Hypoglycemic and hypolipidemic activity of the leaf of *Samallanthus sonchifolius* in genetically type 2 diabetic mice

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The hypoglycemic and hypolipidemic activity of *Samallanthus sonchifolius* (Compositae) was investigated in KK-Ay mice, an animal model of genetically type 2 diabetes. The water extract of the leaf of *Samallanthus sonchifolius* (Yacon) (500 mg/kg body weight) reduced the blood glucose (p<0.01) and cholesterol (p<0.05) of KK-Ay mice 6 weeks after repeated administration. However, Yacon did not affect the blood glucose in normal mice. Yacon also improved hyperglycemia after glucose tolerance. These results suggest that Yacon is useful for hyperglycemia and hyperlipidemia of type 2 diabetes.

Key words *Samallanthus sonchifolius*, hypoglycemic activity, hypolipidemic activity, KK-Ay mouse.

Introduction

Despite considerable progress in the management of diabetes mellitus by synthetic drugs, the search for indigenous natural antidiabetic agents is ongoing. The plant kingdom offers a wide field to look for effective oral hypoglycemics. More than 400 species have been reported to display hypoglycemic effects, but only a few of them have been investigated.1,2) We screened hypoglycemic materials in longevity food.

Yacon is the Oriental medical name given to *Samallanthus sonchifolius* (Compositae). The medicine has been used traditionally for longevity in the Andes area of Peru.3) Terada et al. reported Yacon suppressed the elevation of glucose level after loading starch in normal rats.4)

Ayber et al. also reported hypoglycemic effect in normal animal model.5) However, adequate characterization of their effect is yet to be done and no study has been performed on type 2 diabetes model. In the present study, we examined the effect of Yacon on blood glucose and lipid in type 2 diabetic mice.

Materials and Methods

Plant materials. The water extracts of the leaf of *Samallanthus sonchifolius* (Yacon) which was provided by Latina, Inc (Tokyo, Japan) was used for the experiment. The used Yacon was made in Peru. Yacon was extract with water on a heating bath (60 °C, 1hour). The water extract were lyophilized and stored at room temperature until use. The yield is 8.3%.

Animals. Adult male ddY mice (SLC, Shizuoka, Japan) weighing 22-25 g and KK-Ay mice (Clea, Tokyo, Japan), 12 weeks old, were used. KK-Ay mice with blood glucose level above 300 mg/100ml were considered to be diabetic and used in this study. The mice were housed in an air-conditioned room at 22±2 °C with a 12 hour light-12 hour dark cycle (light: 9:00 am to 9:00). The animals were kept in an experimental animal room for 7 days with free access to food (CE-2, Clea, Tokyo) and water (tap water). Blood samples were withdrawn from the caudal sinus with a capillary to determine blood glucose levels under non-anesthesia and non-fasting. Yacon was dissolved in distilled water. The distilled water was administered to the control mice. The studies were started at 10:00-11:00 a.m., and blood samples after repeated administration of Yacon were taken at 10:00-11:00 a.m. Yacon was administered orally on a compulsory basis (repeated administration, once a day). Animals were treated in accordance with the Guideline for the Care and Use of Laboratory Animals (the Prime Minister's Office no.6, 1980). Four to six animals were used for each group.

Oral glucose tolerance test. Oral glucose tolerance tests were performed at the end of the repeated administration. After overnight (18 hours) fasting, the glucose (2 g/kg body weight) solution was administered orally to the KK-Ay mice. Blood samples were collected before the administration of the glucose and 30, 60 and 120 minutes later.

Insulin tolerance test. Insulin tolerance tests were performed at the end of the repeated administration. After overnight (18 hours) fasting, the insulin (Humalin N, Eli Lilly Japan K. K) (0.5 U/kg body weight) solution was administered subcutaneously (s.c.) to the KK-Ay mice. Blood samples were collected before administration of the insulin and 30, 60 and 120 minutes later.

Determination of blood glucose. Blood glucose levels in the mice were determined by the glucose oxidase method,9) and blood cholesterol and triglyceride were measured by cholesterol-E test and Triglyceride G test (Wako).10,11) All the data were expressed as mean ± S.E.M., and Student's t test and ANOVA was used for statistical analysis. The values were considered to be significant when the p value was less than 0.05.

