender, male : female	7 : 3	6 : 4
Mean age, year (SD)	54.5 (9.5)	27.6 (2.9)
Mean FPG, mg/dL (SD)	151.0 (57.1)	83.4 (11.3)
Mean HbA1c, % (SD)	7.7 (1.1)	5.8 (0.3)
Mean creatinine, mg/dL (SD)	0.9 (0.5)	0.8 (0.2)
Mean cholesterol, mg/dL (SD)	175.5 (26.6)	204.0 (35.7)
Mean triglyceride, mg/dL (SD)	131.2 (56.7)	85.0 (26.4)
Mean AST, U/L (SD)	32.2 (13.6)	16.9 (5.7)
Mean ALT, U/L (SD)	46.6 (21.0)	29.7 (5.3)
Mean bilirubin, mg/dL (SD)	0.6 (0.3)	0.6 (0.4)

were excluded. Informed, written consent was obtained from all subjects after explanation of the nature, purpose, and potential risks of the study.

2.2. Plant Material and Fraction Preparation. The stems of *T. crispa* were collected from Supanburi and Nakhonsithammarat provinces, Thailand. Plant material was identified by Dr. Kongkathip N, Department of Chemistry, Faculty of Science, Kasetsart University. Coarse powder of *T. crispa* stem was defatted with petroleum ether (60–80°C) and dried material was extracted with 70% ethanol using soxhlet apparatus at 65–70°C for 7 days. The extract was dried under vacuum in a rotary evaporator. Powder was used microcrystalline cellulose at 7% of powder weight and using dry granulation technique. Powder of 125 and 250 mg *T. crispa* stem was prepared in form of capsule [6]. We designed to use 250 mg of *T. crispa* dry powder capsule because in previous study, 250 mg twice a day *T. crispa* can reduce fasting blood glucose significantly from baseline in metabolic syndrome patients [7].

2.3. Methods. After the screening visit, all subjects adhered to an alcohol-free, high-carbohydrate diet (>150 g/d) and discontinued all oral hypoglycemic agents at least 72 hours before the study. Exercise was discontinued 24 hours before and fasting was instituted 12 hours till the morning of the study. The study was performed in three visits, 1 to 2 weeks apart. The doses at each visit were as follows: 75 g of glucose at first visit; 75 g of glucose and 125 mg of *T. crispa* dry powder capsule at second visit; 75 g of glucose and 250 mg of *T. crispa* dry powder capsule at third visit. Venous blood was drawn and then ingestion of 75 g glucose with or without ingestion of 125 or 250 mg of *T. crispa*. Additional venous blood samples were drawn at 30, 60, 90, 120, and 180 minutes after ingestion. Serum glucose was obtained by an automated glucose oxidase method and serum insulin was measured by radioimmunoassay kit. All participants were examined and blood was taken for complete blood count, liver enzyme profile, and renal function at entry and end of the study.

2.4. Statistical Analyses. Areas under the curve (AUC) for increase in serum glucose and serum insulin were calculated

FIGURE 1: Mean serum glucose level at timed intervals during glucose tolerance test for 10 diabetic and 10 healthy participants. Mean serum glucose levels in mg/dL without (o) and with 125 (•) and 250 mg (×) ingestion of *Tinospora crispa* diabetic participants, and without (△) and with 125 (▲) and 250 mg (*) ingestion of *Tinospora crispa* in healthy participants.

by trapezoidal rule, and means were tested for significance by paired *t*-test. Mean glucose and insulin blood levels of all subjects were calculated for each time point. $P < 0.05$ was considered statistically significant.

3. Results

All of the 20 participants who had enrolled completed the study. At the dosage used there were no adverse effects reported by our subjects. During the treatment period no elevations in serum transaminase were detected. The baseline characteristics of the participants are shown in Table 1.

3.1. Glucose Levels with and without Ingestion of *Tinospora crispa*. Table 2 shows incremental serum glucose AUC (time 0 to 180 min) over the baseline in mg min/mL for 75 g glucose ingestion with and without 125 or 250 mg of *T. crispa* for each participant. The mean serum glucose AUC in both diabetic and healthy participants was not significantly different between with and without *T. crispa*. In diabetic participants the mean serum glucose AUC were slightly lesser when 250 mg of *T. crispa* was ingested, but not reaching statistical significance (478 and 444 mg min/mL, resp., $P = 0.57$). The mean glucose levels at each time interval showed small differences with *T. crispa* ingestion (Figure 1).

