原　著

Effect of the water extract of *perilla leaves* on glucose metabolism in diabetic rats

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Abstract

We examined the effect of the water extract of *perilla leaves* on glucose metabolism in normal and neonatal streptozotocin-induced diabetic (NSZ) rats that are one of the animal models of type 2 diabetes mellitus. The water extract of *perilla leaves* lowered the blood glucose concentration after glucose load in both normal and NSZ rats in the oral glucose tolerance test. The plasma insulin levels of normal and NSZ rats that took the water extract of *perilla leaves*, however, did not change in the oral glucose tolerance test. These results suggest that the water extract of *perilla leaves* improved glucose tolerance, in part, by the inhibition of glucose absorption in the small intestine.

Introduction

The proportion of diabetes mellitus in lifestyle diseases has increased remarkably in recent years. The cause has to do with diet, the decrease of exercise and the stressful society. The relation between diabetes and the dietary habit is obvious, so diet therapy is useful in the first stage of diabetes. Blood glucose is increased by the intake of glucose, and its concentration reflects the condition of intracellular metabolism of glucose. Recently, several kinds of tea have come on market. Some of them lower the rapid elevation of blood glucose concentration by inhibiting the absorption of glucose in the small intestine. *Perilla leaves* are easy to buy in supermarkets, because perilla is a year-round plant. It contains a particularly large variety of vitamins, and is similar to other vegetables in other components. However, there is no experimental evidence for the anti-diabetic effect of *perilla leaves*. In the present study, we examined the effect of the water extract of *perilla leaves* on glucose metabolism in diabetic rats.

Materials and Methods

The water extract of *perilla leaves* (10 g) was prepared with 1 L boiling water for 60 min, left overnight at room temperature, and filtered by gauze. This extract was referred to as *perilla leaves* extract-1 (PLE-1), and its 2 times dilution (PLE-2) was also prepared. Separated groups of 4-week-old rats were given, respectively, only DW, PLE-1 and PLE-2 to drink for 5 weeks. The amount of DW, PLE-1 and PLE-2 was 200 ml. The quantity taken by the rats was measured, and each liquid was replaced by a fresh batch every 3 days. The number of rats was 3-4 per group.

NSZ rats were produced by subcutaneous injection with 90 mg/kg/bw of streptozocin, freshly dissolved in citrate buffer, pH 4.5. They were similarly divided into DW, PLE-1 and PLE-2 groups.

In oral glucose tolerance test, after overnight fasting, the glucose (2 g/kg/bw) solution was orally administered. Blood samples were collected before the administration of glucose and 30, 60 and 120 mins afterwards. Blood glucose concentration was determined by the glucose oxidase method[1]. Insulin levels were determined by radioimmunoassay using immunoreactive insulin.

All data are expressed as mean ± SEM. Data was analyzed by ANOVA, and statistical significance was defined as $p < 0.05$.

Results

1. The change of the amount of DW, PLE-1 and PLE-2 taken by the rats, and the change of body weight of the rats

The amount of PLE-1 and PLE-2 taken by control 6-week-old rats was significantly greater than that of DW taken by the DW group. However, the amount of DW taken by control 7- and 8-week-old rats was significantly greater than that of PLE-1 and PLE-2 taken by them (Fig. 1-left).

In NSZ rats, the amount of PLE-1 and PLE-2 taken by 6-week-old rats was lower than that of DW. The amount of PLE-2 taken by 6-week-old NSZ rats was lower than the amount of PLE-1. The amount of PLE-1 and PLE-2 taken by 7-week-old NSZ rats was significantly greater than that of DW. The amount of PLE-2 taken by 9-week-old NSZ rats was greater than that of PLE-1. The total amounts of DW, PLE-1 and PLE-2 taken by the diabetic rats were greater than those by control rats (Fig. 1-right).

The body weights increased in both control and NSZ rats (Fig. 2).

