OBSERVATIONS

The Effect of *Ipomoea batatas* (Caiapo) on Glucose Metabolism and Serum Cholesterol in Patients With Type 2 Diabetes

A randomized study

There is considerable and growing interest in neutraceutical products for the treatment of diabetes (1). Recently, it has been shown that caiapo, the extract of white-skinned sweet potato (*Ipomoea batatas*), improves glycemic control in rodents by reducing insulin resistance (2). The aim of our study was to assess the effect of caiapo on glucose metabolism and its tolerability and mode of action in male Caucasian type 2 diabetic patients in a randomized, double-blind prospective study in parallel groups controlled with placebo.

A total of 18 male type 2 diabetic patients (age: 58 ± 8 years; weight: 88 ± 3 kg; BMI: 27.7 ± 2.7 kg/m^2; means ± SEM) treated by diet alone were randomized to receive placebo or 2 (low dose) or 4 g (high dose) caiapo (four tablets each containing 168 or 336 mg powdered white-skinned sweet potato [*I. batatas*], respectively) before breakfast, lunch, and dinner for 6 weeks. The study protocol was approved by the Ethics Committee of the University of Vienna, and informed consent was obtained from all patients before inclusion into the study. Safety parameters (hematology and blood chemistry, including hepatic enzymes and urinanalysis) were controlled before and at the end of the study, and patients were asked to report any adverse events. Patients were seen weekly during the 6-week trial, and fasting blood glucose was measured. Each subject underwent a frequently sampled intravenous glucose tolerance test (FSIGT) in randomized order before and after 6 weeks of caiapo administration for measurement of insulin sensitivity. Plasma glucose was measured using glucose oxidase (Glucose Analyzer II; Beckman, Fullerton, CA) and plasma insulin (coefficents of variation: 8%) by radioimmunoassay (Pharmacia-Upjohn, Uppsala, Sweden).

The FSIGT was performed according to the protocol used for the analysis with the minimal model of glucose disappearance (3). FSIGT data were analyzed by the minimal model method (4), and the insulin sensitivity index (S_I; min^{-1} · μU^{-1} · ml^{-1}), which describes the ability of insulin to promote glucose disappearance, was obtained.

The comparison among the values of the biochemical parameters of the three groups before and after treatment was evaluated by analysis of variance. In every group, paired Student's *t* test was used to assess the statistical significance of the differences of insulin sensitivity. The statistical evaluation was performed using the computer programs Statview (Abacus, Berkley, CA) and S-plus (Insightful, Seattle, WA). Data are expressed as means ± SEM.

The biochemical parameters before and after treatment (Table 1) show a decrease ($P < 0.05$) of fasting plasma glucose as well as of cholesterol (total and LDL cholesterol) after 6 weeks of treatment with high-dose caiapo. No statistically significant changes occurred after treatment with low-dose caiapo or placebo. Body weight and blood pressure remained unchanged in all three groups. In patients receiving low-dose caiapo, the FSIGT demonstrated an increase of S_I by 37% (2.02 ± 0.70 vs. 2.76 ± 0.89 10^4 min^{-1} · μU^{-1} · ml^{-1}, $P < 0.05$); in those on high-dose caiapo, the FSIGT demonstrated an increase of S_I by 42% (1.21 ± 0.32 vs. 1.73 ± 0.40 10^4 min^{-1} · μU^{-1} · ml^{-1}, $P < 0.03$). No changes were seen for S_I in patients receiving placebo (1.52 ± 0.28 vs. 1.35 ± 0.21 10^4 min^{-1} · μU^{-1} · ml^{-1}).

No adverse events have been reported by the patients. The results of the hematology and blood chemistry, including hepatic enzymes (except for glucose and cholesterol [Table 1]) and urinanalysis, were not altered by 6 weeks of treatment with caiapo. Body weight remained stable.

This pilot study demonstrates that ingestion of 4 g caiapo/day for 6 weeks reduces fasting blood glucose and total as well as LDL cholesterol in male Caucasian type 2 diabetic patients previously treated by diet alone. The improvement of insulin sensitivity in the FSIGT indicates that caiapo exerts its beneficial effects via reducing insulin resistance. The treatment was well tolerated, with no apparent side effects.

