Antihypoglycemic effect of Maca in fasted and insulin-induced hypoglycemic mice

Toshihiro MIURA,*[a] Motoki HAYASHI,[a] Yukio NAITO,[b] Ikukatsu SUZUKI[a]

[a]*Suzuka University of Medical Science,*
[b]*Department of Chemistry and Biochemistry, Suzuka National College of Technology*

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Abstract

The antihypoglycemic effect of *Lepidium meyenii* WALP (Maca ; Cruciferas) was investigated in fasted and insulin-induced hypoglycemic mice. The water extract of rhizomes of *L.meyenii* (MW) (1000 mg/kg) increased the blood glucose of fasted mice 30 minutes after oral administration, and also significantly increased the blood glucose of insulin-induced hypoglycemic mice under fasted conditions. But blood glucose did not change in fed mice.

On the other hand, epinephrine-induced hyperglycemic mice did not change the blood glucose. No differences in glycogen content were observed between control and MW-treated mice. These findings indicate that the antihypoglycemic effect of MW may promote glyconeogenesis.

Key words Antihypoglycemic effect, Maca, *Lepidium meyenii* WALP, Cruciferas, Fasted mice, Insulin-induced hypoglycemic mice.

Introduction

Hypoglycemia is induced by fasted condition, exercise and energy deficiency. Now, many energy supplies are shown (for example Guarana).[1] From this concept, drugs to improve hypoglycemia are not yet available clinically.

The rhizomes of *Lepidium meyenii* WALP (Cruciferas) (Maca in oriental medicine) have been used in the Orient as a tonic medicine and energy supply.[2] The constituents of Maca have been chemically investigated including some alkaloids.[2] However, there is no experimental evidence about the energy supply of Maca. The purpose of this study was to examine the antihypoglycemic effect of this medicine.

Materials and Methods

Plant materials used consisted of rhizomes of *Lepidium meyenii* WALP from a market in Peru (South America) by Kimikashuisa Co. LTD. (Japan). The rhizomes (200 g) were extracted with 2 l of water (50°C, 2h, 2 times). The water extracts (MW) were lyophilized and stored at 4°C until use. The yield was 4.8 %.

Animals : Adult male ddY mice (5 weeks old) weighing 22-25 g were used. The mice were housed in an air-conditioned room at 22±2°C with a 12 hour light-12 hour dark cycle. The animals were kept in the experimental animal room for 7 days with free access to food and water. For the determination of blood glucose levels, blood samples were withdrawn from the cavernous sinus with a capillary.

Mice were given the water extract of Maca dissolved in 10 ml of distilled water for oral injection in 100, 300 and 1000 mg/kg body weight.

Fasted and fed mice : After 18 hours fasting (fed mice ; under non-fasting condition), the adult ddY mice were given MW orally. Blood samples were collected at 0, 30, 60 and 120 minutes after the admin-

*〒510-0293 鈴鹿市岸岡町1001-1
鈴鹿医療科学大学 三浦俊宏
1001-1 Kishioka, Suzuka, Mie 510-0293, Japan

istration of MW.

Insulin-induced hypoglycemic mice : After 18 hours fasting, the adult ddY mice were given MW orally and, immediately after, the insulin (0.1 U/kg body weight) solution was administered subcutaneously. Blood samples were collected at 0, 30, 60 and 120 minutes after the administration of insulin.

Epinephrine-induced hyperglycemic mice : After 18 hours, the adult ddY mice were given MW orally and, immediately after, the epinephrine (0.6 mg/kg body weight) solution was administered intraperitoneally. Blood samples were collected after the administration of epinephrine as described above.

Determination of blood glucose: Blood glucose levels in mice were determined by GLUTEST-E (Sanwa Chem. Co.Ltd, Japan).[3)]

Statistics : All the data were expressed as means± S.E. from 5 mice. Statistical analysis was performed by analysis of variance (ANOVA) for significance of differences. The values were considered to be significantly different when the P value was less than 0.05.