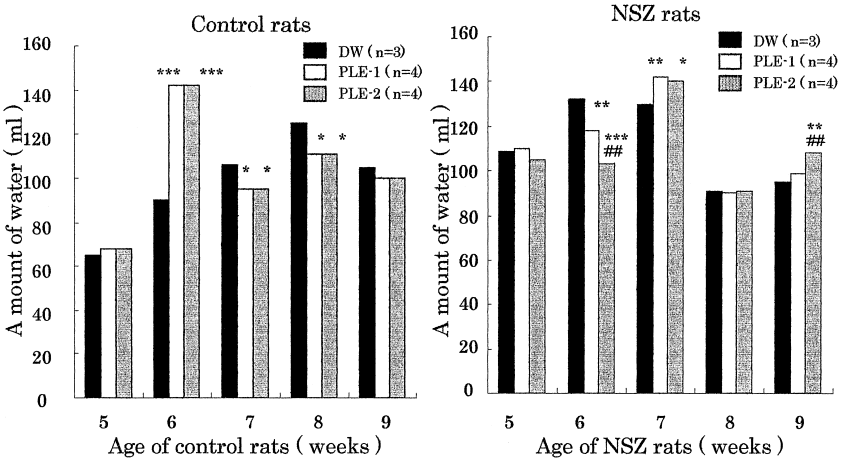

Fig. 1. The amount of DW, PLE-1 and PLE-2 taken by the rats. In control rats, the amount of PLE-1 and PLE-2 taken by 6-week-old rats was greater than that of DW taken by the DW group, but that of DW taken by 7- and 8-week-old rats was greater than that of PLE-1 and PLE-2. In NSZ rats, however, the amount of PLE-1 and PLE-2 taken by 6-week-old rats was lower than that of DW, but that by 7-week-old rats was greater. The amount of PLE-2 taken by 9-week-old NSZ rats increased. The amount of PLE-2 taken by 6-week-old NSZ rats was lower than the amount of PLE-1. However, the amount of PLE-2 was greater in 9-week-old NSZ rats. Each value represents the mean ± S.E.M. Significance of difference from DW: $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$, and from PLE-1, $^{\#\#}p < 0.01$.

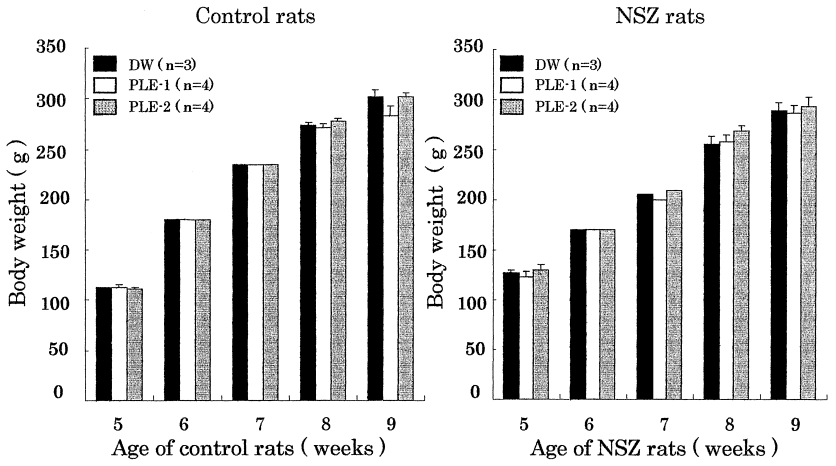

Fig. 2. The change of the body weight of the rats. The body weight increased according to the weeks. There is no statistical difference between the body weight of control and that of NSZ rats. Each value represents the mean ± S.E.M.

2. Oral Glucose Tolerance Test

The blood glucose concentration of the control rats increased and the highest was at 60 min after glucose loading. The glucose concentration of the rats that took PLE-1 significantly decreased at 120 min after the glucose loading. The glucose concentration of the rats that took PLE-2 was lower at 60 and 120 min after glucose loading as compared with that of the rats that took DW. The glucose concentration of the rats that took PLE-2 was lower at 60 min after glucose loading as compared with that of the rats that took PLE-1 (Fig. 3-left).

The highest blood glucose concentration of NSZ rats was at 30 min. PLE-1 and PLE-2 decreased the blood glucose concentration of NSZ rats at 30 and 60 min compared with DW, but no decrease was observed at 120 min. There was no significant difference between the effect of PLE-1 and PLE-2 (Fig. 3-right).

3. The change of plasma insulin in Oral Glucose Tolerance Test

In normal control rats PLE-1 lowered plasma insulin as compared with DW. The plasma insulin of control rats that took DW was higher at 30 and 60 min than that of the PLE-1 group. However, there was no significant difference between DW and PLE-2. The plasma insulin of control rats that took PLE-1 was lower at 60 min than that of those that took PLE-2 (Fig. 4-left).

In NSZ rats, the PLE-1 group showed a significant increase in plasma insulin at 30 and 60 min after the loading of glucose. However, PLE-2 lowered insulin level compared with the PLE-1 and DW groups at 30 min after the glucose loading. However, no significant change was observed at 60 and 120 min (Fig. 4-right).