TABLE 2: Mean of 3 h total area under the curve (AUC) glucose and 3-h total AUC insulin for 75 g oral glucose tolerance test performed with and without 125 or 250 mg of *Tinospora crispa*.

	3 h total AUC for glucose (mg min/mL)			3 h total AUC insulin (mIU min/mL)		
	Without <i>T. crispa</i>	125 mg <i>T. crispa</i>	250 mg <i>T. crispa</i>	Without <i>T. crispa</i>	125 mg <i>T. crispa</i>	250 mg <i>T. crispa</i>
DM	478 ± 135	475 ± 102	444 ± 117	61 ± 56	50 ± 37	39 ± 21
Healthy	165 ± 25	171 ± 38	171 ± 30	73 ± 55	85 ± 34	58 ± 16

FIGURE 2: Mean serum insulin level at timed intervals during glucose tolerance test for 10 diabetic and 10 healthy participants. Mean serum insulin levels in $\mu\text{U/mL}$ without (o) and with 125 (•) and 250 mg (×) ingestion of *Tinospora crispa* in diabetic participants, and without (Δ) and with 125 ($\blacktriangle$) and 250 mg (*) ingestion of *Tinospora crispa* in healthy participants.

3.2. Insulin Levels with and without Ingestion of *Tinospora crispa*. Table 2 shows incremental insulin in $\mu\text{U min/mL}$ AUC (time 0 to 180 min, 75 g glucose tolerance tests without and with 125 or 250 mg of *T. crispa*) for each participant. Mean insulin AUC (Table 2) and mean levels at each time interval (Figure 2) in both diabetic and healthy participants varied, little with *T. crispa* ingestion.

4. Discussion

This study was unable to demonstrate the efficacy of *T. crispa* water extract to dry powder capsule for changes in areas under the serum glucose and insulin curves in healthy or diabetic subjects.

This result was inconsistent with other studies in animal model and metabolic syndrome subjects, Noor et al. [8] showed *T. crispa* aqueous extract to the drinking water for one week. Fasting blood glucose levels were significantly lower and serum insulin levels were significantly higher in treated diabetic rats (10.4 ± 1.0 mmol/l and 12.8 ± 1.1 $\mu\text{U/mL}$, resp.) compared to untreated diabetic controls (17.4 ± 1.7 mmol/l and 8.0 ± 0.7 $\mu\text{U/mL}$, resp.). Kongkathip et al. [9] found that the water extract of *T. crispa* caused a 13.9–15.6% reduction of serum glucose levels in normal rats after 120-minute oral feeding while 70% ethanol extract decreased serum glucose levels by 8.9–13.0% after 120 minute. Acute toxicity testing showed that LD50 values of water extracts are about 20–24 g/kg. It was suggested that the water extract of *T. crispa* is highly safe. Sriyapai et al. [7] presented metabolic syndrome patients who received 250 mg twice a day *T. crispa* dry powder capsule for 2 months

can reduce fasting blood glucose significantly from baseline (6.29 ± 10.47 mg/dL, $P < 0.01$).

on the other hand, Sangsuwan et al. [5] showed that *T. crispa* had no efficacy for therapy in patients with type 2 DM who did not respond to oral hypoglycemic drugs since there were no significant changes in fasting serum glucose between those collected at baseline and during the study period in either group (250 and 245 mg/dL, resp.) or glycosylated hemoglobin (10.3 and 11.2%, resp.). Our study demonstrated that *T. crispa* can not significantly reduce mean serum glucose AUC in diabetic patient but can show a trend to reduce mean glucose AUC 478 to 444 mg mL/min. 250 mg of *T. crispa* may not be adequate dosage to reduce serum glucose and stimulate insulin and another reason is that it may not last long enough to show the effect of treatment. Therefore, we need further investigation about adequate dose of *T. crispa* to reduce serum glucose and stimulate insulin secretion in type 2 diabetic patients.

5. Conclusion

The results suggest that *Tinospora crispa* ingestion cannot affect serum glucose and insulin levels in healthy subjects or patients with type 2 diabetes mellitus.

Acknowledgments

This work was supported by National Innovation Agency of Thailand. Special thanks are expressed to Mrs. Ngampong Kongkathip for her help in the study.

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