Results

Effect of MW on blood glucose in fasted mice

The mean blood glucose levels of fasted mice at various time intervals after oral administration of MW are shown in Fig. 1. These levels were compared with the values in control mice administered distilled water alone. MW (1000 mg/kg) increased the blood glucose of fasted mice 0.5 hours after oral administra-

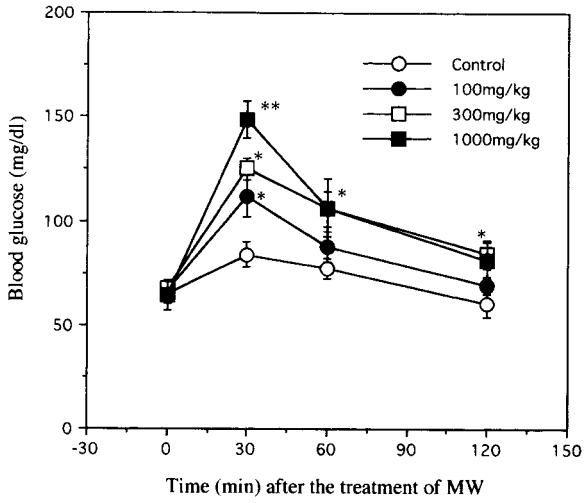

Fig. 1 Effect of MW on blood glucose in fasted mice.
After 18 hours fasting, the adult ddY mice were given MW orally. Blood samples were collected at 0, 30, 60 and 120 minutes after the administration of MW.
Each value represents the mean±S.E. from 5 mice. Significantly different from control, $^{**}p<0.01$.

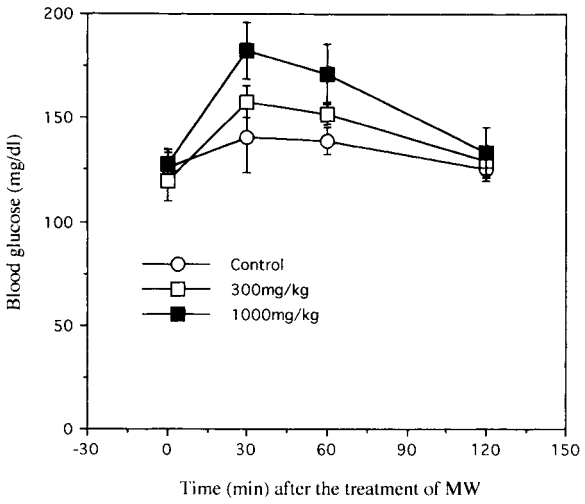

Fig. 2 Effect of MW on blood glucose in fed mice.
Under non-fasting condition, adult ddY mice were given MW orally. Blood samples were collected at 0, 30, 60 and 120 minutes after the administration of MW.
Each value represents the mean±S.E. from 5 mice.

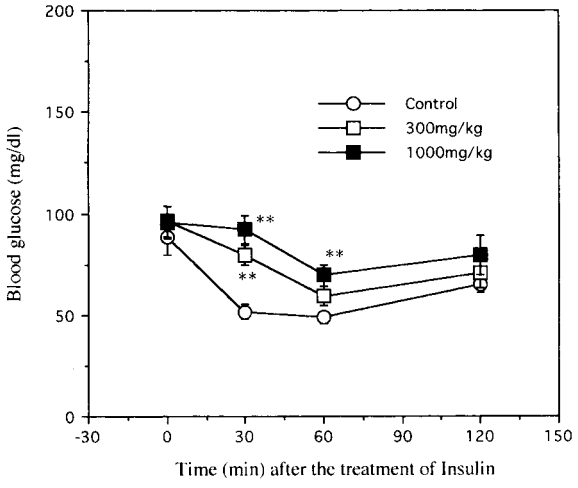

Fig. 3 Effect of MW on blood glucose in insulin-induced hypoglycemic mice.
After 18 hours fasting, the adult ddY mice were given MW orally and, immediately after, the insulin (0.1 U/kg body weight) solution was administered subcutaneously. Blood samples were collected at 0, 30, 60 and 120 minutes after the administration of insulin.
Each value represents the mean±S.E. from 5 mice. Significantly different from control, $^{**}p<0.01$.