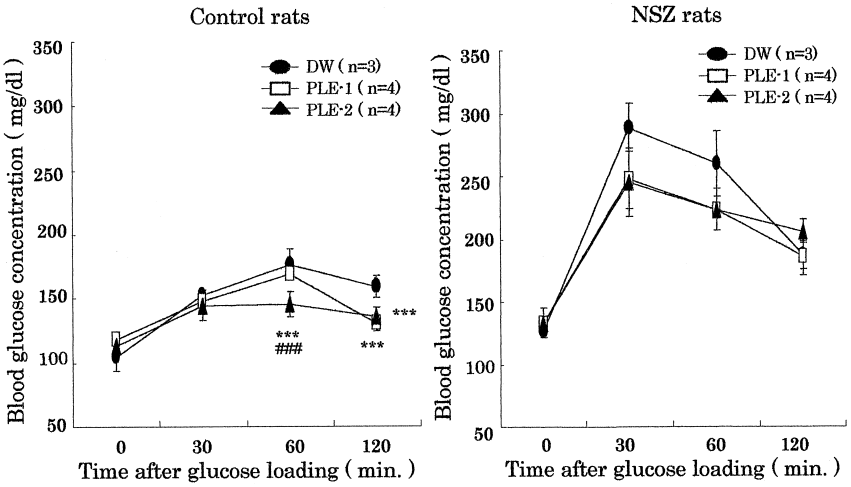

Fig. 3. Effect of PLE on blood glucose concentration in oral glucose tolerance test. In control rats, the highest blood glucose concentration was observed at 60 min. PLE-1 lowered blood glucose concentration at 120 min, and PLE-2 lowered it at 60 min and 120 min. PLE-1 and PLE-2 lowered the blood glucose concentration. Each value represents the mean ± S.E.M. Significance of difference from DW : $^{***}p < 0.001$, and from PLE-1, $^{\#\#\#}p < 0.001$.

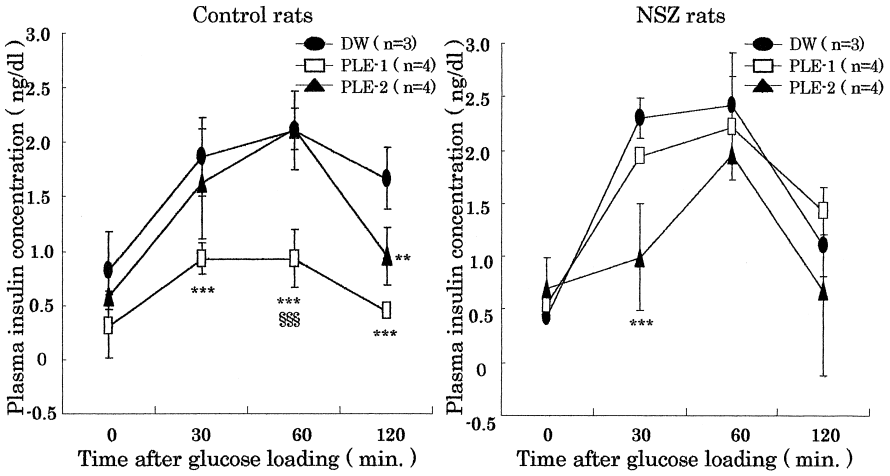

Fig. 4. The change of insulin concentration in oral glucose tolerance test. In normal rats, PLE-1 lowered plasma insulin, at 30, 60 and 120 min. In NSZ rats, PLE-1 did not lower insulin concentration, but PLE-2 lowered it at 30 min after the glucose loading. Each value represents the mean ± S.E.M. Significance of difference from DW: $^{**}p < 0.01$, $^{***}p < 0.001$, and from PLE-2, $^{§§§}p < 0.001$.

Discussion

We examined the effect of the extract of *perilla leaves* on glucose metabolism in normal and diabetic rats. The streptozotocin administration to the neonatal rats caused a type 2 diabetes by regeneration of pancreas β cells[2),3)]. From our findings, the insulin level did not change between control and NSZ rats. It seems likely that NSZ rats are in mild diabetic condition. PLE tended to decrease blood glucose in normal rats, and to inhibit the elevation of blood glucose in NSZ rats. No change in insulin level was observed in PLE-treated rats. It was indicated that PLE inhibited the elevation of blood glucose concentration, without changing insulin level. It is known that *perilla leaves* are rich in dietary fiber, especially soluble fiber[4),5)]. These results suggested the hypoglycemic of PLE is derived, at least in part, from the decrease of the glucose absorption in the small intestine. It is possible to elute soluble fiber in PLE. But there are no significant differences in the extracted concentrations. The improvement of glucose tolerance in PLE may be due to the direct inhibition of glucose absorption in the small intestine.

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