Suppressive Activity of the Fruit of *Momordica charantia* with Exercise on Blood Glucose in Type 2 Diabetic Mice

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Received July 10, 2003; accepted November 17, 2003

The antidiabetic activity of *Momordica charantia* L. (Cucurbitaceae) with exercise was investigated in KK-Ay mice, an animal model with type 2 diabetes with hyperinsulinemia. The water extract of the fruit of *Momordica charantia* L. (MC) with exercise reduced the blood glucose of KK-Ay mice 5 weeks after oral administration (*p* < 0.001), and also significantly lowered the plasma insulin of KK-Ay mice under similar conditions (*p* < 0.01). The blood glucose of MC with exercise is lower than that of MC only or exercise only 5 weeks after the administration. MC with exercise decreased blood glucose in a glucose tolerance test. These results suggest that MC with exercise is useful for type 2 diabetic cure.

Key words antidiabetic activity; exercise; KK-Ay; *Momordica charantia*; Cucurbitaceae

Insulin resistance in peripheral tissue, together with the impairment of glucose-induced insulin secretion from pancreatic beta cells, is known as one of the major pathogenic factors of type 2 diabetes. Therapeutic agents to stimulate insulin secretion (for example, sulfonylureas) have been used for type 2 diabetic patients. But, in the first stage of this condition only, exercise therapy and diet are used.

The fruit of the *Momordica charantia* L. (Cucurbitaceae) (called as Nigauri in Japanese), a plant widely used in traditional medicine as an antidiabetic agent, has been shown to lower blood glucose in laboratory animals. In a previous study, we reported that *Momordica charantia* decreased the blood glucose in genetically type 2 diabetic mice. An important type 2 diabetic cure is exercise therapy and diet. However, no study has been performed on genetically type 2 diabetes models with exercise.

In the present study, we examined the effect of *Momordica charantia* L. with exercise on blood glucose in a type 2 diabetic animal model.

MATERIALS AND METHODS

The fruit of the *Momordica charantia* used in this experiment was obtained in a market in Kagoshima Japan (2001, July). A voucher specimen was deposited at the herbarium of Suzuki University of Medical Science (SUMS). One hundred grams of the fruit was extracted with 21 of water (40 °C, 2 h, 2 times). The water extracts were lyophilized (MC) and stored at room temperature until use. The yield was 18.7%.

The microbiological profile of MC is: (1) total plate count of less than 5000 cfu/g; (2) yeast and mold less than 100 cfu/g; (3) *Escherichia coli*, *Salmonella*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* are absent.

Animals KK-Ay mice (Clea, Tokyo, Japan), 8 weeks old, were used. KK-Ay mice with blood glucose level above 300 mg/100 ml were considered to be diabetic in this study. The mice were housed in an air-conditioned room at 22±2 °C with a 12 h light–12 h dark cycle (light: 9:00 am to 9:00 pm). The animals were kept in the experimental animal room for 7 d with free access to food (CE-2, Clea, Tokyo, Japan) and water (tap water). Blood samples were drawn from the cavernous sinus with a capillary to determine blood glucose levels under non-anesthesia and non-fasting. MC was dissolved in distilled water. The studies were started at 10:00—11:00 am, and blood samples after repeated administrations of MC were taken at 10:00—11:00 am. The oral administration of MC was given on a compulsory basis. In a previous study, we examined the dose-dependence (4, 20, 100 mg/kg) after treatment of MC, and found that it showed antidiabetic activity at 20 and 100 mg/kg after oral administration. Therefore, we studied the effect of the glucose metabolism of MC at the dosage of 20 mg/kg body weight.

**Exercise** For exercise studies, KK-Ay mice were run on a motorized treadmill (Muromachi Kikai Co., Ltd., Osaka, Japan) for 120 min (5 m/min, 7% grade). For exercise studies, mice went without food. MC (20 mg/kg body weight) was administered orally for 5 weeks.

**Oral Glucose Tolerance Test** After overnight (18 h) fasting, KK-Ay mice were given MC orally and 0.5 h later, the glucose (2 g/kg body weight) solution was administered orally. Blood samples were collected before the administration of the glucose and 30, 60 and 120 min later.

**Determination of Blood Glucose and Insulin** Blood glucose levels in mice were determined by the glucose oxidase method, and serum insulin was measured by the double antibody method.

**Statistical Analysis** All the data were expressed as mean±S.E., and analysis of variance (ANOVA) was used for the statistical analysis. The values were considered to be significant when the *p* value was less than 0.05.

RESULTS

The Effect of MC with Exercise on Blood Glucose in KK-Ay The effect of MC with exercise in KK-Ay mice is shown in Fig. 1. MC-treated animals (20 mg/kg body weight) showed lower blood glucose from 1 to 5 weeks after the administration. Exercise only decreased blood glucose 5 weeks. MC with exercise decreased blood glucose from 1 to 5 weeks after the administration. The body weight of the exercise, MC, and MC+exercise mice were not significantly different from that of the control mice (Fig. 2).

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The Effect of MC with Exercise on Plasma Insulin in KK-Ay Mice

The effect of MC with exercise in KK-Ay mice is shown in Fig. 3. The plasma insulin level in MC treated and exercised KK-Ay mice decreased 5 weeks after the administration \( (p<0.001) \) (Fig. 3).

Oral Glucose Tolerance Test

The effect of MC with exercise on glucose tolerance is shown in Fig. 4. MC with exercise decreased blood glucose after 60 min compared with controls \( (p<0.05) \).

DISCUSSION

The present results show that MC with exercise reduces blood glucose and insulin levels in KK-Ay diabetic mice. In a previous study, we reported that MC increased GLUT4 protein content of muscle in KK-Ay mice.\(^7\) KK-Ay mice have been known to genetically induce diabetes, including ob/ob mice\(^10\) and KK mice.\(^11,12\) Hyperinsulinemia occurred as a result of insulin resistance. The blood glucose of MC treatment with exercise was lower than that of MC only or exercise only. Furthermore, the plasma insulin of MC with exercise was lower than that of MC only or exercise only 5 weeks after the administration. From these findings, it could be suggested that the hypoglycemic effect of MC with exercise is a synergistic effect.

MC-treated mice did not show any obvious stimulus action, suggesting that MC did not affect exercise action.

It may be that MC with exercise has a beneficial effect on hyperglycemia in type 2 diabetes. Further investigation will be needed to elucidate the mechanism of these effects.

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