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Results

**KK-Ay and normal mice.** The effect of the repeated administration of Yacon on blood glucose is shown in Fig. 1. Yacon-treated animals (500 mg/kg) showed lower blood glucose levels from 4, 5 and 6 weeks after administration when compared to the pre-value (0 week) or corresponding control. The blood cholesterol level in Yacon-treated KK-Ay mice was decreased 6 weeks after the administration ($p<0.05$ vs control), but the blood triglyceride level was not changed when compared with control (Table 1). Yacon also did not affect the blood glucose in normal mice when compared to the pre-value or corresponding control (Fig. 2). The body weight in Yacon-treated animals did not change in normal and KK-Ay mice when compared with controls (data not shown).

**Oral glucose tolerance test.** The effect of Yacon in glucose tolerance test is shown in Fig. 3. Yacon-treated mice showed a significant decrease in blood glucose after 60 min compared with controls (Fig. 3).

**Insulin tolerance test.** Yacon (500 mg/kg body weight, p.o.) did not change the blood glucose after insulin administration (Fig. 4).

![Fig. 1 Effect of Yacon on blood glucose in KK-Ay mice](image1)

Yacon 500 mg/kg was administered orally to KK-Ay diabetic mice. After 1-6 weeks, blood samples were taken to determine blood glucose level. Each value represents the mean ± S.E. of 5-6 mice. Significantly different from pre-value, $^* p<0.05$, $^{**} p<0.01$. Significantly different from corresponding control, $^* p<0.05$, $^{**} p<0.01$.

**Table 1 Effect of Yacon on blood cholesterol and triglyceride**

<table>
<thead>
<tr>
<th></th>
<th>Blood cholesterol (mg/dl)</th>
<th>Blood triglyceride (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>178 ± 4</td>
<td>166 ± 8</td>
</tr>
<tr>
<td>Control</td>
<td>224 ± 30</td>
<td>352 ± 33</td>
</tr>
<tr>
<td>Yacon</td>
<td>170 ± 7*</td>
<td>281 ± 58</td>
</tr>
</tbody>
</table>

Each value represents the mean ± S.E. from 5-6 mice. Significantly different from Normal, $^* p<0.05$, $^{**} p<0.01$. Significantly different from Control, $^* p<0.05$.

![Fig. 2 Effects of Yacon on blood glucose in normal mice](image2)

Yacon 500 mg/kg was administered orally to ddY normal mice. After 1-6 weeks, blood samples were taken to determine blood glucose level. Each value represents the mean ± S.E. of 5-6 mice.

![Fig. 3 Effect of Yacon on glucose tolerance in KK-Ay mice](image3)

After overnight (18 hours) fasting, 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 minutes later. Each value represents the mean ± S.E. of 4-6 mice. Significantly different from corresponding controls, $^* p<0.05$.
Ay mice, an animal model of type 2 diabetes mellitus. These mice, which are known to genetically induced diabetes and which include ob/ob mice\(^{(1)}\) and KK mice,\(^{(2)}\) had hyperinsulinemia as a result of insulin resistance.\(^{(3)}\) Their treatment with Yacon resulted in hypoglycemia with decreased blood cholesterol. Diabetics also often have elevated blood cholesterol levels. It was known that Yacon contained much dietary fiber.\(^{(4)}\) Dietary fiber inhibited glucose and cholesterol absorption. It is important that Yacon has a beneficial effect on hyperglycemia and hyperlipidemia in type 2 diabetes.

The toxicity of Yacon seems to be very low (LD\(_{50}>>\) 2000 mg/kg body weight) (data not shown). Yacon-treated (2000 mg/kg) mice did not show any obvious stimulus action. Yacon did not change the body weight of KK-Ay mice in repeated administration. These findings suggest that Yacon is a medicine with low toxicity.

Yacon improved hyperglycemia in the glucose tolerance test. Glucose intolerance is known as one of the pathogenic factors of type 2 diabetes, together with insulin resistance in peripheral tissues. Therefore, it is important that Yacon improves glucose tolerance. From fig. 3, Yacon did not affect the fasted blood glucose. From these findings, it seems likely that Yacon exhibits its hypoglycemic effects without decreasing hepatic glucose output.

Further study would show how Yacon could become a useful drug in the treatment of type 2 diabetes. The above experimental results suggest that the hypoglycemic and hypolipidemic activity of Yacon supports the traditional use of longevity.

References


Japanese abstract

ヤーコンの遺伝的2型糖尿病動物（KK−Ay マウス）に対する効果を6週間連続投与を行い、その後糖尿病試験、インスリン負荷試験で検討した。ヤーコン水抽出物は投与6週間後にKK−Ay マウスの血糖値およびコレステロール値を低下させた。しかし、正常マウスの血糖値には影響したかった。ヤーコンはまたKK−Ay マウスの血糖値を上昇を抑制した。これらの結果からヤーコンは2型糖尿病病の高血糖および高コレステロール血症に有効であることが分かった。

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