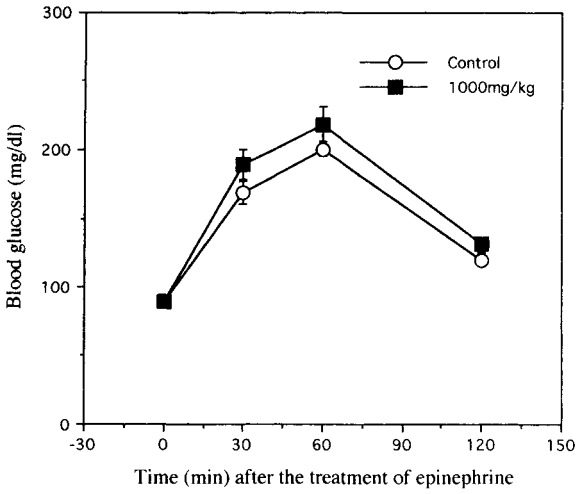

Fig. 4 Effect of MW on blood glucose in epinephrine-induced hyperglycemic mice. After 18 hours, the adult ddY mice were given MW orally and, immediately after, the epinephrine (0.6 mg/kg body weight) solution was administered intraperitoneally. Blood samples were collected at 0, 30, 60 and 120 minutes after the administration of epinephrine.
Each value represents the mean±S.E. from 5 mice.

tion ($p<0.01$). The antihypoglycemic effect of MW was dose-dependent.

Effect of MW on blood glucose in fed mice

The effects of MW on the blood glucose of fed mice are shown in Fig. 2. MW-treated mice tended to increase in blood glucose when compared with the values in control mice.

Insulin-induced hypoglycemic mice

MW-treated animals (300 and 1000 mg/kg body weight, orally) showed a significant increase in blood glucose when compared with controls (Fig. 3, $p<0.01$). The antihypoglycemic effect of MW was dose-dependent.

Effect of MW on blood glucose in epinephrine-induced hyperglycemic mice

The effect of MW treated orally on epinephrine-induced hyperglycemia is shown in Fig. 4. MW-treated animals (1000mg/kg body weight, orally) showed no change on blood glucose levels when compared with control group.

Discussion

The present study clearly showed that the water extract of the rhizomes of (MW) produces consistent antihypoglycemic effects in both fasted and insulin-induced hypoglycemic mice. MW-treated groups showed a striking increase of glucose levels in fasted mice. However, the level of blood glucose in fed mice did not significantly change in both normal and MW-treated mice. The increase of blood glucose in fasted mice was higher than that of fed mice. These findings indicate that the antihypoglycemic effect of MW needs the fasting condition in order to act. Thus, we made our examination under a fasting condition.

MW also increased blood glucose in insulin-induced hypoglycemic mice. However, there is no difference on liver glycogen content between MW-treated and control mice in fasted mice (data not shown). In the basic study, we examined the dose-dependence (0, 0.2, 0.4, 0.6, 0.8, 1.0 mg/kg) after treatment of epinephrine, and found that 0.6 mg/kg is the maximum dose of epinephrine in the blood glucose.[4] It is suggested that epinephrine at 0.6 mg/kg induced maximum gluconeogenesis. MW-treated mice did not change the blood glucose in epinephrine-induced hyperglycemic mice. On the other hand, gluconeogenesis is induced under fasting condition. From these findings, the antihypoglycemic function of MW may promote glyconeogenesis. However, it is possible to decrease glucose uptake in peripheral tissue.

In regards to toxicity, the toxicity of MW seems to be very low ($LD_{50}>>3000$ mg/kg) (data is not shown). Moreover, MW-treated (3000 mg/kg) mice did not show any obvious stimulus action, suggesting that MW is a medicine with lower toxicity.

These findings indicate that Maca may be useful for the treatment of energy supply on hypoglycemic condition.

和文抄録

マカの抗低血糖作用を絶食およびインスリン誘発低血糖マウスを用いて検討した。マカの根茎の水抽出物(1000 mg/kg)は経口投与後30分に絶食マウスの低血糖を改善した。また，インスリン誘発低血糖も同様に改善した。しかし，飽食マウスにおいては血糖の変化は見られなかった。また，エピネフリン誘発高血糖マウスの血糖値にも変化は見られなかった。これらのことから，マカの抗低血糖作用機序として糖新生を促進する可能性が考えられた。

References

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