The increase of insulin sensitivity has been observed for both the low- and the

Table 1—*Metabolic parameters before (upper line) and after (lower line) treatment with caiapo in the single groups*

	Placebo	Low dose	High dose
n	6	6	6
Fasting plasma glucose (mmol/l)	8.2 ± 0.2	8.8 ± 0.4	8.3 ± 0.6
	8.4 ± 0.3	8.4 ± 1.1	7.2 ± 0.4*
Fasting plasma insulin (pmol/l)	8.7 ± 1.7	8.3 ± 1.6	13.4 ± 2.5
	8.7 ± 1.2	9.0 ± 1.8	13.2 ± 2.5
Total cholesterol (mmol/l)	5.69 ± 0.23	6.05 ± 0.31	4.97 ± 0.21
	5.66 ± 0.31	5.68 ± 0.34	4.45 ± 0.18*
LDL cholesterol (mmol/l)	3.72 ± 0.23	4.11 ± 0.28	3.12 ± 0.16
	3.78 ± 0.41	3.80 ± 0.28	2.72 ± 0.16*
HDL cholesterol (mmol/l)	1.40 ± 0.10	1.27 ± 0.10	1.16 ± 0.05
	1.42 ± 0.16	1.16 ± 0.10	1.11 ± 0.05
Triglycerides (mmol/l)	1.26 ± 0.15	1.45 ± 0.35	1.52 ± 0.19
	1.37 ± 0.30	1.61 ± 0.30	1.33 ± 0.13
HbA_{1c} (%)	7.0 ± 0.3	7.3 ± 0.4	7.1 ± 0.3
	7.0 ± 0.2	7.3 ± 0.4	6.8 ± 0.3
Blood pressure (mmHg)	134 ± 13	147 ± 18	135 ± 20
	130 ± 18	133 ± 19	128 ± 21
BMI (kg/m^2)	28.9 ± 0.9	25.5 ± 0.8	28.6 ± 1.3
	29.2 ± 0.8	25.8 ± 0.9	28.1 ± 1.5

Data are means ± SEM. *$P < 0.05$ compared with pretreatment.

high-dose caiapo group according to the FSIGT data. The results of the dynamic study (FSIGT) indicate that an increase of insulin sensitivity independent of body weight seems to be the mechanism responsible for the improvement of metabolic control with caiapo administration. This mechanism of action is supported by beneficial changes in hyperinsulinemia (by 50%), free fatty acids, and glucose tolerance in response to 100 mg · kg^{-1} · day^{-1} caiapo powder in obese Zucker fatty rats (2). In this model, this effect was similar to the effect of treatment with 50 mg · kg^{-1} · day^{-1} troglitazone. The direct effect on insulin sensitivity was demonstrated in this study by an enhanced ^{14}C-glucose uptake in isolated adipocytes. Parallel histological examinations of the pancreas showed a remarkable regranulation of pancreatic B-cells. Contrary to troglitazone, no weight gain could be seen after caiapo treatment in the animals.

Recently, the antidiabetic component of caiapo was isolated as an acidic glycoprotein (5) that is currently subject to further characterization. Unexpectedly, a simultaneous lowering of total and LDL cholesterol was observed after treatment with high-dose caiapo in our study. This effect could be independent of improved insulin sensitivity and suggests that caiapo also could contain more than one metabolically active ingredient. In regard to triglyceride levels, no significant changes were observed, despite an improvement of insulin resistance. This might be due to the relatively short period of the study.

Despite careful randomization, the subjects in the high-dose group showed higher insulin levels, whereas those in the low-dose group were leaner and more insulin-sensitive compared with those in the high-dose and placebo groups. We cannot exclude that the higher baseline insulin level of high-dose subjects might have predisposed these subjects to a better treatment effect. In this regard, however, it is remarkable that low-dose caiapo exerted its effect on insulin sensitivity, even in those moderately insulin-resistant patients, which further supports the contention of caiapo as an insulin-sensitizing agent.

In conclusion, this pilot study shows beneficial effects of high-dose caiapo on plasma glucose and total as well as LDL cholesterol levels in patients with type 2 diabetes. These effects relate to a decrease in insulin resistance, as also described in rodents (2), and were observed without affecting body weight or causing side effects. Therefore, the results of this pilot study indicate that caiapo could potentially play a role in the treatment of type 2 diabetes.

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